Coronary angiography after out-of-hospital cardiac arrest without ST-elevation

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on behalf of the TOMAHAWK investigators

Heart Center Leipzig and University Heart Center Lübeck, Germany
Causes of OHCA – Registry

714 OHCA admitted to ICU

435 w/o obvious extracardiac etiology

134 ST elevation (31%)
- 128 with significant lesion (96%)
- 6 w/o significant lesion (4%)

301 other ECG patterns (69%)
- 176 with significant lesion (58%)
- 125 w/o significant lesion (42%)

92 PCI attempted (31%)

Respiratory failure n=131
Brain injury n=17
Metabolic disorders n=15
Hemorrhage n=10
Miscellaneous n=106

714 OHCA admitted to ICU

Pros and Cons
of Immediate Angiography after OHCA

**Pro**
- Prevention of
  - Large myocardial injury
  - Hemodynamic deterioration
  - Heart failure
in presence of a treatable culprit lesion

**Con**
- Delay in diagnosis and treatment for etiologies other than ACS
- Risk of complications
  - Renal damage
  - Reperfusion injury
  - Stent thrombosis
  - Bleeding
  - Cerebral damage by application of contrast in the setting of compromised blood-brain barrier after OHCA
In resuscitated OHCA patients without ST-segment elevation, routine immediate coronary angiography (possibly followed by revascularization) is superior to a delayed or selective approach regarding 30-day all-cause mortality.
Survivor of out-of-hospital cardiac arrest without ST-segment elevation

Check in- and exclusion criteria

Informed consent

Randomization

Immediate angiography (direct transport to cath)

Initial intensive care evaluation with delayed angiography if indicated

Primary endpoint: 30-day mortality

Follow-up at 6 and 12 months (telephone)

Design

31 active sites in Germany and Denmark
Key In- and Exclusion Criteria

**Inclusion criteria**
- Documented resuscitated OHCA of possible cardiac origin and return of spontaneous circulation
- Age ≥30 years
- Informed consent

**Exclusion criteria**
- ST-segment elevation or left bundle branch block
- No ROSC upon hospital admission
- Severe hemodynamic or electrical instability requiring immediate coronary angiography/intervention (delay clinically not acceptable)
- Obvious extra-cardiac etiology
- In-hospital cardiac arrest
- Known or likely pregnancy
- Participation in another intervention study interfering with the research questions of the TOMAHAWK trial
**Statistical Methodology**

**Primary endpoint**
- 30-day all-cause mortality

**Sample size**
- Estimated 34% event rate in immediate vs. 46% in delayed/selective angiography for primary endpoint
- 1 interim analysis (after 109 events)
- 2-sided test time-to-event analysis; power 80%; alpha=0.034 for final analysis
- To compensate for losses in follow-up → 558 patients

**Secondary endpoints at 30 day follow-up**
- Myocardial infarction at 30 days
- Severe neurological deficit (cerebral performance categories 3-5)
- Composite endpoint of all-cause mortality or severe neurological deficit at 30 days
- Length of intensive care unit stay
- Serial Simplified Acute Physiology Score (SAPS) II
- Rehospitalization for congestive heart failure within 30 days
- Peak release of myocardial enzymes
- Moderate and severe bleeding (BARC definition types 2–5)
- Stroke
- Acute renal failure requiring renal replacement therapy

**Primary endpoint**

**Sample size**

**Secondary endpoints at 30 day follow-up**

**To compensate for losses in follow-up → 558 patients**
Analyzed (n=265)

Excluded from analysis (n=16)
- Withdrawal of informed consent (n=14)
- Violation of in-/exclusion criteria [in hospital cardiac arrest] (n=2)

Immediate angiography (n=281)
Received allocated intervention (n=260)
Did not receive allocated intervention (n=21)
- No catheterization at all (n=6)
- No catheterization in first 24h (n=1)
- No record on file due to withdrawal of informed consent (n=14)

Randomization (n=554)

Not included (n=4)
- No completion of informed consent process (n=4)

Considered for inclusion (n=558)

Immediate angiography (n=281)
Delayed/selective angiography (n=273)

Received allocated intervention (n=245)
Did not receive allocated intervention (n=28)
- Catheterization before 24h without fulfilling crossover criteria for early catheterization (n=22)
- No record on file due to withdrawal of informed consent (n=6)

Excluded from analysis (n=8)
- Withdrawal of informed consent (n=6)
- Violation of in-/exclusion criteria [STEMI] (n=2)

Immediate angiography (n=281)

