# A New Risk Score to Predict Bleeding Events in ST Elevation Myocardial Infarction Patients Underwent Primary Percutaneous Coronary Intervention

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# Background – Bleeding in ACS
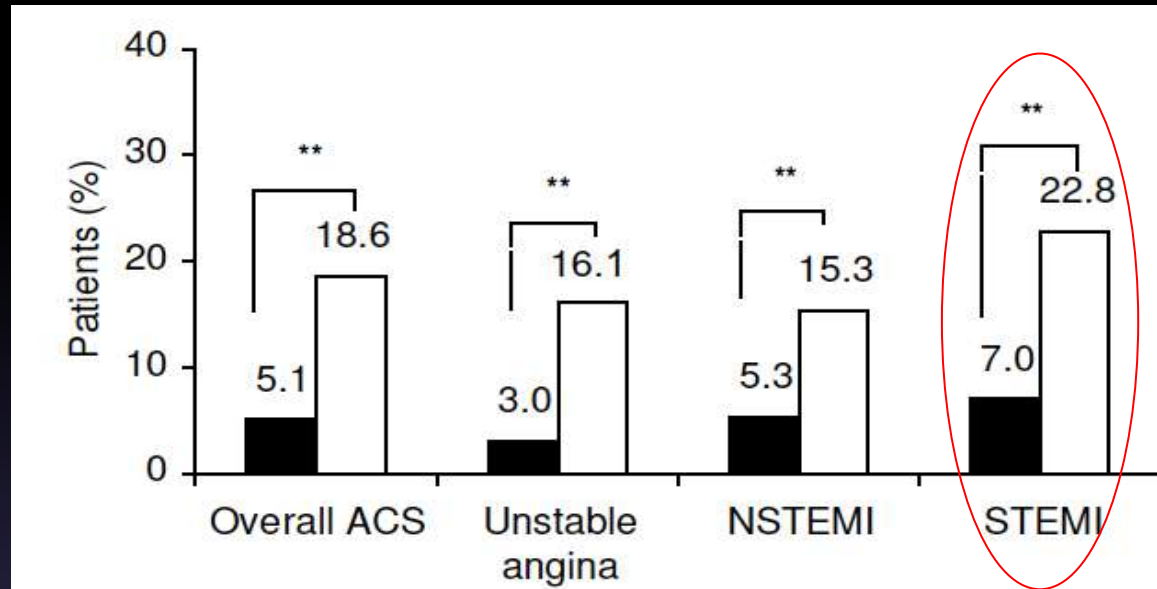


*Moscucci M, et al. Predictors of major bleeding in ACS: GRACE registry. European Heart Journal 2003*

- One of the main complication of ACS Treatment
- Very high mortality compared to ACS without bleeding
- Most frequently found in STEMI patients
- In STEMI yields highest mortality increasement

# Background

Current Available Bleeding Prediction in ACS:
None specialized for STEMI population

| CRUSADE | ACUITY-HORIZON | ACTION-GWTG |
|---|---|---|
| Population: NSTEMI | Population: NSTEMI + STEMI | Population: NSTEMI + STEMI |

**Why Special Bleeding Prediction for STEMI?**
– Most frequent bleeding frequency than other ACS
– Mortality in STEMI with bleeding events is higher than other ACS
– Different Management approach (Primary PCI in for STEMI)

# Aim / Purpose

- To Identify factors associated with bleeding events in STEMI patients underwent Primary PCI

- To make a bleeding prediction system from these identified factors

# Methods

Cohort Retrospective, NCCHK Jakarta, N=579

**Inclusion:**
STEMI ≤ 12 hours, done PPCI

**Exclusion:**
Done or History of Fibrinolytic Therapy

Identified Factors

**Bleeding Definition:**
Inhospital Bleeding
Type 3 BARC Bleeding  (ESC, 2011)

**Model testing: C-Statistic and Diagnostic test**

# Result – Baseline Characteristic

| Variable | |
|---|---|
| Age (years)* | 55.0 (50.0, 61.0) |
| Male | 86.0 % |
| BMI (kg/m²)* | 24.5 (22.9 – 26.9) |
| Diabetes | 41.3% |
| History of CVD / Stroke | 6.0% |
| Creatinin (mg/dL)* | 1.0 (0.9, 1.3) |
| KILLIP Class III or IV | 6.6% |
| Gp2b3a before PCI | 73.1% |
| Femoral Access | 70.3% |
| TPM Implantation | 6.9% |
| Heparin maintenance | 41.3% |
| IABP Support | 3.3% |
| **In-Hospital Events** | |
| Bleeding Events | 7.3% |
| Death | 1.6 % |

*Median (25th, 75th percentile)

579 Samples

42 Bleeding Events

# Multivariable Predictors of Bleeding

| | Variable | p | OR | 95% CI | |
|---|---|---|---|---|---|
| | | | | min | max |
| Demographic & Clinical | Female | 0.015 | 2.71 | 1.31 | 5.55 |
| | Age ≥ 62 y.o | 0.051 | 2.42 | 1.27 | 4.59 |
| | Body Mass Index ≥ 25 | 0.147 | 1.75 | 0.92 | 3.34 |
| | Killip Class III - IV | <0.001 | 9.18 | 4.26 | 19.78 |
| LAB | White Blood Count > 12.000 | 0.066 | 2.68 | 1.29 | 5.57 |
| | Creatinine > 1.5 mg/dL | 0.067 | 3.12 | 1.52 | 6.42 |
| INTER-VENTION | Femoral Access | 0.132 | 3.16 | 1.22 | 8.19 |
| | Multiple Coronary Lesion | 0.017 | 2.46 | 1.15 | 5.24 |
| | TPM Implantation | 0.013 | 6.19 | 2.83 | 13.55 |
| C-Statistic | | 0.84 | | | |

