Unprotected Left Main Trunk Angioplasty (ULTRA) Registry in Japan

Update in ULTRA Registry
--- Is it still risky? ---

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Unprotected Left Main Trunk Angioplasty

ULTIMA Registry
(Unprotected Left Main Trunk Intervention Multi-center Assessment)
1994-1996, from 25 centers

✓ 1st multi-center registry for unprotected LM angioplasty

107 pts: 91 pts electively or 16 pts as acute MI
stents(50%), DCA(24%) & POBA(20%)

In-hospital death:
- Acute MI (n=16) 69%
- Elective/CABG candidate (n=68) 5.9%
- Elective/not CABG candidate (n=23) 30.4%

Cardiac death within 6 mos after PCI: 10.6%
Unprotected Left Main Trunk Angioplasty

ULTIMA Registry (1st Report)
(Unprotected Left Main Trunk Intervention Multi-center Assessment)
1994-1996, from 25 centers

✓ Initial results for selected pts appear promising,

✓ LM angioplasty should not be considered an alternative to CABG, until early cardiac death after discharge can be minimized.

✓ F/u angiogram 6 to 8 wks after PCI is advisable.
Unprotected Left Main Trunk Angioplasty

ULTIMA Registry (Final Report)
(Unprotected Left Main Trunk Intervention Multi-center Assessment)
1993-1998, from 25 centers


✓ 279 pts: 46% inoperable or at high surgical risk
   stents(69%), DCA(17%) & POBA(15%)
   In-hospital death: 13.7%

✓ 32% pts <65yrs with LVEF>30% and without shock: no in-hospital death and 3.4% 1-y-mortality
### Correlates of All-cause Mortality (In-hospital and during F/U)

<table>
<thead>
<tr>
<th>Event</th>
<th>% of Study</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF(&lt;30%)</td>
<td>14.3</td>
<td>4.21</td>
<td>2.27-7.81</td>
<td>0.001</td>
</tr>
<tr>
<td>MR grades 3 or 4</td>
<td>4.1</td>
<td>3.66</td>
<td>1.61-8.30</td>
<td>0.001</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>13.7</td>
<td>3.56</td>
<td>1.73-7.34</td>
<td>0.001</td>
</tr>
<tr>
<td>Cr &gt; 2 mg/dl</td>
<td>5.8</td>
<td>3.10</td>
<td>1.30-7.39</td>
<td>0.001</td>
</tr>
<tr>
<td>Severe lesion calc.</td>
<td>8.9</td>
<td>2.32</td>
<td>1.13-4.76</td>
<td>0.022</td>
</tr>
</tbody>
</table>

ULTIMA Registry (Final Report)
(Unprotected Left Main Trunk Intervention Multi-center Assessment)
1993-1998, from 25 centers n=279

In conclusion,

- LMT PCI **may be an alternative to CABG** for a select population proportion of elective pts,

- **may also be appropriate for highly symptomatic inoperable pts.**

- **Meticulous follow-up of hospital survivor is required.**

Results and Long-term Predictors of Adverse Clinical Events after Elective PCI on ULMTD


- 67 pts in Centro Cuore Columbus, 1993-2001
  - Stents (n=39), DCA/Stent (n=13), Rotastent (n=12), DCA alone (n=3)
- 3-y Mortality: 9%
- Restenosis: 31.4%, TVR 23.9%
- Independent covariate of cardiac death: preserved LV function
- The most important predictors of favorable follow-up:
  - Ref. vessel size and LV function

Elective ULMT angioplasty has good long-term results in pts with low surgical risk and large reference vessel size.
Elective Stenting of Unprotected LM Coronary Artery Stenosis

Effect of Debulking before Stenting and IVUS Guidance—

- 127 pts with ULMD and normal LV function
  - IVUS guide (n=77) vs. Angio. guide (n=50)
  - debulking+stent (n=40) vs. stenting alone (n=87)
- Larger lumen in IVUS guide
- Lower restenosis in debulking+stent (8.3% vs. 25%)
- 2-y Mortality: 3%

Stenting for ULMTD might be favorable long-term results in selected pts and debulking before stenting seems to be effective in reducing the restenosis.
Unprotected Left main TRunk Angioplasty (ULTRA) Registry in Japan