Excluded from analysis (n=28)
- Violation of in-/exclusion criteria [in hospital cardiac arrest] (n=2)
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Immediate angiography (n=265)</th>
<th>Delayed/selective angiography (n=265)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years); median (IQR)</strong></td>
<td>69 (59-78)</td>
<td>71 (60-79)</td>
</tr>
<tr>
<td><strong>Female sex; n/total (%)</strong></td>
<td>80/265 (30.2)</td>
<td>81/265 (30.6)</td>
</tr>
<tr>
<td><strong>Known coronary artery disease; n/total (%)</strong></td>
<td>79/229 (34.5)</td>
<td>93/229 (40.6)</td>
</tr>
<tr>
<td><strong>Diabetes mellitus; n/total (%)</strong></td>
<td>71/244 (29.1)</td>
<td>74/251 (29.5)</td>
</tr>
<tr>
<td><strong>Arrest witnessed; n/total (%)</strong></td>
<td>236/259 (91.1)</td>
<td>226/257 (87.9)</td>
</tr>
<tr>
<td><strong>Shockable first monitored rhythm; n/total (%)</strong></td>
<td>126/241 (52.3)</td>
<td>142/242 (58.7)</td>
</tr>
<tr>
<td><strong>Bystander cardiopulmonary resuscitation; n/total (%)</strong></td>
<td>142/247 (57.5)</td>
<td>152/252 (60.3)</td>
</tr>
<tr>
<td><strong>Time from arrest to basic life support (min); median (IQR)</strong></td>
<td>2 (0-8)</td>
<td>1 (0-5)</td>
</tr>
<tr>
<td><strong>Time from arrest to return of spontaneous circulation (min); median (IQR)</strong></td>
<td>15 (10-20)</td>
<td>15 (8-20)</td>
</tr>
<tr>
<td><strong>Glasgow Coma Scale on admission; median (IQR)</strong></td>
<td>3 (3-3)</td>
<td>3 (3-3)</td>
</tr>
<tr>
<td><strong>Left ventricular ejection fraction on admission (%); median (IQR)</strong></td>
<td>45 (38-56)</td>
<td>44 (30-50)</td>
</tr>
</tbody>
</table>
## Characteristics and Treatment of CAD

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Immediate angiography (n=265)</th>
<th>Delayed/selective angiography (n=265)</th>
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<tbody>
<tr>
<td>Coronary angiography performed; n/total (%)</td>
<td>253/265 (95.5)</td>
<td>165/265 (62.2)</td>
</tr>
<tr>
<td>Time from arrest to coronary angiography (h); median (IQR)</td>
<td>2.9 (2.2-3.9)</td>
<td>46.9 (26.1-116.6)</td>
</tr>
<tr>
<td>Severity of coronary artery disease; n/total (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No significant disease</td>
<td>99/252 (39.3)</td>
<td>46/165 (27.9)</td>
</tr>
<tr>
<td>1-vessel disease</td>
<td>37/252 (14.7)</td>
<td>21/165 (12.7)</td>
</tr>
<tr>
<td>2-vessel disease</td>
<td>32/252 (12.7)</td>
<td>26/165 (15.8)</td>
</tr>
<tr>
<td>3-vessel disease</td>
<td>84/252 (33.3)</td>
<td>72/165 (43.6)</td>
</tr>
<tr>
<td>Culprit lesion identified; n/total (%)</td>
<td>94/247 (38.1)</td>
<td>67/156 (43.0)</td>
</tr>
<tr>
<td>PCI performed; n/total (%)</td>
<td>93/250 (37.2)</td>
<td>70/162 (43.2)</td>
</tr>
</tbody>
</table>
Primary Endpoint

Survival probability over Days after Randomization for Immediate and Delayed/Selective angiography.

Hazard ratio 1.28 (95% CI 1.00-1.63)
Log-rank p=0.06

Immediate angiography:
- Days: 265
- Values: 265, 195, 151, 138, 129, 123, 117

Delayed/Selective angiography:
- Days: 265
- Values: 265, 207, 163, 149, 139, 138, 133
## Secondary Endpoints at 30 days

