# Clinically Relevant Myocardial Infarction Associated with PCI
## Practical and Clinical Trial Aspect

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# Background

- Clinical significance of periprocedural MI remained controversial.

- This uncertainty leads to unnecessary medical test, increased cost, and longer hospital stay in clinical practice.

- Clinical trials frequently counted periprocedural MI as MI events with spontaneous MI. This approach may obscure appropriate interpretation of trial results unless prognostic value of periprocedural and spontaneous MI was equivalent.

# Is This Difference Clinically Relevant?

## BIOFLOW V
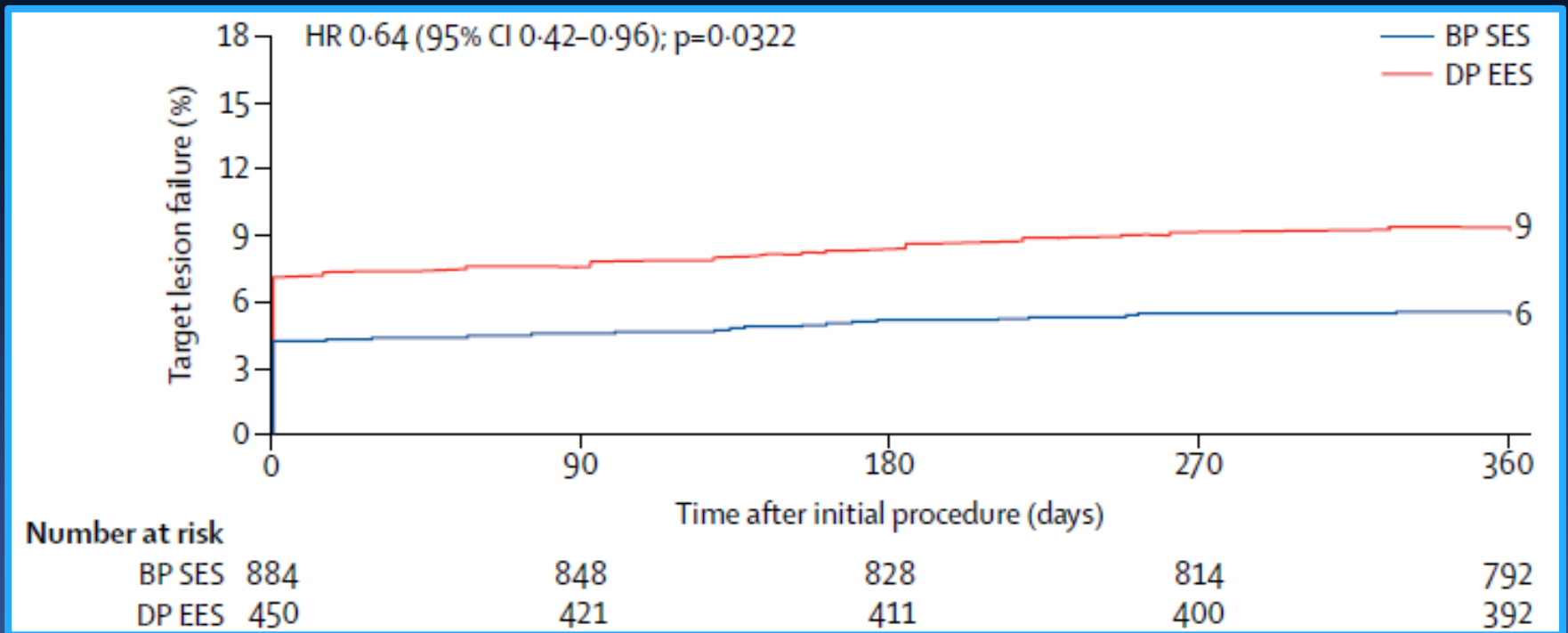
# Objective

- We aimed to determine the clinically relevant periprocedural MI criteria using the combination of cardiac enzyme and supportive clinical features in patients with normal baseline cardiac biomarker.

- Clinically relevant periprocedural MIs were evaluated in 2 steps:

  *1) Those with a higher risk of mortality*
  *2) Those with mortality similar to spontaneous MI*

# Study Population

- From 4 prospective large contemporary registries

  - IRIS-DES registry: Multicenter (45 centers)

  - ASAN PCI registry: Single center

  - ASAN MAIN registry: Single center

  - ASAN MV registry (PCI cohort): Single center

- Eligible patients were men and women *without creatine kinase-MB (CK-MB) elevation before PCI and with serial (every 8 hours) CK-MB measurement after PCI*

# Study Flow



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┌────────────────────┐  ┌────────────────────┐  ┌────────────────────────┐  ┌──────────────────────────┐
│ IRIS-DES Registry  │  │ ASAN-PCI Registry  │  │ PCI Cohort of ASAN-MV  │  │ PCI Cohort of ASAN-MAIN  │
│   (2007-2015)      │  │   (2003-2011)      │  │ Registry (2003-2013)   │  │ Registry (2003-2017)     │
│   N=17555          │  │   N=10059          │  │   N=6252               │  │   N=1567                 │
└────────────────────┘  └────────────────────┘  └────────────────────────┘  └──────────────────────────┘
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A pooled data from 4 registries after eliminating patients overlapped
(N=26260)

- Not available data (N=497)
- *Baseline CK-MB elevation X 1 URL (N = 8573)*

*Study population Without CK-MB elevation*
*(N=17190)*

# Collecting Variables for MI

## Common eCRF

**Major Event Data**
**Myocardial Infarction**

Subject Number : IE010376    Subject Initial : KYK    Date of index procedure : 2011-11-22

Date of event * [          ] (yyyy-mm-dd)