# Scoring Development: Complete Model (Model-1)

| Variable | Score |
|---|---|
| Female | 12 |
| Age ≥ 62 y.o | 8 |
| BMI ≥ 25 | 8 |
| Killip Class III - IV | 25 |
| WBC > 12.000 | 8 |
| Creatinine > 1.5 | 8 |
| Femoral Access | 10 |
| Multiple Coronary Lesion | 8 |
| TPM Implantation | 13 |
| TOTAL | 100 |

**94%**

Probability of Having Bleeding Events

Bleeding Risk Category (Total Score)

Low (0-39)  Moderate (40-61)  High (62-77)  Very High (78-100)
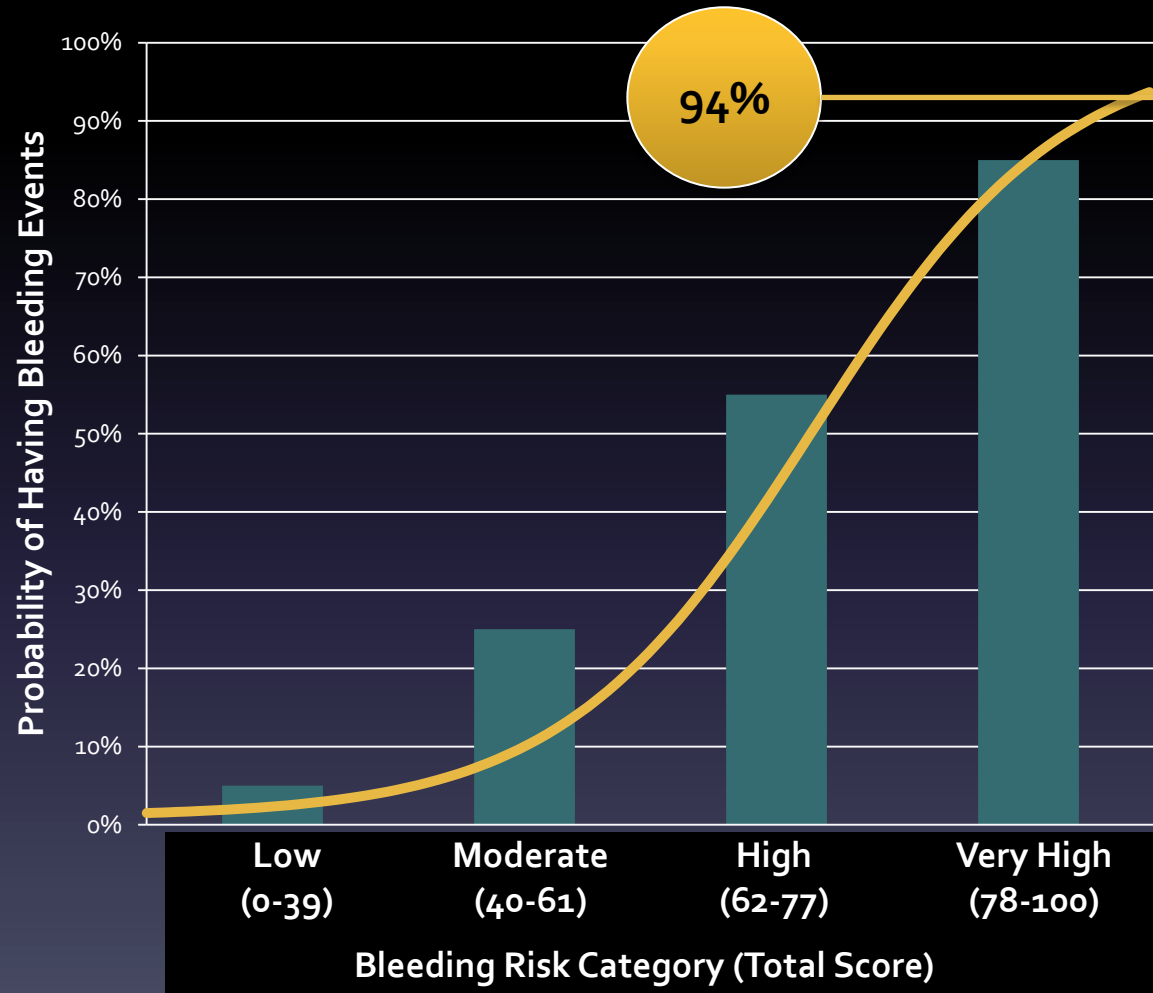
$y = -5.318 + (0.080 \times Total\ Score)$

$p = 1 / ( 1 + exp (-y) )$

# Statistical Analysis for Model-1

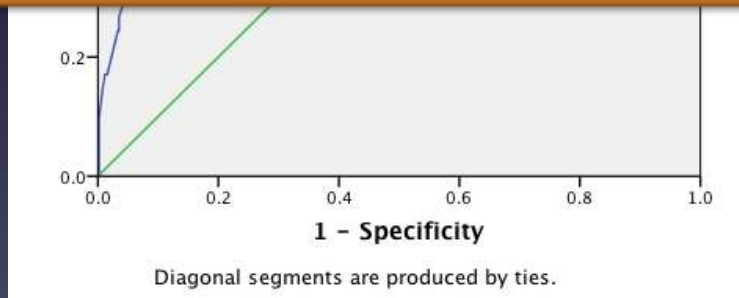| Step | Chi-square | df | Sig. |
|------|------------|-----|------|
| 1 | 8.596 | 7 | .283 |

Hosmer and Lomeshow test: P > 0.05 → Good calibration

## C-Statistic 0.84

## Negative Predictive Value 93.4%

## False Negative Rate 6.62%

## (Good to Rule Out Disease)



| Specificity | Pr( −\|~D) | 99.22% |
|-------------|-----------|--------|
| Positive predictive value | Pr( D\| +) | 55.56% |
| Negative predictive value | Pr(~D\| −) | 93.38% |
| | | |
| False + rate for true ~D | Pr( +\|~D) | 0.78% |
| False − rate for true D | Pr( −\| D) | 87.80% |
| False + rate for classified + | Pr(~D\| +) | 44.44% |
| False − rate for classified − | Pr( D\| −) | 6.62% |