<table>
<thead>
<tr>
<th></th>
<th>Immediate angiography (n=265)</th>
<th>Delayed/selective angiography (n=265)</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction; n/total (%)</td>
<td>0/248 (0)</td>
<td>2/250 (0.8)</td>
<td>RR 0 (0-1.93)</td>
</tr>
<tr>
<td>Severe neurological deficit; n/total (%)</td>
<td>21/112 (18.8)</td>
<td>16/126 (12.7)</td>
<td>RR 1.48 (0.82-2.67)</td>
</tr>
<tr>
<td>All-cause mortality or severe neurological deficit; n/total (%)</td>
<td>164/255 (64.3)</td>
<td>138/248 (55.6)</td>
<td>RR 1.16 (1.002-1.34)</td>
</tr>
<tr>
<td>Peak release of myocardial enzymes</td>
<td></td>
<td></td>
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<tr>
<td>Troponin T (µg/L); median (IQR)</td>
<td>0.39 (0.14-1.26)</td>
<td>0.34 (0.12-1.07)</td>
<td>HLE 0.04 (-0.03-0.11)</td>
</tr>
<tr>
<td>Troponin I (µg/L); median (IQR)</td>
<td>1.46 (0.42-5.69)</td>
<td>1.10 (0.40-5.75)</td>
<td>HLE 0.06 (-0.37-0.49)</td>
</tr>
<tr>
<td>Moderate and severe bleeding (BARC 2-5)*; n/total (%)</td>
<td>2/260 (4.6)</td>
<td>8/232 (3.4)</td>
<td>RR 1.34 (0.57-3.14)</td>
</tr>
<tr>
<td>Stroke*; n/total (%)</td>
<td>4/258 (1.6)</td>
<td>5/242 (2.1)</td>
<td>RR 1.13 (0.33-3.84)</td>
</tr>
<tr>
<td>Acute renal failure requiring renal replacement therapy*; n/total (%)</td>
<td>49/259 (18.9)</td>
<td>38/241 (15.8)</td>
<td>RR 1.14 (0.78-1.68)</td>
</tr>
</tbody>
</table>

*Assessed in safety (as treated) population

RR = Relative risk, HLE = Hodges-Lehmann estimator for location shift
### Subgroup Analysis

<table>
<thead>
<tr>
<th></th>
<th>Immediate angiography</th>
<th>Delayed/selective angiography</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of patients with event/total no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥65 years</td>
<td>104/164 (0.63)</td>
<td>99/175 (0.54)</td>
<td>1.29 (0.97-1.73)</td>
</tr>
<tr>
<td>&lt;65 years</td>
<td>40/102 (0.4)</td>
<td>26/90 (0.31)</td>
<td>1.37 (0.84-2.23)</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No</td>
<td>82/173 (0.47)</td>
<td>69/177 (0.39)</td>
<td>1.32 (0.95-1.83)</td>
</tr>
<tr>
<td>Yes</td>
<td>49/71 (0.69)</td>
<td>46/74 (0.62)</td>
<td>1.19 (0.78-1.81)</td>
</tr>
<tr>
<td>First monitored rhythm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-shockable</td>
<td>84/115 (0.73)</td>
<td>68/100 (0.68)</td>
<td>1.24 (0.88-1.75)</td>
</tr>
<tr>
<td>Shockable</td>
<td>49/126 (0.39)</td>
<td>43/142 (0.3)</td>
<td>1.44 (0.99-2.19)</td>
</tr>
<tr>
<td>Confirmed myocardial infarction as OHCA trigger</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>73/145 (0.5)</td>
<td>63/159 (0.4)</td>
<td>1.34 (0.95-1.89)</td>
</tr>
<tr>
<td>Yes</td>
<td>18/47 (0.38)</td>
<td>18/43 (0.42)</td>
<td>0.97 (0.5-1.9)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>50/90 (0.62)</td>
<td>37/81 (0.46)</td>
<td>1.04 (1.06-2.54)</td>
</tr>
<tr>
<td>Male</td>
<td>94/185 (0.51)</td>
<td>86/184 (0.47)</td>
<td>1.14 (0.84-1.53)</td>
</tr>
<tr>
<td>Targeted temperature management</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>28/59 (0.47)</td>
<td>25/56 (0.45)</td>
<td>1.34 (0.77-2.33)</td>
</tr>
<tr>
<td>Yes</td>
<td>114/204 (0.56)</td>
<td>96/206 (0.47)</td>
<td>1.25 (0.96-1.67)</td>
</tr>
<tr>
<td>Time from arrest to ROSC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥15 min</td>
<td>99/171 (0.58)</td>
<td>97/170 (0.57)</td>
<td>1.02 (0.76-1.36)</td>
</tr>
<tr>
<td>&lt;15 min</td>
<td>20/39 (0.54)</td>
<td>17/37 (0.3)</td>
<td>1.51 (0.78-2.90)</td>
</tr>
</tbody>
</table>
Conclusions

• Among patients with resuscitated OHCA of possible cardiac origin with shockable and non-shockable arrest rhythm and no ST-elevation, a strategy of immediate unselected coronary angiography was not found to be beneficial over a delayed and selective approach with regard to the 30-day risk of all-cause death.

• The findings of the TOMAHAWK trial support results from a previous randomized trial (COACT) of OHCA patients with shockable arrest rhythms only, which found no significant differences in clinical outcome between immediate and delayed coronary angiography at 90 days and 1 year.
Trial Network and Organization

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Homepage
https://tomahawk.dzhk.de/
Angiography after Out-of-Hospital Cardiac Arrest without ST-Segment Elevation