Procedure time    Start [▼] hr [▼] min - End [▼] hr [▼] min

Type of MI *    ○ Q wave MI    ○ Non Q wave MI

Time of MI *    ○ Periprocedural MI    ○ Inhospital MI    ○ F /U MI

Angina symptom *    ○ Yes    ○ No

Location of infarction *    ○ Anteior    ○ Anterolateral    ○ Inferior    ○ Posterior    ○ Undetermined

Any diagnostic ECG finding? *    ○ Yes    ○ No
☐ New pathologic Q waves    ☐ New ST elevation    ☐ New ST depression
☐ New T wave inversion    ☐ LBBB    ☐ Others [          ]

Cardiac biomarker measurements *

| | | Baseline | Baseline value | Before treatment | Before treat value | Peak |
|---|---|---|---|---|---|---|
| CK (IU/L) | Date | [    ] ND | [    ] | Date [    ] ND | [    ] ND | Date [    ] ND |
| | Time | [▼] hr [▼] min | ND | Time [▼] hr [▼] min | | Time [▼] hr [▼] min |
| CK-MB (ng/mL) | Date | [    ] ND | [    ] | Date [    ] ND | [    ] ND | Date [    ] ND |
| | Time | [▼] hr [▼] min | ND | Time [▼] hr [▼] min | | Time [▼] hr [▼] min |
| Troponin I (ng/mL) | Date | [    ] ND | [    ] | Date [    ] ND | [    ] ND | Date [    ] ND |
| | Time | [▼] hr [▼] min | ND | Time [▼] hr [▼] min | | Time [▼] hr [▼] min |
| Troponin T (g/L) | Date | [    ] ND | [    ] | Date [    ] ND | [    ] ND | Date [    ] ND |
| | Time | [▼] hr [▼] min | ND | Time [▼] hr [▼] min | | Time [▼] hr [▼] min |

Angiography done related to this event *    ○ Yes    ○ No
• Total occlusion : ○ Yes ○ No
• Visible thrombus: ○ Yes ○ No

Related to target vessel *    ○ Yes    ○ No    ○ Unknown

Related to stent thrombosis *    ○ Yes    ○ No    ○ Unknown

Treatment related to this event *    ○ Medication only    ○ Thrombolysis    ○ PCI    ○ CABG

## Collecting Variables

Chest pain
Electrocardiographic change
- Q wave
- Left bundle branch block
- T wave inversion
- ST segment elevation
- ST segment depression

Angiographic mechanism
- Side branch occlusion
- Main vessel complications
  - Coronary perforation
  - Distal embolization
  - No reflow
  - Thrombus
  - Flow limiting coronary dissection

* All data of interest were centrally collected, verified, and carefully adjudicated by an independent committee.

# Endpoint, Definition and FU

- The primary endpoint: *All-Cause Mortality*

- Spontaneous MI:

  Any cardiac enzyme elevation with ischemic symptom and sign not related with the PCI procedure

- Patients were clinically followed at 1, 6, and 12 months and annually thereafter.

# Statistical Analysis

- Stratified Cox proportional hazards models were used to estimate the adjusted association between various categories of periprocedural MI, spontaneous MI, and mortality

- To determine the criteria of periprocedural MI with mortality similar to spontaneous MI, we calculated the age-adjusted standardized mortality rates (SMRs) of periprocedural MI according to the CK-MB level.

- Standardized mortality rate was calculated as annualized mortality rate multiplied by a ratio of observed mortality to expected mortality in each category. Expected mortality was determined by applying indirect standardization method for age.

- All reported P values were two sided, and a value of $P < 0.05$ was considered statistically significant. SAS software, version 9.1 (SAS Institute, Inc., Cary, NC), was used for all statistical analyses.

# Patient Characteristics

| Patient | N=17109 |
|---|---|
| Age | 63.2 ±10.1 |
| Gender (Male) | 11664 (68.2) |
| Unstable angina | 6837 (40.0) |
| Body mass index | 25.0 ±3.1 |
| Hypertension | 10719 (62.7) |
| Diabetes | 5665 (33.1) |
| Current smoking | 4108 (24.0) |
| Hyperlipidemia | 7297 (42.7) |
| Previous CABG | 397 (2.3) |
| Previous MI | 1241 (7.3) |
| Previous PCI | 2698 (15.8) |
| Previous CHF | 297 (1.7) |
| Previous stroke | 1221 (7.1) |
| PAD | 380 (2.2) |

| Patients | N=17109 |
|---|---|
| Chronic renal failure | 486 (2.8) |
| Chronic lung disease | 318 (1.9) |
| Ejection fraction | |
| >50% | 15717 (91.9) |
| 40-50% | 944 (5.5) |
| <40% | 448 (2.6) |
| Multivessel disease | 9492 (55.5) |
| Location of target vessel | |
| Left main | 1694 (9.9) |
| LAD | 11758 (68.7) |
| LCX | 4810 (28.1) |
| RCA | 5918 (34.6) |
| Number of stent | 1.8 ±1.1 |