ULTRA I Registry: 7 centers

ULTRA II Registry: 12 centers
Purpose

We evaluated the immediate and long-term outcomes of consecutive patients undergoing unprotected left main coronary artery angioplasty, considered unsuitable for coronary artery bypass graft surgery or who desired angioplasty, in a multicenter registry.
Methods

- Emergent and elective angioplasty for unprotected left main trunk disease (LMD)

- Registration:
  ULTRA II: Jan. 1, 2001 ~ Until DES approval

- Study Design: Multicenter prospective study
The ULTRA I Study

The Unprotected Left main TRunk Angioplasty Study

Investigators

Hideo Nishikawa, Kazuki Nakajima; Yamada Red Cross Hospital
Hideo Tamai, Kunihiko Kosuga; Shiga Medical Center for Adults
Tohru Kobayashi, Etsuo Tsuchikane; Osaka Medical Center for Cancer and Cardiovascular Diseases
Osamu Katoh; Kyoto Katsura Hospital
Yoshiaki Yokoi; Kishiwada Tokusyuikai Hospital
Kinzo Ueda; Takeda Hospital
Takahiko Suzuki, Mariko Ehara; Toyohashi Heart Center

CCT 2003 in Kobe
Inclusion Criteria

- De novo unprotected left main trunk disease
- Left main stenosis > 50%
- Need for revascularization
- The absence of patent bypass graft to the left coronary artery
Exclusion Criteria

- Catheter-induced left main stenosis

- The presence of good collateral flow from the right coronary artery
Clinical and Angiographic Follow-up

- Follow-up period: 5 years
- Clinical follow-up; Clinical event (every year)
  - Death
  - AMI
  - AP
  - CHF
  - CABG
  - Re-intervention
- Angiographic follow-up; 1mo 3mos 6mos 1yr 3yrs 5yrs
The ULTRA I Study
Patients registered: n=284
Patients registered: n=284

AMI 50

17% 83%

Non-AMI 234

AMI: related to LM lesion


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Patients registered: \( n=284 \)

Emergent 101

- Emergent: 35%
- Elective: 65%


CCT 2003 in Kobe
Reason for Catheter Intervention

Emergency
High risk

56%

44%

(patient/physician preference)

(including inoperative cases)
### Clinical Characteristics (1)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>68 ± 10</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>79</td>
</tr>
<tr>
<td>Acute myocardial infarction (%)</td>
<td>17</td>
</tr>
<tr>
<td>Recent myocardial infarction (&lt;2wks) (%)</td>
<td>11</td>
</tr>
<tr>
<td>Stable angina (%)</td>
<td>33</td>
</tr>
<tr>
<td>Unstable angina (%)</td>
<td>27</td>
</tr>
<tr>
<td>Prior myocardial infarction (%)</td>
<td>37</td>
</tr>
<tr>
<td>Prior CABG (%)</td>
<td>7</td>
</tr>
</tbody>
</table>

$n=284$
Clinical Characteristics (2)  

\[ n = 284 \]

LVEF (%)  
52 ± 17

Coronary Risk Factors;  
- Diabetes mellitus (%)  
  36  
- Current smoker (%)  
  37  
- Hypercholesterolemia (%)  
  39  
- Hypertension (%)  
  54  
- Obesity (%)  
  11
## Angiographic Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion length (mm)</td>
<td>$8.1 \pm 4.9$</td>
</tr>
<tr>
<td>Lesion location (%)</td>
<td></td>
</tr>
<tr>
<td>Ostial</td>
<td>31</td>
</tr>
<tr>
<td>Midshaft</td>
<td>35</td>
</tr>
<tr>
<td>Distal</td>
<td>59</td>
</tr>
<tr>
<td>LVEF</td>
<td>$0.49 \pm 0.20$</td>
</tr>
<tr>
<td>No. of diseased vessels except LMD (%)</td>
<td>7 / 31 / 39 / 23</td>
</tr>
<tr>
<td>Reference diameter (mm)</td>
<td>$3.3 \pm 0.6$</td>
</tr>
<tr>
<td>Percent stenosis (%)</td>
<td>$65 \pm 15$</td>
</tr>
</tbody>
</table>
Non-AMI (n=234) vs. AMI (n=50)

- **Non-AMI (n=234)**
  - Stent: 43%
  - POBA: 46%
  - CB: 37%
  - Rotablator: 7%