C-Statistic 0.84 → Good discrimination      Good NPV and low False Negative Rate
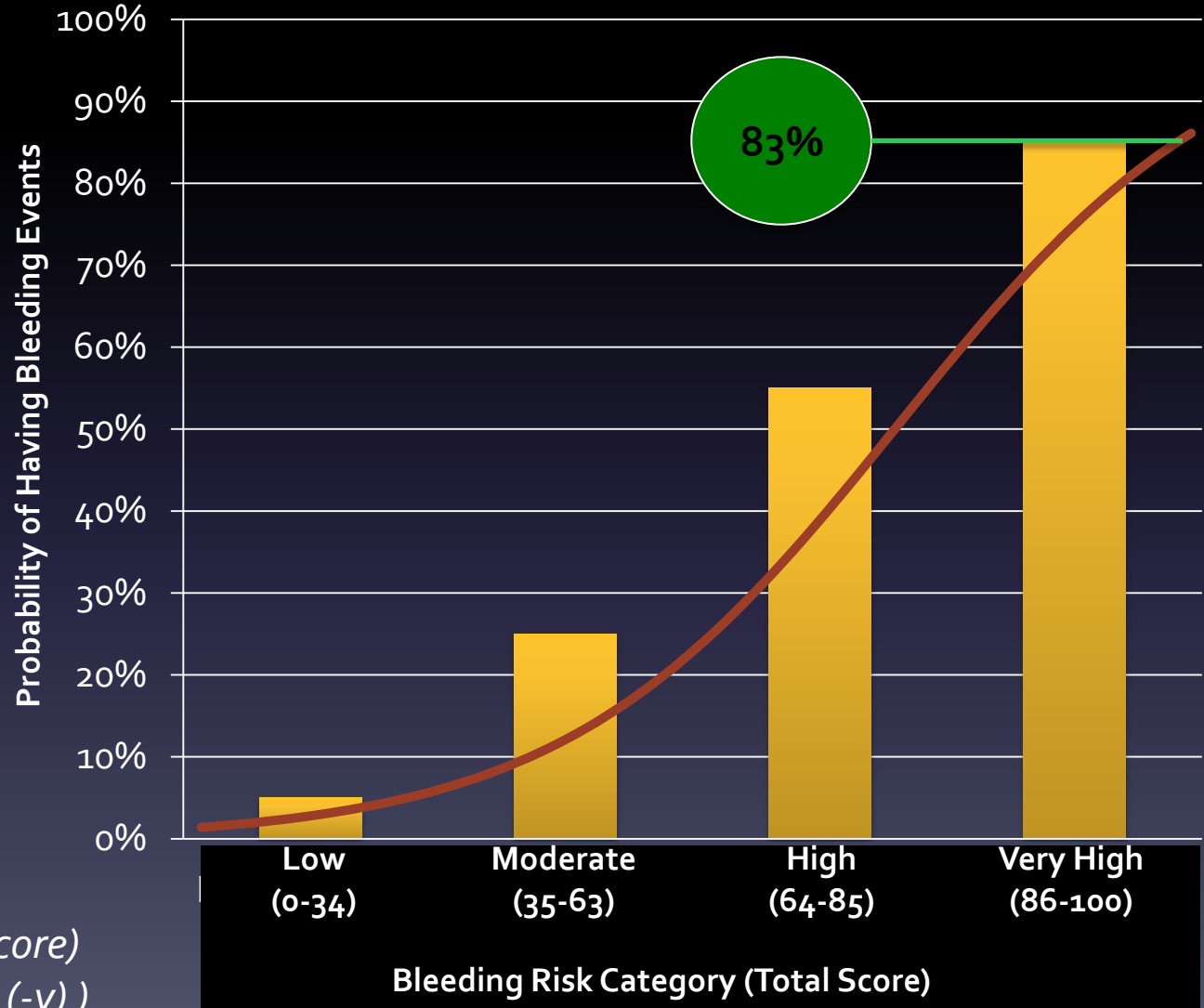
# Multivariable Predictors of Bleeding: Eliminates Interventional-related Variables

| | Variable | p | OR | 95% CI | |
|---|---|---|---|---|---|
| | | | | min | max |
| **Demographic & Clinical** | Female | 0.013 | 2.87 | 1.25 | 6.58 |
| | Age ≥ 62 y.o | 0.013 | 2.60 | 1.22 | 5.55 |
| | BMI ≥ 25 | 0.060 | 1.96 | 0.97 | 3.96 |
| | Killip Class III - IV | <0.001 | 7.74 | 3.24 | 18.49 |
| **LAB** | WBC > 12.000 | 0.033 | 2.34 | 1.07 | 5.11 |
| | Creatinine > 1.5 | 0.025 | 2.51 | 1.12 | 5.60 |
| | *C-Statistic* | *0.82* | | | |

## For Risk Stratification before Primary PCI

# Scoring Development: Alternative Model (Model-2)

| Variable | Score |
|---|---|
| Female | 14 |
| Age ≥ 62 y.o | 12 |
| BMI ≥ 25 | 10 |
| Killip Class III - IV | 40 |
| WBC > 12.000 | 12 |
| Creatinine > 1.5 | 12 |
| TOTAL | 100 |

83%

Probability of Having Bleeding Events

100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%

| Low (0-34) | Moderate (35-63) | High (64-85) | Very High (86-100) |

Bleeding Risk Category (Total Score)

$y = -4.512 + (0.059 \times total\ score)$

$p = 1 / (1 + exp(-y))$

# Statistical Analysis for Model 2

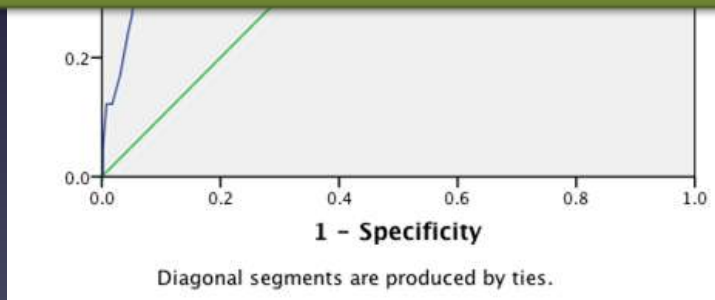| Step | Chi-square | df | Sig. |
|------|-----------|-----|------|
| 1 | 9.329 | 6 | .156 |