# Chest Pain*

**48.1%**
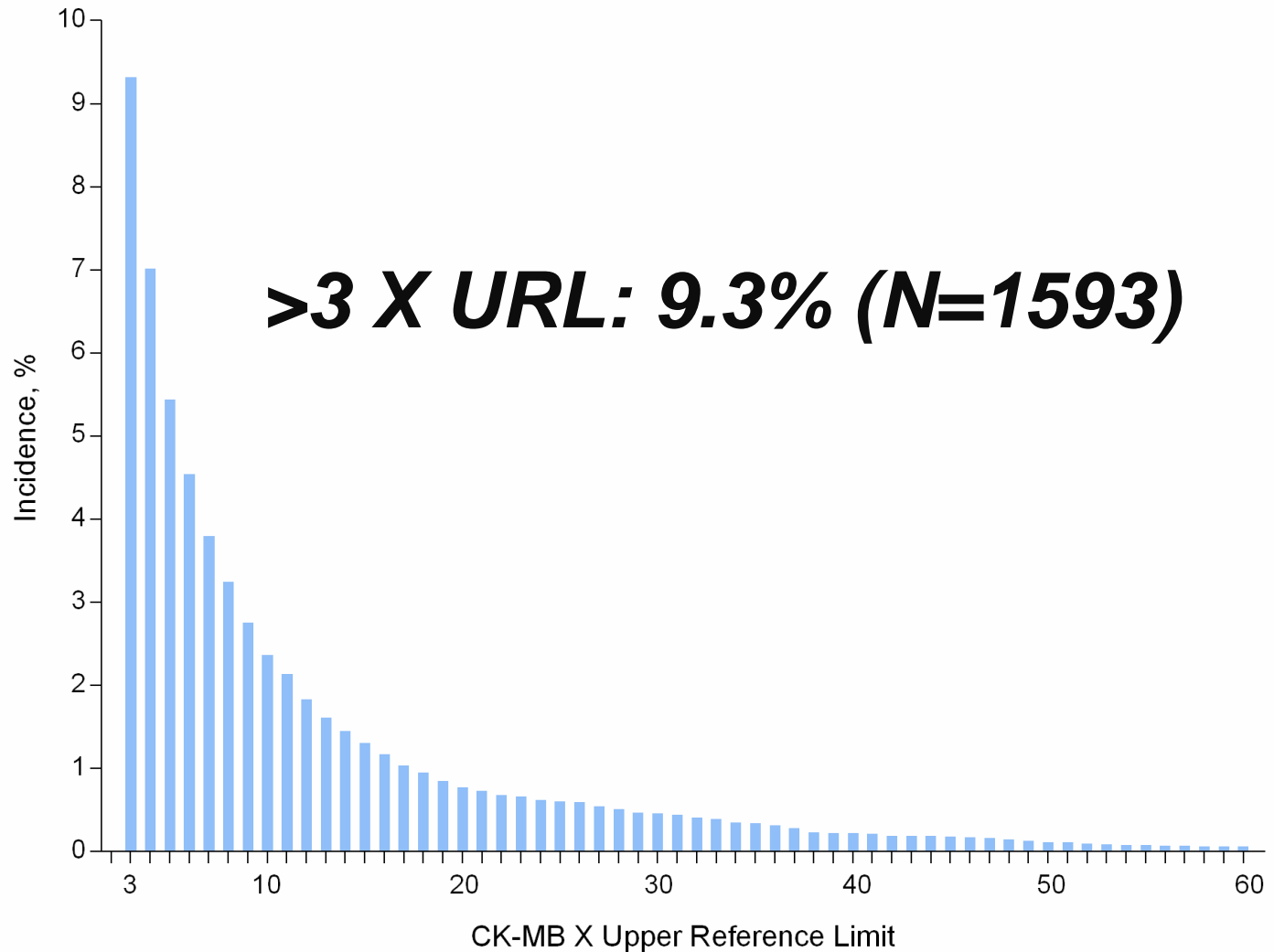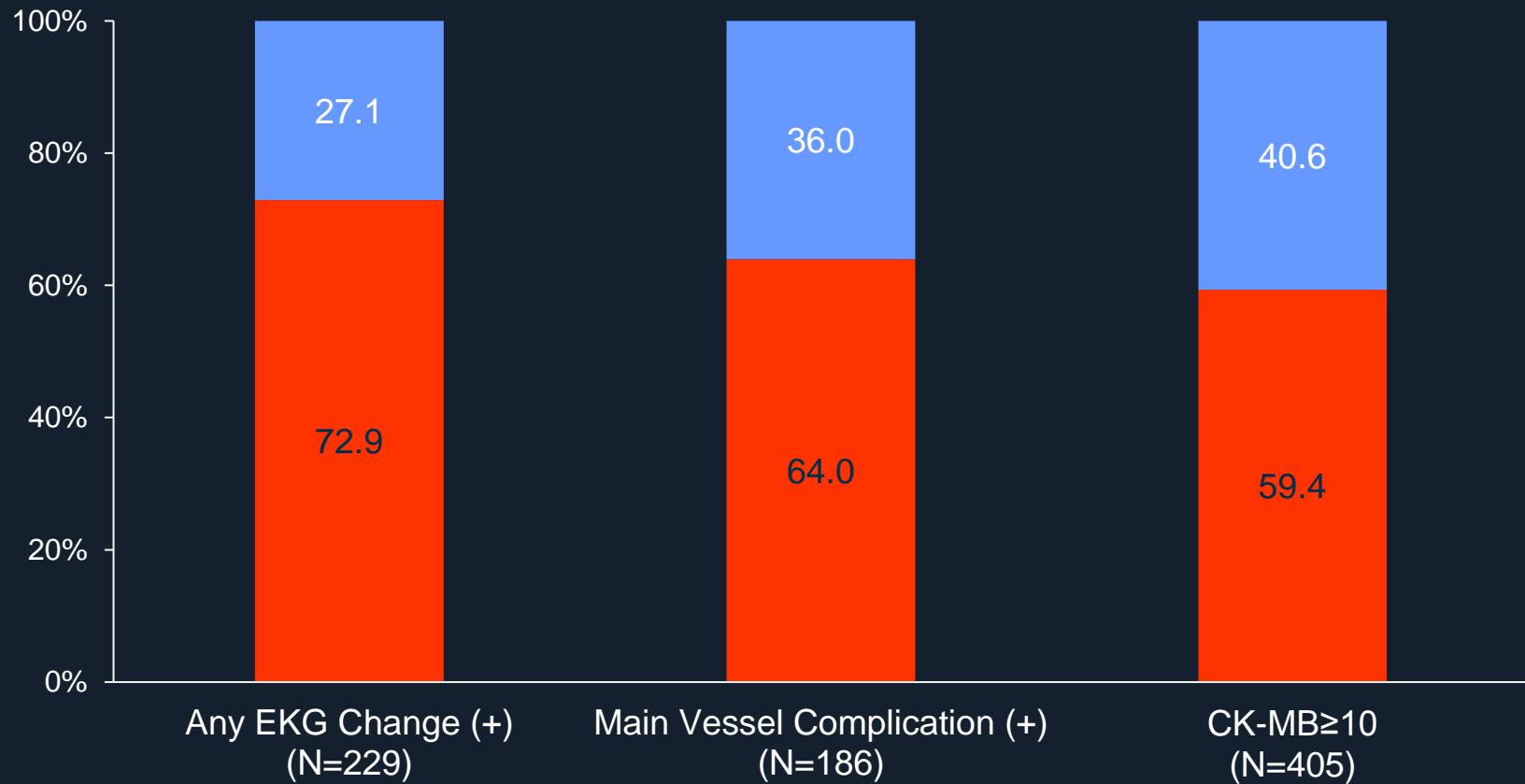


*Chest pain requiring EKG assessment and/or morphine injection

# Any EKG Change

**14.4%**

■ Yes ■ No



| | 3-5 (N=663) | 5-10 (N=526) | 10-20 (N=272) | ≥20 (N=133) |
|---|---|---|---|---|
| No | 93.2 | 85.8 | 81.3 | 56.4 |
| Yes | 6.8 | 14.2 | 18.7 | 43.6 |

