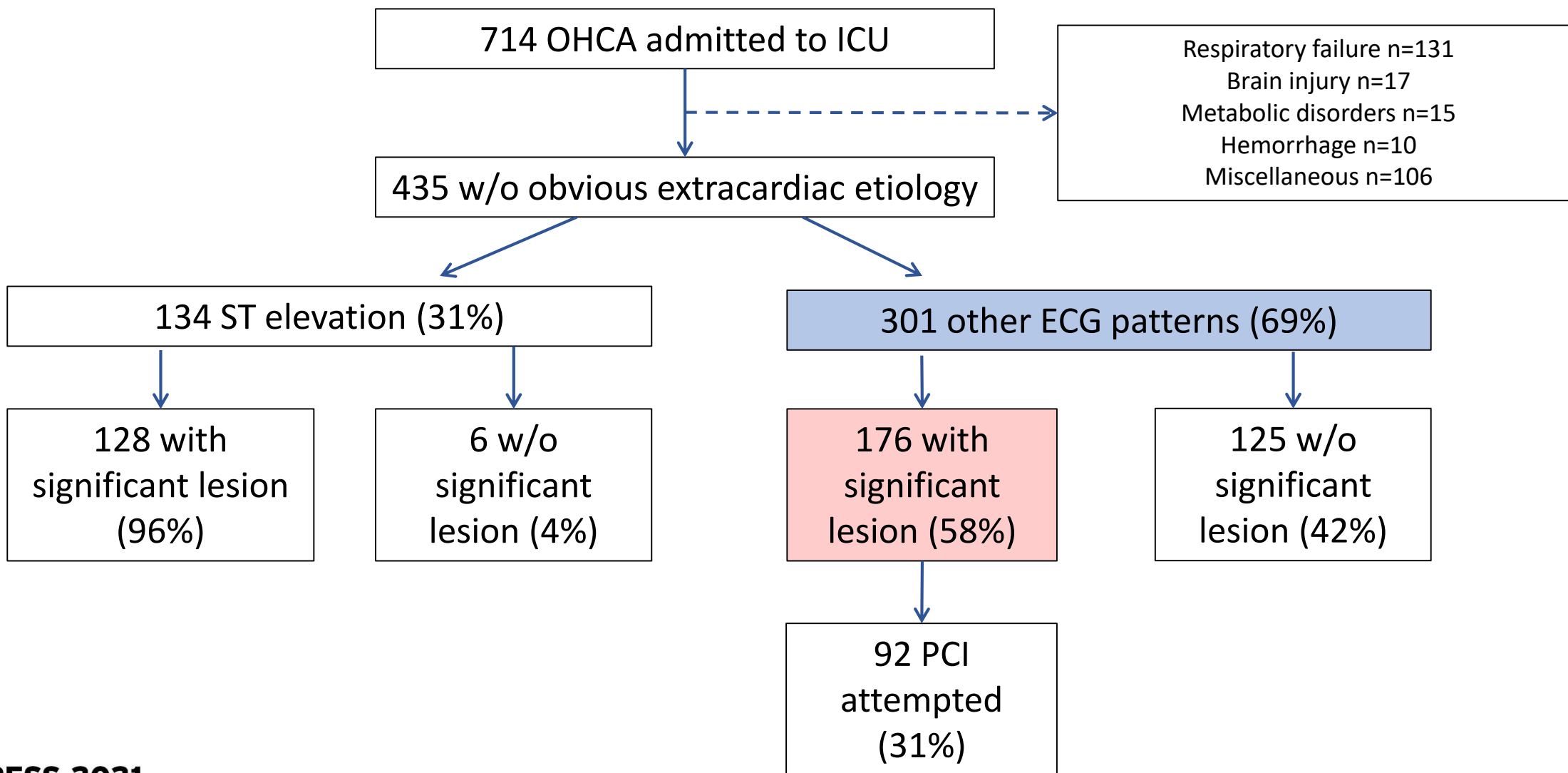# Coronary angiography after out-of-hospital cardiac arrest without ST- elevation