Hosmer and Lomeshow test: P > 0.05 → Good calibration

## C-Statistic 0.82

## Negative Predictive Value 93.4%

## False Negative Rate 6.56%

## (Good to Rule Out Disease)



```
                                    Specificity              Pr( -|~D)    99.23%
0.2-                                Positive predictive value Pr( D| +)   55.56%
                                    Negative predictive value Pr(~D| -)   93.44%
                                    -----------------------------------------------
                                    False + rate for true ~D  Pr( +|~D)    0.77%
0.0-                                False - rate for true D   Pr( -| D)   87.80%
   0.0  0.2  0.4  0.6  0.8  1.0     False + rate for classified + Pr(~D| +) 44.44%
          1 - Specificity           False - rate for classified - Pr( D| -)  6.56%
```

Diagonal segments are produced by ties.

C-Statistic 0.82 → Good discrimination          Good NPV and low False Negative Rate

# Discussion – Comparison with Previous Study

| | CRUSADE (2009) | ACUITY-HORIZONS (2010) | ACTION-GWTG (2011) | New Score (2013) |
|---|---|---|---|---|
| ACS Population | NSTEMI | NSTEMI STEMI | NSTEMI STEMI | STEMI |
| Variable | Female Diabetic Creatinin clearance Vascular Disease Hematocrit <36% Heart Failure Heart Rate Systolic < 110 mmHg Diastolic > 180 mmHg | Female Age Creatinin Leucocyte Anemia Clinical appearance Antithrombotic | Female Age Weight Warfarin Diabetic Vascular Disease Hemoglobin Creatinin Heart Failure/Shock Heart Rate Systolic BP ECG Changes | Female Age BMI Killip Class Creatinin Leucocyte Femoral Access Multipel Coronary Lesion Temporary Pacemaker |
| C-statistic | 0.71 | 0.74 | 0.73 | 0.84 (Model 1) 0.82 (Model 2) |

Better C-Statistic value → 	* Interventional factors inclusion
	* STEMI population only

# Summary

- Retrospective cohort study to identify factors related to in-hospital bleeding events in STEMI underwent PPCI

- 9 variables found related to bleeding events

- 2 models of scoring systems developed:

  - Complete model (Model-1) contains all variables

  - Alternative model (Model-2) eliminates interventional-related variables for early bleeding stratification

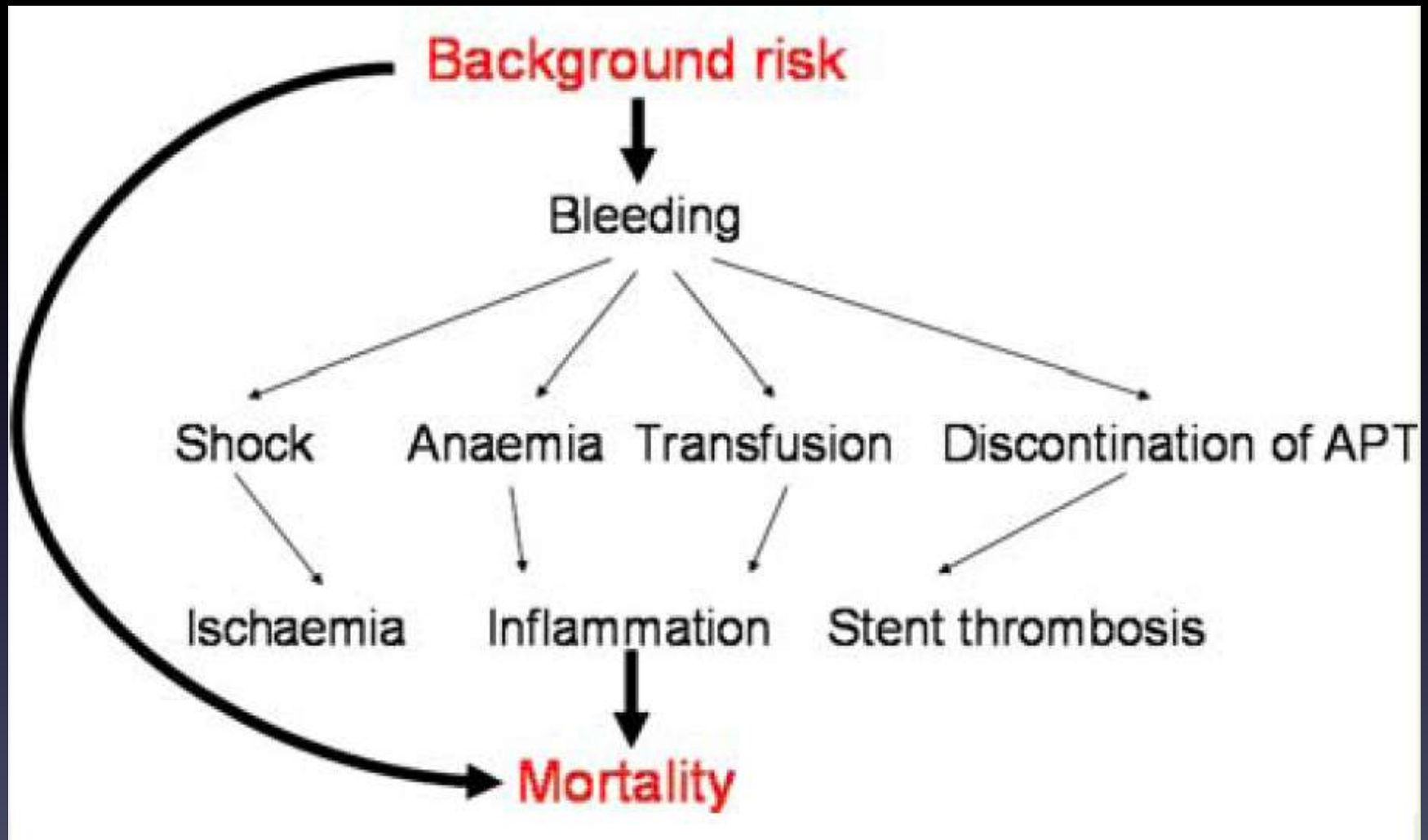- Both models performed well in testing and hopefully can help to elevate STEMI Care