CK-BM X URL
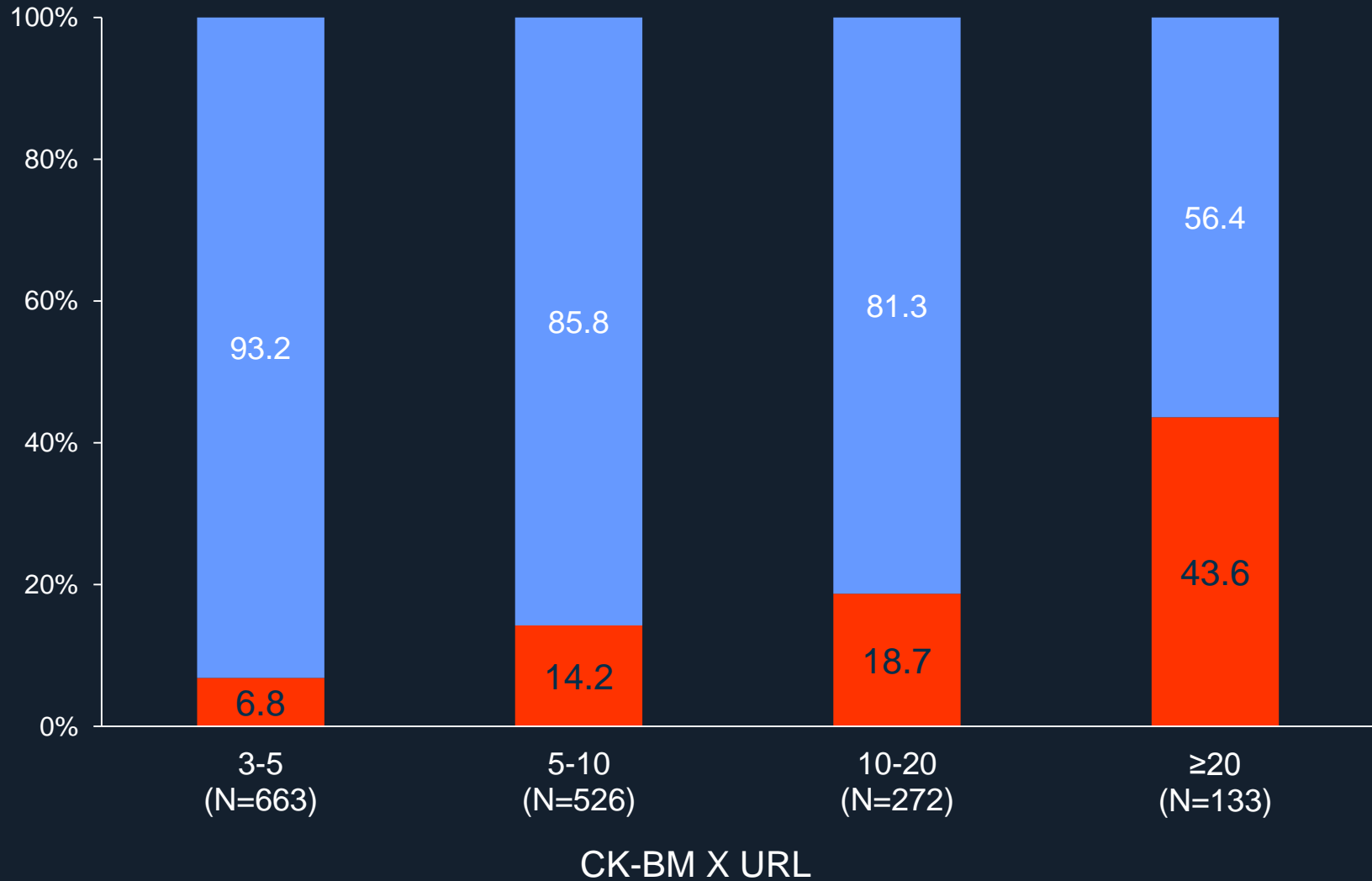
# Angiographic Mechanism

## 70.3%
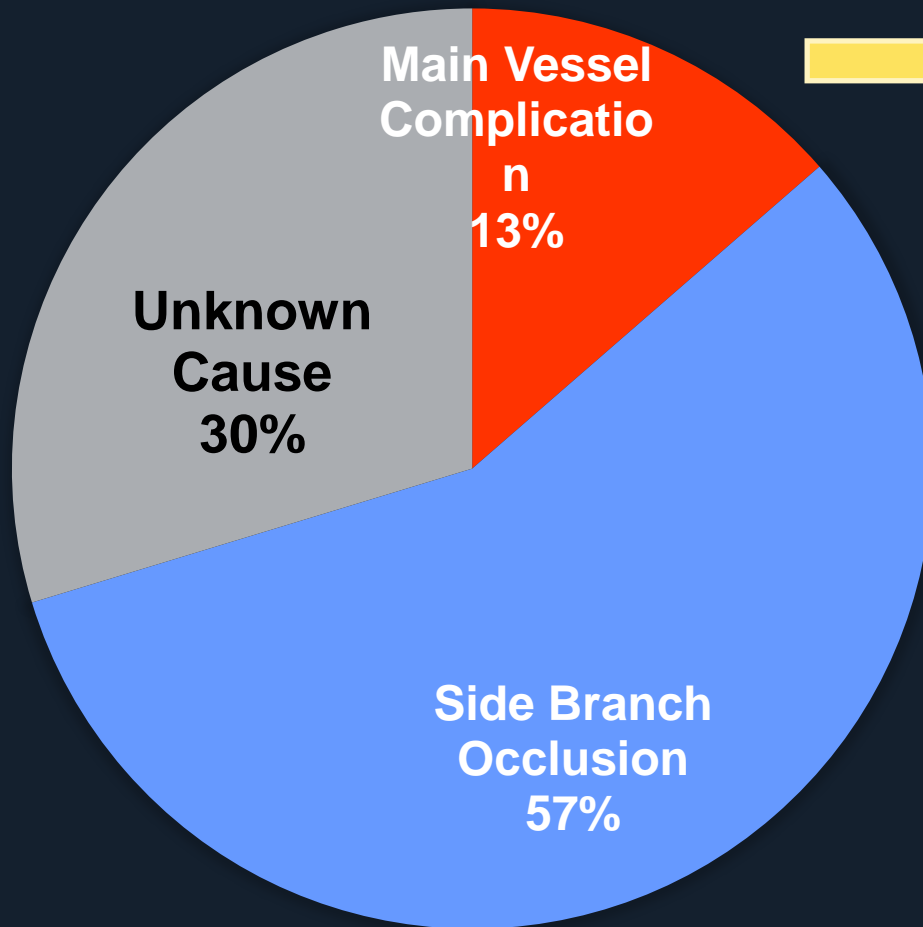


| Main Vessel Cx (Number) |
| --- |
| • Perforation (10) |
| • Distal Embolization (52) |
| • No Reflow (46) |
| • Thrombus (29) |
| • Flow Limiting Dissection (34) |
| • Others (15) |

Pie chart:
- Main Vessel Complication 13%
- Side Branch Occlusion 57%
- Unknown Cause 30%