## Steffen Desch, MD

## on behalf of the TOMAHAWK investigators

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# Causes of OHCA – Registry



714 OHCA admitted to ICU

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

435 w/o obvious extracardiac etiology

134 ST elevation (31%)

301 other ECG patterns (69%)

128 with significant lesion (96%)

6 w/o significant lesion (4%)

176 with significant lesion (58%)

125 w/o significant lesion (42%)

92 PCI attempted (31%)

Dumas et al. Circ Cardiovasc Interv 2010;3:200-207

# 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
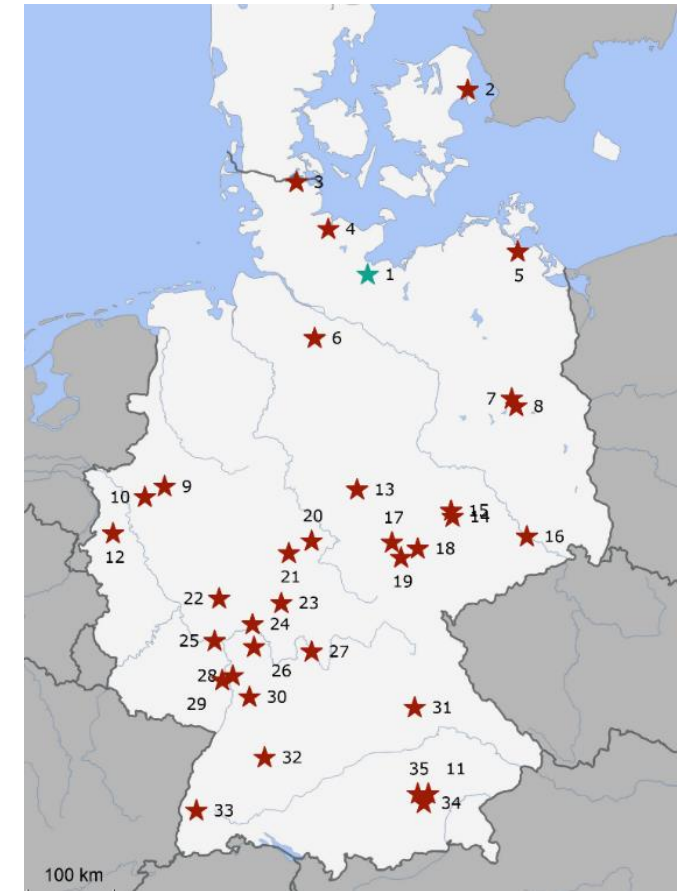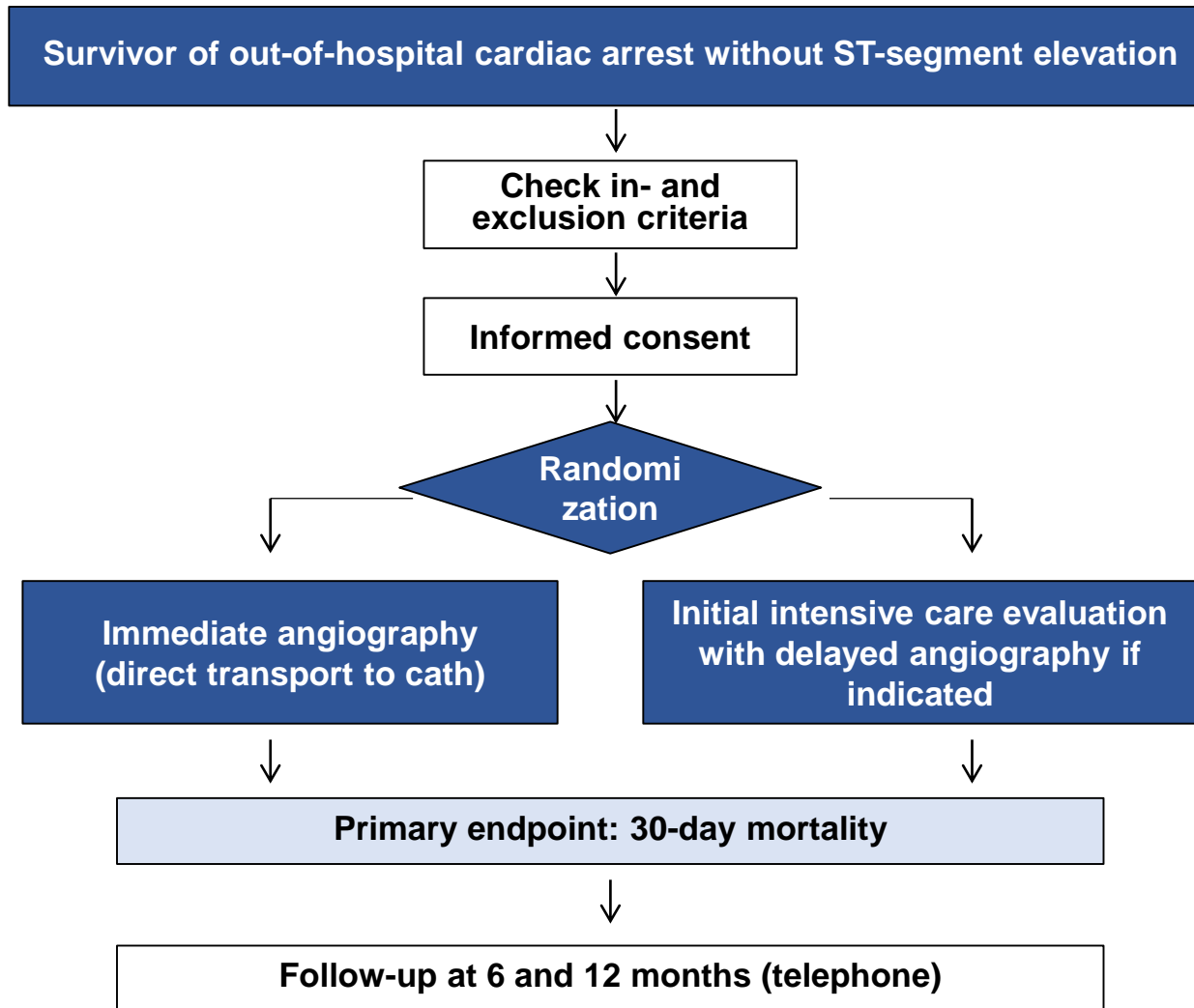
# Study Hypothesis