# Limitations & Future Directions

- Restrospective Study

- Has not been validated (ongoing)

- Relatively small samples compared to previous studies

- Lack of study regarding this issue – Need more researches

**THANK YOU**

# WHY INCREASED MORTALITY?

**Intracranial bleeding**

**Blood transfusion**
↓O₂ delivery
Prothrombotic?
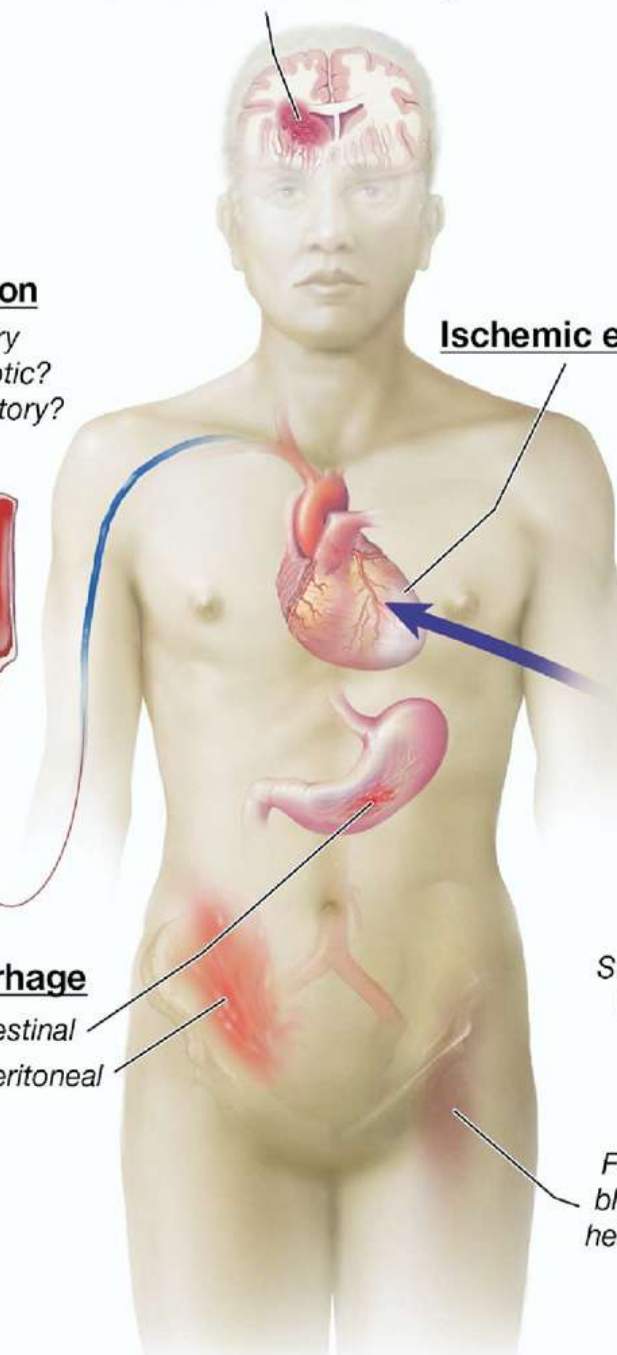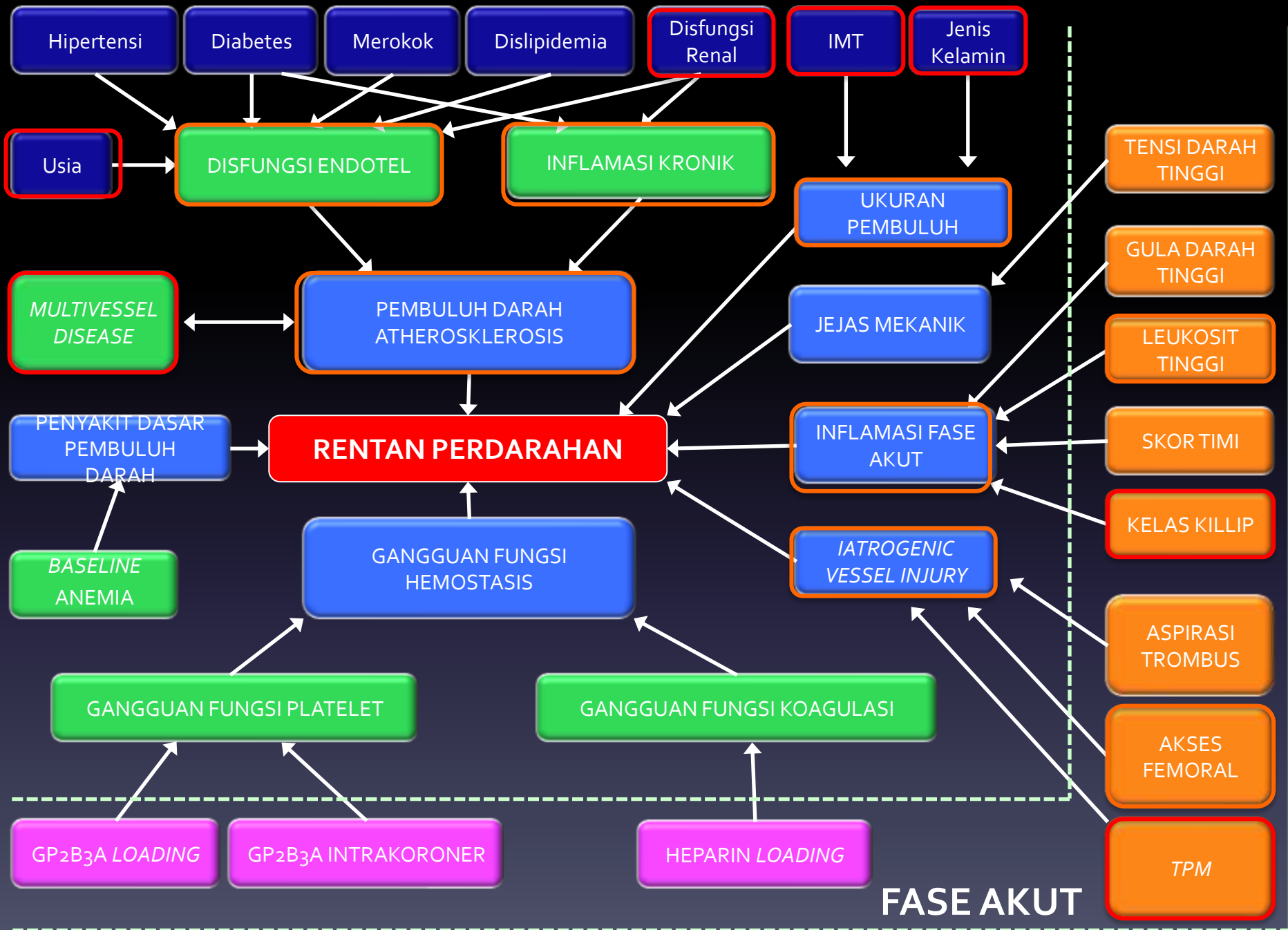Proinflammatory?