- **AMI (n=50)**
  - Stent: 76%
  - POBA: 24%
  - CB: 0%
  - Rotablator: 0%

**Final Procedure**

- **n=284**
  - Stent: 49%
  - DCA: 37%
  - POBA: 8%
  - CB: 6%
  - Rotablator: 2%
### Procedural Characteristics

<table>
<thead>
<tr>
<th>Type of Stent (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>P-S stent</td>
<td>29</td>
</tr>
<tr>
<td>ML stent</td>
<td>21</td>
</tr>
<tr>
<td>gfx/s670 stent</td>
<td>18</td>
</tr>
<tr>
<td>NIR stent</td>
<td>15</td>
</tr>
<tr>
<td>Wiktor stent</td>
<td>12</td>
</tr>
<tr>
<td>GR stent</td>
<td>5</td>
</tr>
</tbody>
</table>

| IABP (%)                | 57   |
| PCPS (%)                | 8    |
## Angiographic Results

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reference diameter (mm)</strong></td>
<td>3.3 ± 0.6</td>
<td>3.7 ± 0.6</td>
</tr>
<tr>
<td><strong>Diameter stenosis (%)</strong></td>
<td>64.7 ± 14.2</td>
<td>12.5 ± 12.6</td>
</tr>
<tr>
<td><strong>Minimal lumen diameter (mm)</strong></td>
<td>1.2 ± 0.5</td>
<td>3.1 ± 0.6</td>
</tr>
<tr>
<td><strong>Maximal balloon inflation pressure (atm)</strong></td>
<td>13.0 ± 2.4</td>
<td></td>
</tr>
</tbody>
</table>

*Follow-up values are averages of pre- and post-values.*
Initial Results in Patients with AMI

Procedural success (%) 49 / 50 (98%)
In-hospital death 17 / 50 (34%)
Emergency CABG 2 / 50 (4%)
Elective CABG 3 / 50 (6%)
Clinical success 32 / 50 (64%)

n=50
### Initial Results in Patients without AMI

\( n = 234 \)

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Procedural success</strong></td>
<td>233</td>
<td>(99.6%)</td>
</tr>
<tr>
<td><strong>In-hospital death</strong></td>
<td>11</td>
<td>(4.7%)</td>
</tr>
<tr>
<td><strong>Q-MI</strong></td>
<td>2</td>
<td>(0.9%)</td>
</tr>
<tr>
<td><strong>nonQ-MI</strong></td>
<td>12</td>
<td>(5.1%)</td>
</tr>
<tr>
<td><strong>Emergency CABG</strong></td>
<td>1</td>
<td>(0.4%)</td>
</tr>
<tr>
<td><strong>Clinical success</strong></td>
<td>220</td>
<td>(94.5%)</td>
</tr>
</tbody>
</table>
## Initial Results in Elective Cases

*n = 183*

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Procedural success</strong></td>
<td>182</td>
<td>99.5%</td>
</tr>
<tr>
<td><strong>In-hospital death</strong></td>
<td>1</td>
<td>0.5%</td>
</tr>
<tr>
<td><strong>Q-MI</strong></td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td><strong>nonQ-MI</strong></td>
<td>6</td>
<td>3.3%</td>
</tr>
<tr>
<td><strong>Emergency CABG</strong></td>
<td>1</td>
<td>0.5%</td>
</tr>
<tr>
<td><strong>CVA</strong></td>
<td>2</td>
<td>1.1%</td>
</tr>
<tr>
<td><strong>Clinical success</strong></td>
<td>181</td>
<td>98.9%</td>
</tr>
</tbody>
</table>
## Late Outcomes

**Follow-up (months)**  
29.8 ± 10.9  

**Clinical follow-up rate (>1yr)**  
97%  

<table>
<thead>
<tr>
<th>Event</th>
<th>Rate</th>
</tr>
</thead>
</table>
| Restenosis             | 51 / 230   | (22%)  
| TLR                    | 47 / 230   | (20%)  
| Cardiac Death          | 16         | (6%)   
| MI                     | 22         | (9%)   
| CABG                   | 13         | (5%)   |

1-Y-Event (MACE) free survival  
89%
Overall Cumulative Survival Curve

- Survival rate: 62.6%
- Death: 70 cases
- Kaplan-Meier
- $n=284$
Cumulative Survival Curve