# Angiographic Mechanism



**70.3%**

Legend: ■ Unknown cause  ■ Side Branch Occlusion  ■ Main Vessel Complication

| CK-BM X URL | Unknown cause | Side Branch Occlusion | Main Vessel Complication |
|---|---|---|---|
| 3-5 (N=562) | 41.5 | 50.7 | 7.8 |
| 5-10 (N=468) | 29.5 | 60.5 | 10.0 |
| 10-20 (N=225) | 13.3 | 67.6 | 19.1 |
| ≥20 (N=112) | 4.5 | 49.1 | 46.4 |
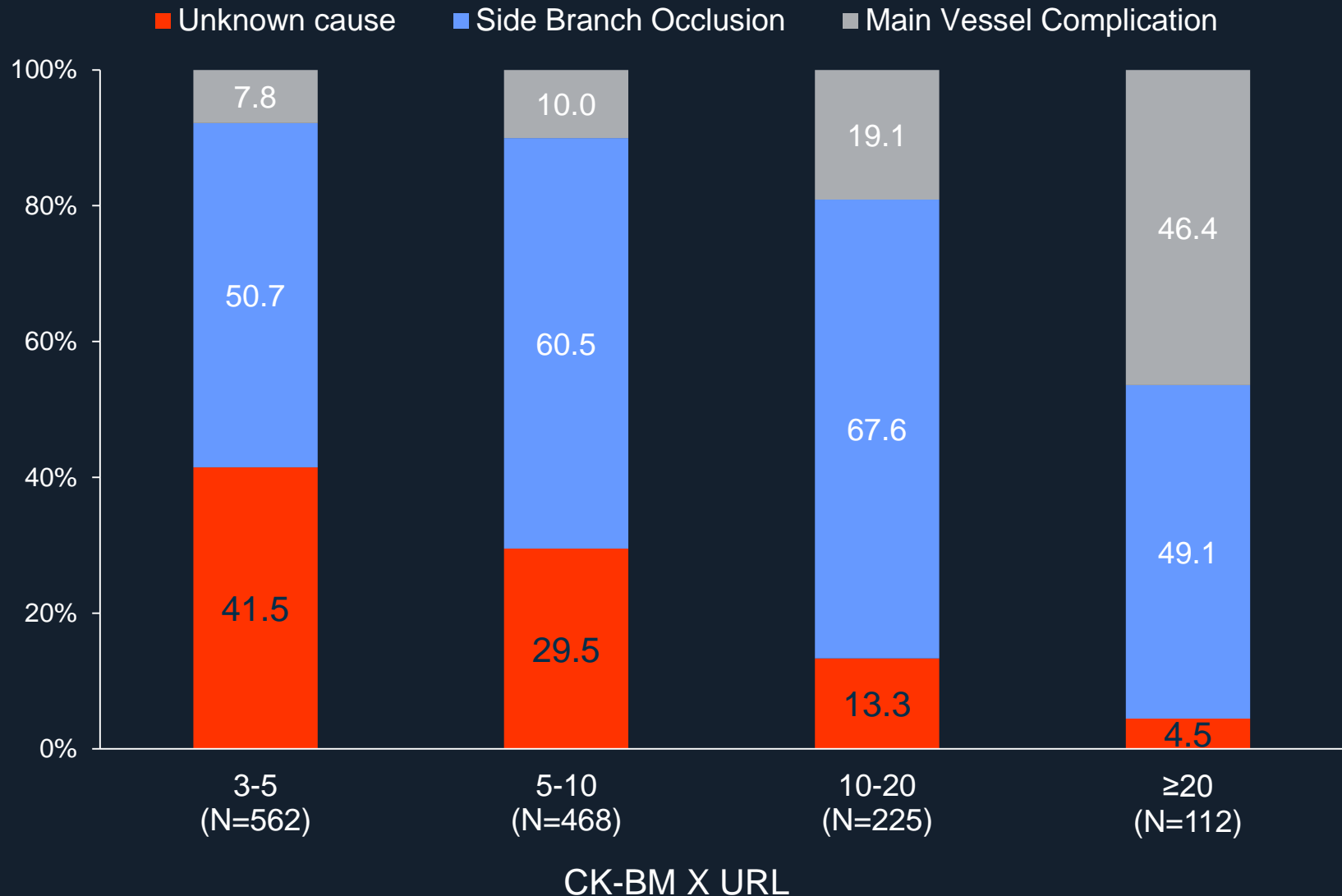
# Long-Term Follow-Up