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.

# Design



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)

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

# Study Flow

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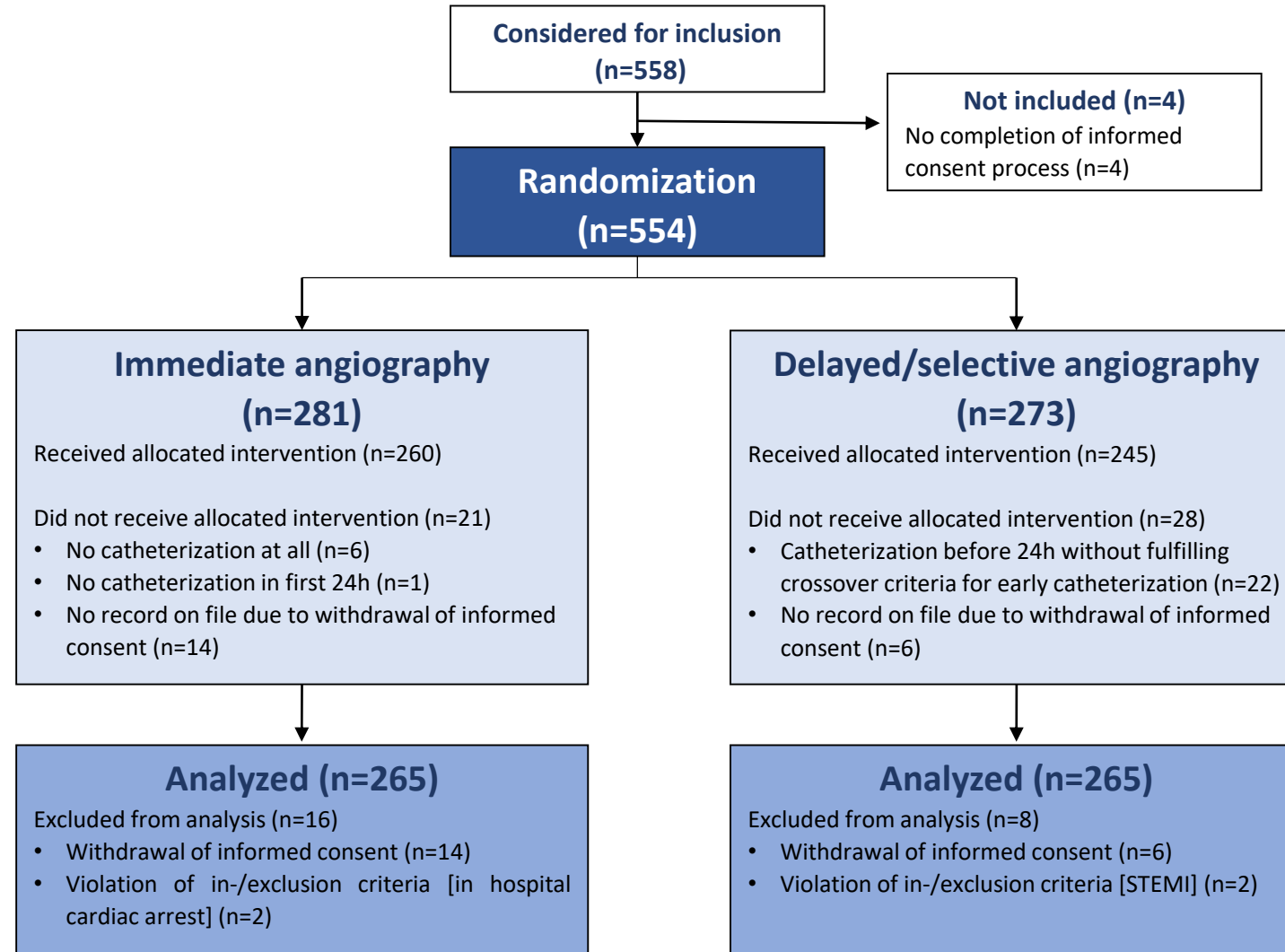
| | Immediate angiography (n=265) | Delayed/selective angiography (n=265) |
|---|---|---|
| Age (years); median (IQR) | 69 (59-78) | 71 (60-79) |
| Female sex; n/total (%) | 80/265 (30.2) | 81/265 (30.6) |
| Known coronary artery disease; n/total (%) | 79/229 (34.5) | 93/229 (40.6) |
| Diabetes mellitus;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