**Ischemic events**

Stent
thrombosis

**Severe hemorrhage**
Gastrointestinal
Retroperitoneal

Stop antiplatelet therapy
Prothrombotic state?

Femoral
bleeding,
hematoma
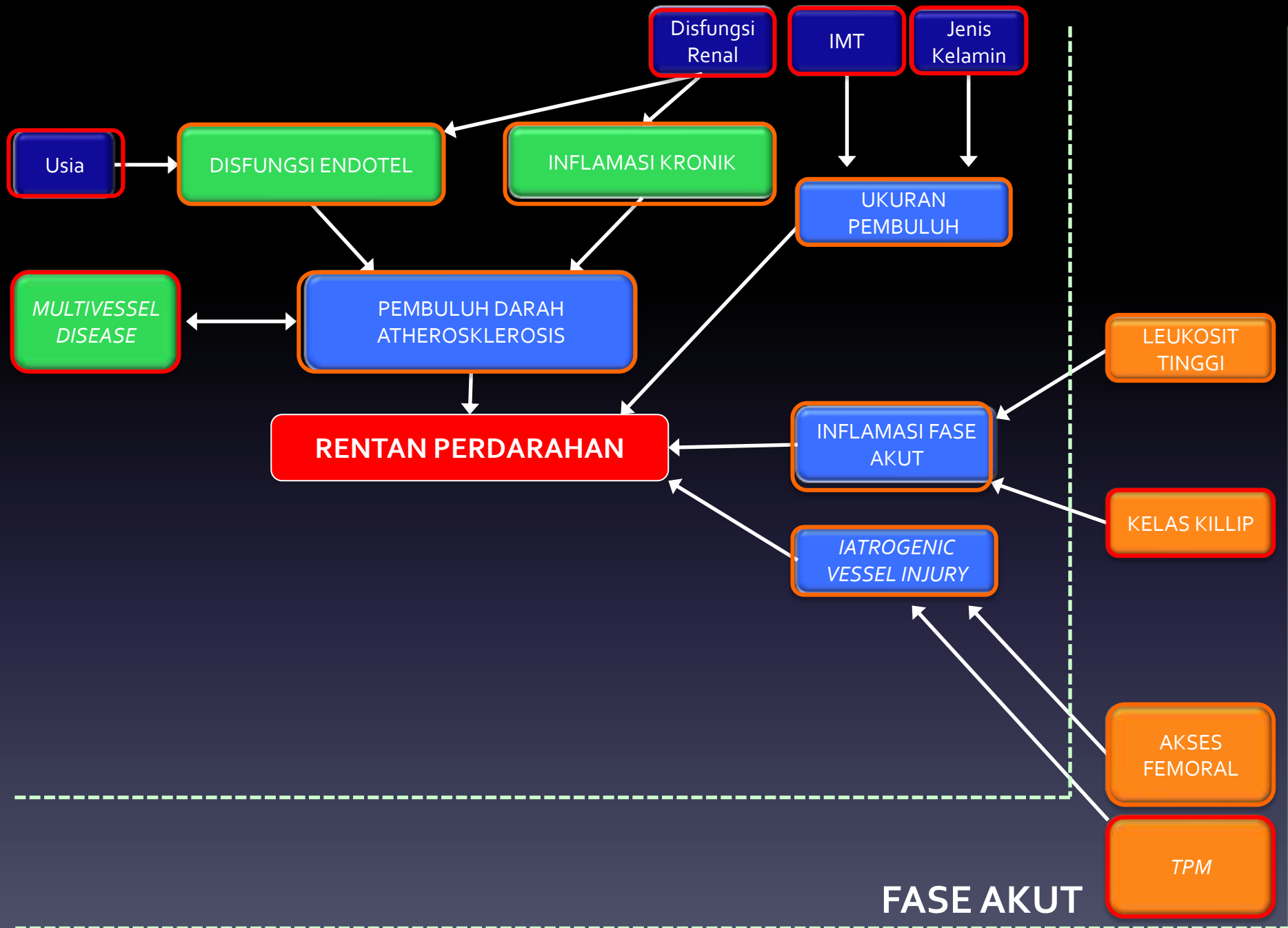
# Bleeding Definition

* Inhospital Bleeding

* BARC Bleeding definition (ESC, 2011)

*Type 3a:*     - Overt bleeding plus hemoglobin drop of 3 to <5 g/dL
                 - Any transfusion with overt bleeding

*Type 3b:*     - Overt bleeding plus hemoglobin drop ≥5 g/dL
                 - Cardiac tamponade
                 - Bleeding requiring surgical intervention
                 - Bleeding requiring IV vasoactive agents

*Type 3c*:     - Intracranial hemorrhage
                 - Subcategories confirmed by autopsy or imaging or lumbar puncture.
                 - Intraocular bleed compromising vision.