Without acute MI

81%  
\(n=284\)

With acute MI

53%  
\(n=50\)

Log-Rank \(p=0.0001\)
Wilcoxon \(p=0.0001\)

\(n=234\)

CCT 2003 in Kobe
**Cumulative Survival Curve**

- **With elective procedure**: 
  - Survival: 83% \( n=183 \)
  - Log-Rank: \( p=0.0001 \)
  - Wilcoxon: \( p=0.0001 \)

- **With emergency procedure**: 
  - Survival: 54% \( n=101 \)

**CCT 2003 in Kobe**
Contemporary surgical outcomes

Spectrum of surgical risk for LM stenoses:
Benchmark for potentially competing PCI


- Cleveland Clinic Foundation, 1990-1995
- Overall In-hospital Mortality: 2.3% (for 1585 pts)
  Correlates: Renal insuff., Age & CHF(class 3 or 4)

- Overall 3-y Mortality: 15.6%
  Correlates: Age, Renal insuff., COPD
  - Group I: 4.5%
  - Group II: 6.5%
  - Group III: 20.0%
  - Group IV: 39.8% (high risk)
The ULTRA II Study

The Unprotected Left main TRunk Angioplasty Study

Investigators

Hideo Nishikawa; Yamada Red Cross Hospital
Hideo Tamai, Kunihiko Kosuga; Shiga Medical Center for Adults
Tohru Kobayashi, Etsuo Tsuchikane; Osaka Medical Center for Cancer and Cardiovascular Diseases
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Kinzo Ueda; Takeda Hospital
Yasushi Asakura; Keio University Hospital
Kenshi Fujii; Sakurabashi Watanabe Hospital
Haruo Hirayama; Nagoya Daini Red Cross Hospital
Hirotaka Oda; Niigata City General Hospital
Akitsugu Oida; Dokkyo University Hospital
Takahiko Suzuki, Mariko Ehara; Toyohashi Heart Center
Patients registered: n=178

AMI 31

17%

Non-AMI 147

83%

AMI: related to LM lesion
Patients registered: $n=178$

Emergent  67

38%

elective  111

62%
Reason for Catheter Intervention

Emergency
High risk

Desire

58%
42%

(patient/physician preference)

(including inoperative cases)


CCT 2003 in Kobe
## Clinical Characteristics (1)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n=178</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>69 ± 11</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>78</td>
</tr>
<tr>
<td>Acute myocardial infarction (%)</td>
<td>17</td>
</tr>
<tr>
<td>Recent myocardial infarction (&lt;2wks) (%)</td>
<td>10</td>
</tr>
<tr>
<td>Stable angina (%)</td>
<td>34</td>
</tr>
<tr>
<td>Unstable angina (%)</td>
<td>27</td>
</tr>
<tr>
<td>Prior myocardial infarction (%)</td>
<td>34</td>
</tr>
<tr>
<td>Prior CABG (%)</td>
<td>8</td>
</tr>
</tbody>
</table>
Clinical Characteristics (2)

n=178

LVEF (%)  
51 ± 18

Coronary Risk Factors:

- Diabetes mellitus (%)  38
- Current smoker (%)  34
- Hypercholesterolemia (%)  38
- Hypertension (%)  55
- Obesity (%)  13
## Angiographic Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion length (mm)</td>
<td>$8.4 \pm 4.6$</td>
</tr>
<tr>
<td>Lesion location (%)</td>
<td></td>
</tr>
<tr>
<td>Ostial</td>
<td>30</td>
</tr>
<tr>
<td>Midshaft</td>
<td>36</td>
</tr>
<tr>
<td>Distal</td>
<td>60</td>
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<tr>
<td>LVEF</td>
<td>$0.48 \pm 0.21$</td>
</tr>
<tr>
<td>No. of diseased vessels except LMD (%)</td>
<td></td>
</tr>
<tr>
<td>Zero / One / Two / Three</td>
<td>6 / 32 / 39 / 23</td>
</tr>
<tr>
<td>Reference diameter (mm)</td>
<td>$3.5 \pm 0.7$</td>
</tr>
<tr>
<td>Percent stenosis (%)</td>
<td>$66 \pm 14$</td>
</tr>
</tbody>
</table>
Final Procedure