# Characteristics and Treatment of CAD

|  | Immediate angiography (n=265) | Delayed/selective angiography (n=265) |
|---|---|---|
| **Coronary angiography performed; n/total (%)** | 253/265 (95.5) | 165/265 (62.2) |
| **Time from arrest to coronary angiography (h); median (IQR)** | 2.9 (2.2-3.9) | 46.9 (26.1-116.6) |
| **Severity of coronary artery disease; n/total (%)** | | |
| **No significant disease** | 99/252 (39.3) | 46/165 (27.9) |
| **1-vessel disease** | 37/252 (14.7) | 21/165 (12.7) |
| **2-vessel disease** | 32/252 (12.7) | 26/165 (15.8) |
| **3-vessel disease** | 84/252 (33.3) | 72/165 (43.6) |
| **Culprit lesion identified; n/total (%)** | 94/247 (38.1) | 67/156 (43.0) |
| **PCI performed; n/total (%)** | 93/250 (37.2) | 70/162 (43.2) |
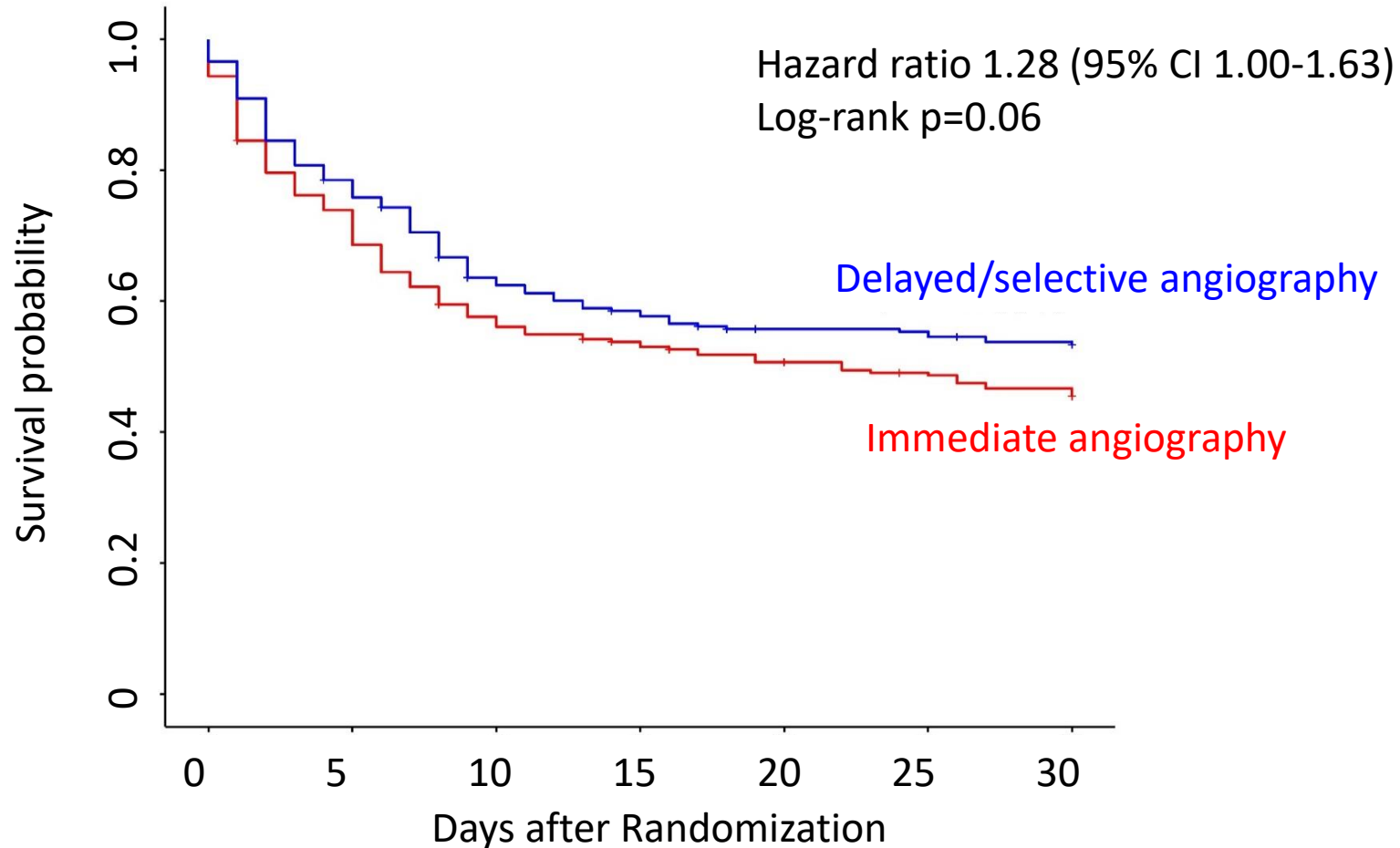
# Secondary Endpoints at 30 days