Not included: Bleeding related to operation (CABG)

No. _____ | Bleeding: Ya / Tidak | Jenis Perdarahan: _____

# Formulir Penelitian Prediktor Kejadian Perdarahan Pada Pasien Infark Miokard Akut Dengan ST Elevasi Yang Dilakukan Intervensi Perkutan Primer

Stiker Pasien

Nama : _____     Tanggal Lahir : ___/___/_____     No. Telfon : _____
No. Rekam Medis : _____     Pasien Baru : 0. Tidak     1. Ya

Gender : 0. Perempuan     1. Laki-laki     Usia : _____tahun     Etnis : _____

Tanggal Admission : ___/___/_____     Jam ___:___     Tanggal Keluar : ___/___/_____     Lama Rawat : ____ hari

## Faktor Risiko

| | | | |
|---|---|---|---|
| Diabetes Mellitus | 0. Tidak | 1. Ya | |
| Hipertensi | 0. Tidak | 1. Ya | |
| Merokok | 0. Tidak | 1. Ya | |
| Dislipidemia | 0. Tidak | 1. Ya | |
| Riwayat Keluarga | 0. Tidak | 1. Ya | |
| Menopause | 0. Tidak | 1. Ya | |

**Riwayat Pengobatan Rutin (≥7 hari terakhir)**
Antiplatelet     0. Tidak     1. Ya
Antikoagulan     0. Tidak     1. Ya

## Riwayat Penyakit

| | | |
|---|---|---|
| Asma | 0.Tidak | 1.Ya |
| Riwayat Stroke | 0.Tidak | 1.Ya |
| Jenis    1. Iskemik    2. Hemoragik | | |
| Gastritis | 0.Tidak | 1.Ya |
| Heart Failure | 0.Tidak | 1.Ya |
| Riwayat CKD | 0.Tidak | 1.Ya |
| Riwayat CAD | 0.Tidak | 1.Ya |
| Riwayat PCI | 0.Tidak | 1.Ya |
| Riwayat CABG | 0.Tidak | 1.Ya |
| Riwayat MI | 0.Tidak | 1.Ya |
| Riwayat PAD | 0.Tidak | 1.Ya |
| Riwayat Perdarahan | 0.Tidak | 1.Ya |

## Saat masuk UGD

Tekanan Darah : _____/_____ mmHg          Heart Rate : _____ bpm
Jenis Irama    1. Sinus    2. TAVB    3. _____     Roentgen : CTR >58%    0. Tidak    1. Ya

## Lab Saat Masuk

| | | | | | | |
|---|---|---|---|---|---|---|
| Hb | :_____ | Ur | :_____ | | | |
| Ht | :_____ | Cr | :_____ | | | |
| Leu | :_____ | GDS | :_____ | | | |
| Trop T / Hs: _____ | | Trombo: _____ | | | | |
| LED | :_____ | CRP | :_____ | | | |

## Lab Selama Perawatan

| | | | |
|---|---|---|---|
| Hb terendah : _____ | | Chol Tot : _____ | |
| Ht terendah : _____ | | HDL : _____ | |
| OGTT | : _____ / _____ | LDL : _____ | |
| HbA1c | : _____ | Trig : _____ | |
| | | Chol Rat : _____ | |

Lokasi STEMI     : 1. Anterior     2. Posterior     3. Lateral     4. Inferior     5. RV
6. Anteroseptal     7. InferoPosterior     8. Inferior RV     9. AnteroLateral
10. AnteriorExtensive     11. _____

Onset STEMI _____ Jam          TIMI : _____/14          Killip : _____
Diagnosa tambahan     1. _____     2. _____     3. _____

| | | | | | |
|---|---|---|---|---|---|
| Loading dose Aspilet | 0. Tidak | 1. Ya | Dosis: _____ mg |
| Loading dose Clopidogrel | 0. Tidak | 1. Ya | Dosis: _____ mg |
| Loading dose Ticagrelor | 0. Tidak | 1. Ya | Dosis: _____ mg |
| Gp2b3a di EMG | 0. Tidak | 1. Ya | |

Terjadi VT pulseless/VF     0. Tidak     1. Ya          DC Shock / Kardioversi     0. Tidak     1. Ya

## Tindakan di Cath Lab

Jenis Tindakan     1. PCI     2. POBA saja     3. None
Jenis Stent     1. DES     2. BMS     3. Mixed     4. None
     Jumlah Stent : _____ buah
Culprit Lesion : 1. LM     2. LAD     3. LCx     4.RCA     5. Intermediate
Vessel Diseased : 1. Single     2. Multi

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Berat Badan : _____ kg          Tinggi Badan : _____ cm          IMT : _____

| | | | | | |
|---|---|---|---|---|---|
| Puncture Site | 1. Radial | 2.Femoral | 3. Brachial | Pemasangan TPM     0. Tidak     1. Ya | |
| Pindah Puncture Site | 0. Tidak | 1. Ya | | Door to Device time : _____ menit | |
| Aspirasi Thrombus | 0. Tidak | 1. Ya | | Total Heparin : _____ unit | |
| Bolus Gp2b3a di cathlab | 0. Tidak | 1. Ya | | Intracoroner Gp2b3a     0. Tidak     1. Ya | |
| Terjadi VT pulseless/VF | 0. Tidak | 1. Ya | | DC Shock / Kardioversi     0. Tidak     1. Ya | |