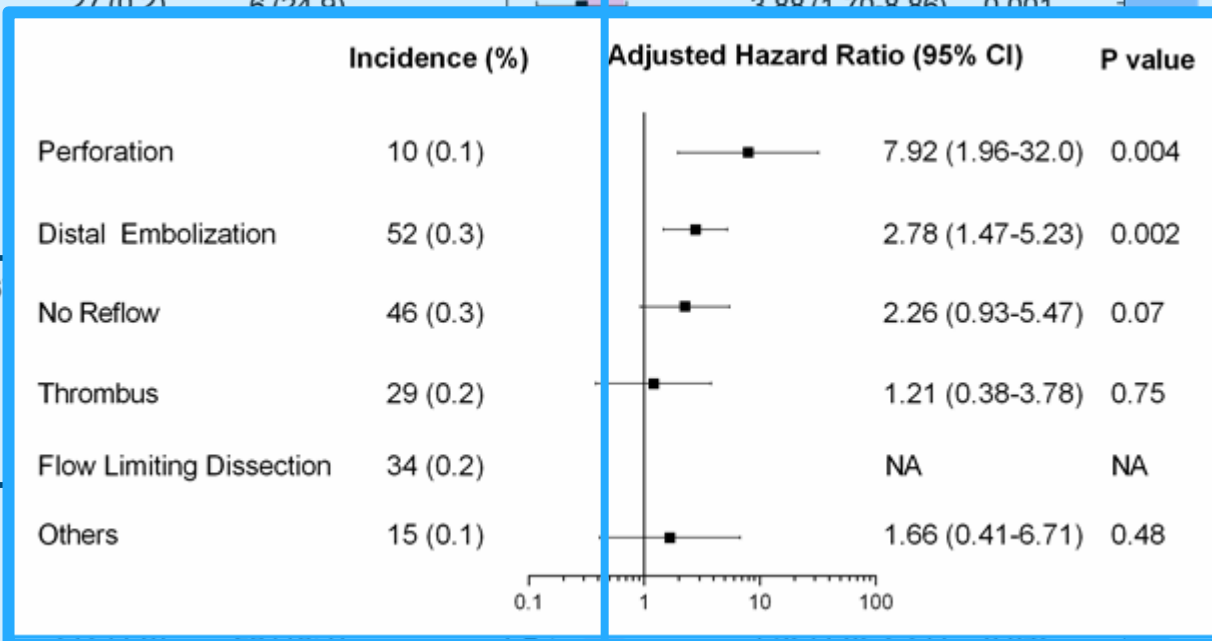- During the median follow up of 4.5 yrs (IQR: 3.2 to 5.2 years), *1167* deaths from any causes occurred.