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

\*Assessed in safety (as treated) population
RR = Relative risk, HLE = Hodges-Lehmann estimator for location shift
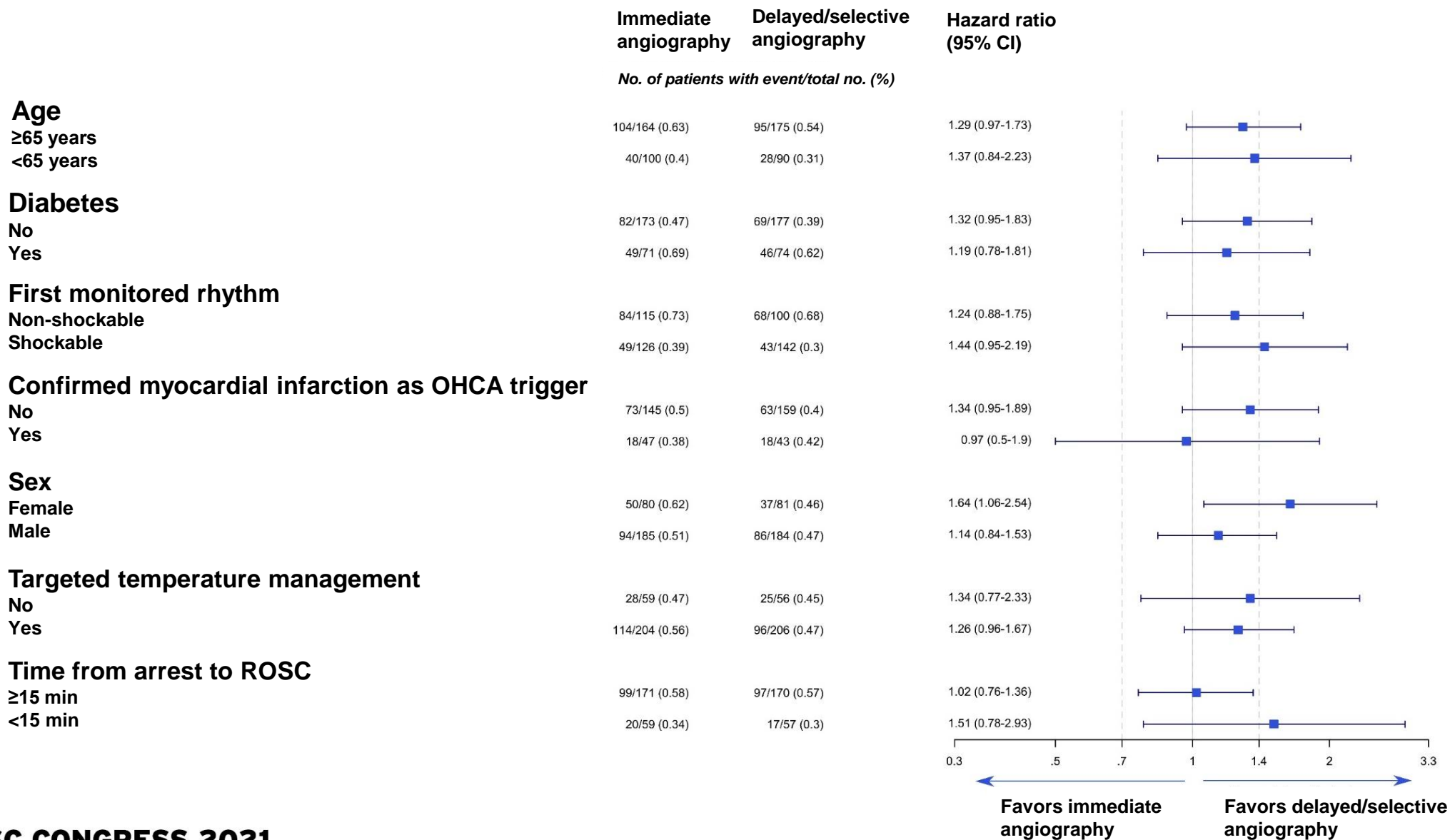
# Conclusions

- 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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