## Selama Perawatan

| | | | | |
|---|---|---|---|---|
| Maintenance Aspirin | 0. Tidak | 1. Ya | Support IABP     0. Tidak     1. Ya | |
| Maintenance Clopi | 0. Tidak | 1. Ya | Support Ventilator     0. Tidak     1. Ya | |
| Maintenance Tica | 0. Tidak | 1. Ya | Support CVVH     0. Tidak     1. Ya | |
| Heparinisasi post PPCI | 0. Tidak | 1. Ya | Lain-lain : _____ | |
| Jenis    1. UFH    2. Enoxaparin    3. Fondaparinux | | | | |
| Maintenance GP2b3a | 0. Tidak | 1. Ya | | |
| Antikoagulan oral | 0. Tidak | 1. Ya | | |

**Echo Post Primary**

Terjadi VT pulseless /VF 0. Tidak     1. Ya
DC Shock / Kardioversi  0. Tidak     1. Ya

Penyulit selama perawatan:
     1. _____
     2. _____

Tanggal : ___/___/___
EDD : _____ mm
ESD : _____ mm
EF : _____ %
TAPSE : _____ cm
Lain-lain: _____

## Perdarahan Selama Perawatan

Terjadi Perdarahan     (Any bleeding)     0. Tidak     1. Ya     Tanggal : ___/___/_____
Gangguan Hemodinamik (Life Threatening)     0. Tidak     1. Ya
Jenis Perdarahan :

| | | |
|---|---|---|
| Stroke Hemoragik | 0. Tidak | 1. Ya |
| Hematuria | 0. Tidak | 1. Ya |
|     Gross | 0. Tidak | 1. Ya |
| Hematemesis | 0. Tidak | 1. Ya |
| Melena | 0. Tidak | 1. Ya |
| Perdarahan retroperitoneal | 0. Tidak | 1. Ya |
| Cardiac Tamponade | 0. Tidak | 1. Ya |
| Hematom puncture site | 0. Tidak | 1. Ya |
|     Ukuran Hematom | 1. <5cm | 2. >=5cm |

Perdarahan Minimal (Epistaksis/mild hematuria)     0. Tidak     1. Ya

Transfusi :     0. Tidak     1. Ya
     Jenis Transfusi :     1. PRC     2. FFP     3. Trombosit     4. Whole Blood     5. Cryo

| | | |
|---|---|---|
| Tindakan bedah untuk kontrol perdarahan | 0. Tidak | 1. Ya |
| Obat vasoaktif untuk kontrol perdarahan | 0. Tidak | 1. Ya |
| Stop antiplatelet karena perdarahan | 0. Tidak | 1. Ya |
| Stop antikoagulan karena perdarahan | 0. Tidak | 1. Ya |

Bleed Score     : ___ S + ___ I + ___ A = _____ (Pooled)

| | | |
|---|---|---|
| S (Superficial) | : Lebam (kebiruan), perdarahan dari luka kecil, petechia, ecchymosis | (1 poin per kejadian) |
| I (Internal) | : Hematom, epistaksis, perdarahan dari mulut, vagina, melena, perdarahan daerah mata, hematuria, hematemesis | (3 poin per kejadian) |
| A (Alarming) | : Butuh transfusi, perdarahan intrakranial, mengancam jiwa | (6 poin per kejadian) |

# No Standard Bleeding Definition : Problem for Inter-Study Analysis

| Classification | Severity | Criteria |
|---|---|---|
| TIMI | Major | Intracranial bleeding. Overt bleeding with a decrease in haemoglobin $\geq 5$ g/dL or decrease in haematocrit $\geq 15\%$ |
| | Minor | Spontaneous gross haematuria. Spontaneous haematemesis. Observed bleeding with decrease in haemoglobin $\geq 3$ g/dL but haematocrit $\leq 15\%$ |
| | Insignificant | Blood loss insufficient to meet criteria listed above |
| GUSTO | Severe | Deadly bleeding. Intracerebral bleeding or substantial haemodynamic compromise requiring treatment |
| | Moderate | Bleeding requiring transfusion |
| | Mild | Other bleeding not requiring transfusion or causing haemodynamic compromise |
| ACUITY | Major | Intracranial or intraocular bleeding, haemorrhage at the access site requiring intervention, haematoma with a diameter of at least 5 cm, a reduction in haemoglobin levels of at least 4 g/dL without an overt bleeding source or at least 3 g/dL with such a source, reoperation for bleeding, or transfusion of a blood product |
| PLATO | Major life-threatening bleeding | Fatal bleeding, intracranial bleeding, intrapericardial bleeding with cardiac tamponade, hypovolemic shock or severe hypotension due to bleeding and requiring pressors or surgery, a decline in haemoglobin level of 5.0 g per deciliter or more, or the need for transfusion of at least 4 units of red cells |
| | Other major | Bleeding that led to clinically significant disability (e.g. intraocular bleeding with permanent vision loss) or bleeding either associated with a drop in the haemoglobin level of at least 3.0 g per deciliter but less than 5.0 g per deciliter or requiring transfusion of 2 to 3 units of red cells |
| | Minor | Any bleeding requiring medical intervention but not meeting the criteria for major bleeding |
| GRACE | Severe | Bleeding requiring transfusion of $\geq 2$ units of packed red blood cells; bleeding resulting in a $\geq 10\%$ decrease in haematocrit or death; or intracranial/subdural bleeding |
| STEEPLE | Major | Fatal bleeding; retroperitoneal, intracranial, or intraocular bleeding; bleeding that causes haemodynamic compromise requiring specific treatment; bleeding that requires intervention (surgical or endoscopic) or decompression of a closed space to stop or control the event; clinically overt bleeding, requiring any transfusion of $\geq 1$ unit of packed red cells or whole blood; clinically overt bleeding, causing a decrease in haemoglobin of $\geq 3$ g/dL (or, if haemoglobin level not available, a decrease in haematocrit of $\geq 10\%$) |
| ISTH | Major | Fatal bleeding or symptomatic bleeding in a critical area or organ (e.g. intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, pericardial, or intramuscular), or a bleeding causing haemoglobin decrease of $> 2$ g/dL, or requiring $> 2$ U transfusion |