**Long-Term Risk of Peri-MI and Subgroup**

| | Incidence n/total n (%) | 5 Year Mortality* (%) | Adjusted Hazard Ratio (95% CI) | | P value | Peak CK-MB (X URL) |
|---|---|---|---|---|---|---|
| **Spontaneous myocardial infarction** | 189 (1.1) | 44 (22.3) | | 5.95 (4.24-8.34) | <0.001 | 19.2 |
| **Periprocedural myocardial infarction** | | | | | | |
| CK-MB elevation ≥ 3 X URL | 1594 (9.3) | 126 (9.3) | | 1.18 (0.97-1.43) | 0.096 | 9.4 |
| CK-MB elevation ≥ 3 X URL with | | | | | | |
| Chest pain | 767 (4.5) | 56 (8.3) | | 1.15 (0.87-1.52) | 0.33 | 10.6 |
| Electrocardiographic changes | | | | | | |
| Q wave | 27 (0.2) | 6 (24.9) | | 3.88 (1.70-8.86) | 0.001 | 22.3 |
| Left bundle branch block | | | | | | 14.6 |
| T wave inversion | | | | | | 12.4 |
| ST segment elevation | | | | | | 22.3 |
| ST segment depression | | | | | | 13.1 |
| Angiographic mechanism (N=136...) | | | | | | |
| Major vessel complication† | | | | | | 18.2 |
| Side branch occlusion | | | | | | 9.0 |
| Unknown cause | | | | | | 6.1 |
| Peak CK-MB category | | | | | | |
| ≥ 20 X URL | | | | | | 36.9 |
| 10-20 X URL | | | | | | 13.9 |
| 5-10 X URL | 526 (3.1) | 41 (9.2) | | 1.10 (0.80-1.52) | 0.56 | 7.1 |
| 3-5 X URL | 663 (3.9) | 42 (7.6) | | 0.98 (0.71-1.34) | 0.89 | 3.9 |
| < 3 X URL | 15515 (90.7) | 802 (6.5) | | 1 (reference) | | |

| | Incidence (%) | Adjusted Hazard Ratio (95% CI) | P value |
|---|---|---|---|
| Perforation | 10 (0.1) | 7.92 (1.96-32.0) | 0.004 |
| Distal Embolization | 52 (0.3) | 2.78 (1.47-5.23) | 0.002 |
| No Reflow | 46 (0.3) | 2.26 (0.93-5.47) | 0.07 |
| Thrombus | 29 (0.2) | 1.21 (0.38-3.78) | 0.75 |
| Flow Limiting Dissection | 34 (0.2) | NA | NA |
| Others | 15 (0.1) | 1.66 (0.41-6.71) | 0.48 |

# New Criteria

- $\geq$ CK-MB X 3 URL plus

    Newly developed Q Wave

    Major Vessel Complications


- $\geq$ CK-MB X 10 URL

# Proportion of New Criteria



Cardiac Enzyme ≥10 X URL (N=405)

Q Wave on EKG (N=27)

Major Vessel Complication (N=186)

302 · 8 · 8 · 9 · 86 · 2 · 89
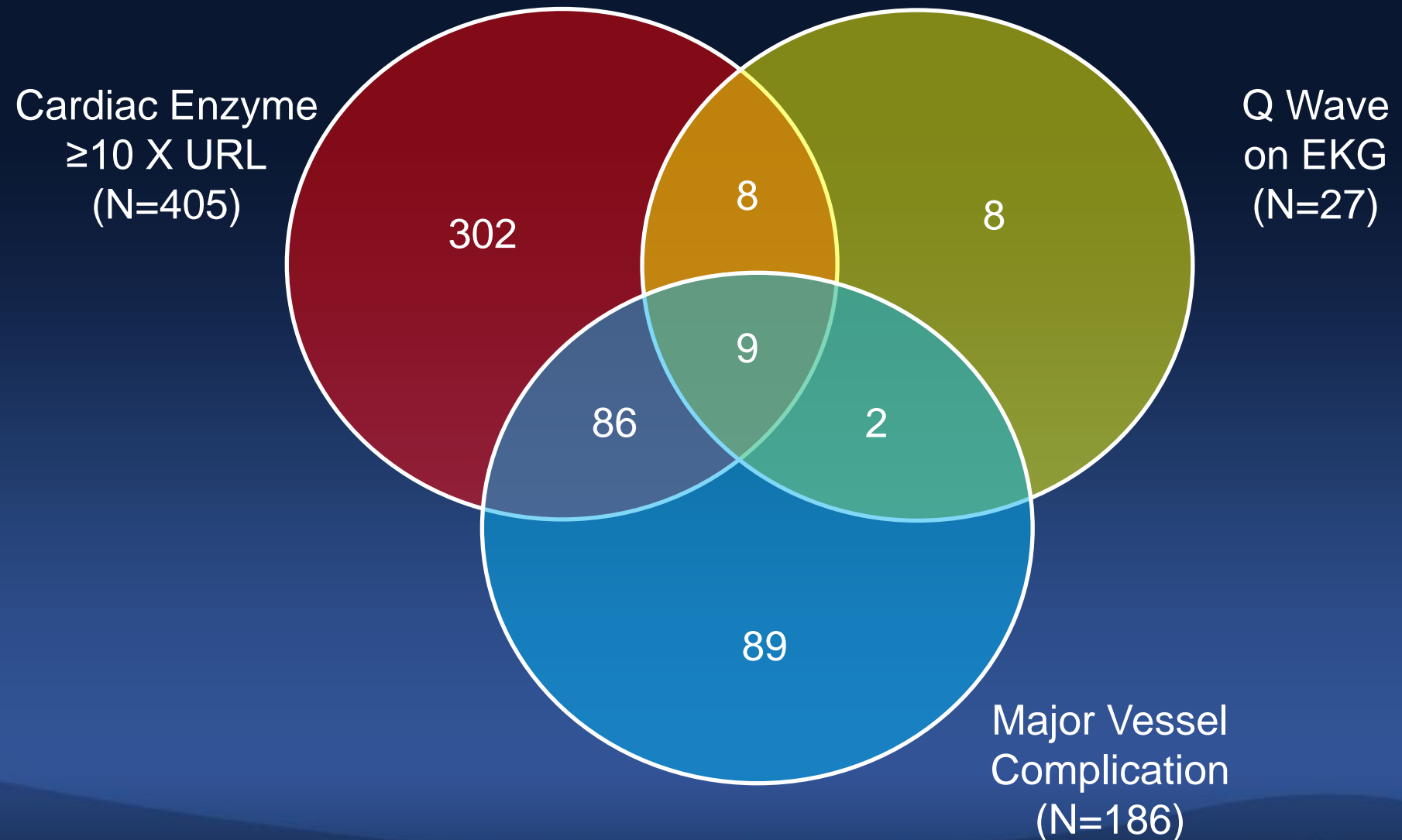
# Long-Term Risk of Mortality