N=178

Non-AMI (n=147)
- Stent: 65
- DCA: 2
- Rota: 2
- CB: 2
- POBA: 2

AMI (n=31)
- Stent: 12
- DCA: 3
- Rota: 3
- CB: 65
- POBA: 82

CCT 2003 in Kobe
## Procedural Characteristics

<table>
<thead>
<tr>
<th>Type of stent (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ML stent</strong></td>
<td>37</td>
</tr>
<tr>
<td><strong>Bx stent</strong></td>
<td>32</td>
</tr>
<tr>
<td><strong>gfx/s670 stent</strong></td>
<td>18</td>
</tr>
<tr>
<td><strong>NIR stent</strong></td>
<td>13</td>
</tr>
</tbody>
</table>

| IABP (%) | 56 |
| PCPS (%) | 8  |
## Angiographic Results

<table>
<thead>
<tr>
<th></th>
<th>ULTRA II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reference diameter (mm)</strong></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>3.5 ± 0.7</td>
</tr>
<tr>
<td>Post</td>
<td>3.8 ± 0.6</td>
</tr>
<tr>
<td><strong>Diameter stenosis (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>65.7 ± 14.1</td>
</tr>
<tr>
<td>Post</td>
<td>11.1 ± 12.1</td>
</tr>
<tr>
<td>Follow-up</td>
<td>29.1 ± 16.0</td>
</tr>
<tr>
<td><strong>Minimal lumen diameter (mm)</strong></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>1.2 ± 0.5</td>
</tr>
<tr>
<td>Post</td>
<td>3.2 ± 0.6</td>
</tr>
<tr>
<td>Follow-up</td>
<td>2.7 ± 0.7</td>
</tr>
<tr>
<td><strong>Maximal balloon inflation pressure (atm)</strong></td>
<td>14.7 ± 2.9</td>
</tr>
</tbody>
</table>
Initial Results in Patients with AMI

Procedural success (%) 31 / 31 (100%)
In-hospital death 11 / 31 (35%)
Emergency CABG 2 / 31 (6%)
Elective CABG 2 / 31 (6%)
Clinical success 19 / 31 (61%)

n=50
**ULTRA II**

**Initial Results in Patients without AMI**

\[ n=147 \]

- **Procedural success**: 146 (99.3%)
- **In-hospital death**: 5 (3.4%)
- **Q-MI**: 1 (0.7%)
- **nonQ-MI**: 8 (4.6%)
- **Emergency CABG**: 1 (0.7%)
- **Clinical success**: 140 (95.2%)
## Initial Results in Elective Cases

$n=111$

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural success</td>
<td>110</td>
<td>(99.1%)</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>0</td>
<td>(0%)</td>
</tr>
<tr>
<td>Q-MI</td>
<td>0</td>
<td>(0%)</td>
</tr>
<tr>
<td>nonQ-MI</td>
<td>4</td>
<td>(3.6%)</td>
</tr>
<tr>
<td>Emergency CABG</td>
<td>0</td>
<td>(0%)</td>
</tr>
<tr>
<td>CVA</td>
<td>1</td>
<td>(0.9%)</td>
</tr>
<tr>
<td>Clinical success</td>
<td>110</td>
<td>(99.1%)</td>
</tr>
</tbody>
</table>
Conclusion

Catheter interventions for selected and elective patients with unprotected LMD could be accomplished safely and effectively with new devices in this registry. The benefit of angioplasty for patients with acute MI was, however, undetermined.

Mid to long term follow-up results are favorable in patients with elective angioplasty for unprotected LMD.
Unprotected Left Main Trunk Angioplasty

--- Is it still risky? ---

It is safe with new devices.
However, we need a large-scale, randomized study.
**Left Main Rapamycin-Coated Stent**


Case 47y/o male
a history of recurrent PCI
Rapamycin-coated stent
(Bx Velocity 4.0x18mm)

At 6-mo f/u:
no symptoms
no intimal hyperplasia

**Drug eluting stent is not available in Japan!**

Conventional angiogram

Multislice spiral CT

Intravascular ultrasound
Unprotected Left Main Trunk Angioplasty

- PCI for LMD might be superior to CABG in drug eluting stent era.

- We have to do a large-scale, randomized study after the approval.
Surgeons for CABG
END

Thank you for your attention.