| | % | 5-year Mortality | Adjusted HR | P |
|---|---|---|---|---|
| *Spontaneous MI* | *1.1%* | *22.3%* | *5.95 (4.24-8.34)* | *<0.001* |
| Periprocedural MI | | | | |
| 2nd Universal Definition | 9.3% | 9.3% | 1.18 (0.97-1.43) | 0.098 |
| 3rd Universal Definition | 4.2% | 11.5% | 1.48 (1.15-1.89) | 0.002 |
| SCAI consensus document | 2.4% | 12.2% | 1.61 (1.18-2.20) | 0.002 |
| *New Criteria* | *2.9%* | *11.6%* | *1.61 (1.20-2.14)* | *0.001* |

# Cardiac Enzyme Threshold
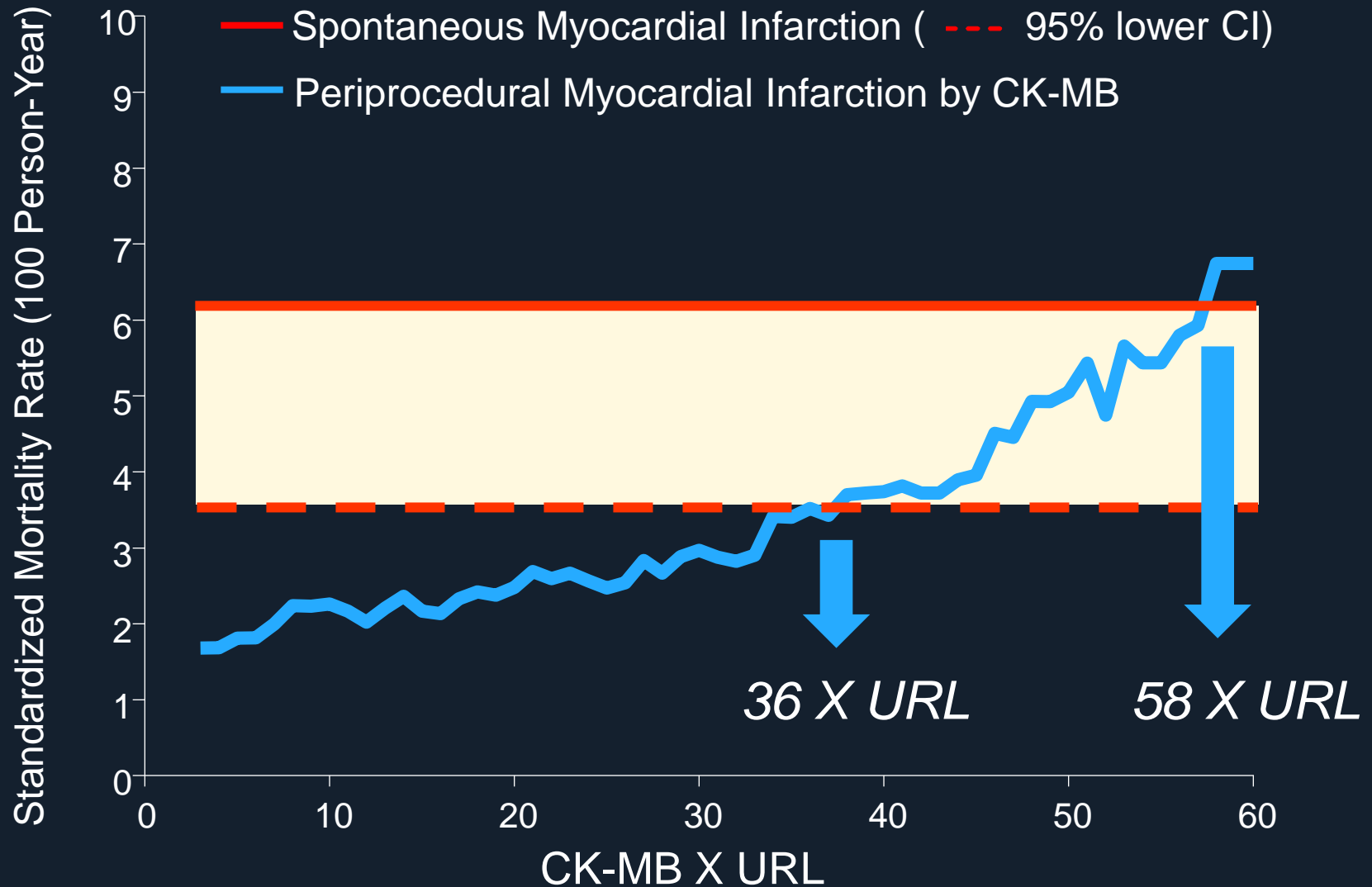
# Summary (1)

- This large, prospective observational study is the first to systematically demonstrate the criteria of clinically relevant periprocedural MI based on cardiac enzyme and supportive clinical features in patients without CK-MB elevation before PCI.

- The criteria of periprocedural MI significantly associated with a higher risk of mortality was newly developed Q wave or main vessel complications with CK-MB elevation ≥3 times the URL or CK-MB elevation >10 times the URL.

# Summary (2)

- Nevertheless, clinically relevant periprocedural MI showed a lower mortality rate compared with spontaneous MI.

- This study provided valuable information for redefining the criteria of clinically relevant periprocedural MI. In addition, the finding of the inequivalent prognostic value between periprocedural MI and spontaneous MI should be considered in daily practice and in appropriate interpretation and design of clinical trials.

Thank you.