CLINICAL CARDIOLOGY   WILEY

Outcomes of anemic patients presenting with acute coronary syndrome: An analysis of the Cooperative National Registry of Acute Coronary Care, Guideline Adherence and Clinical Events
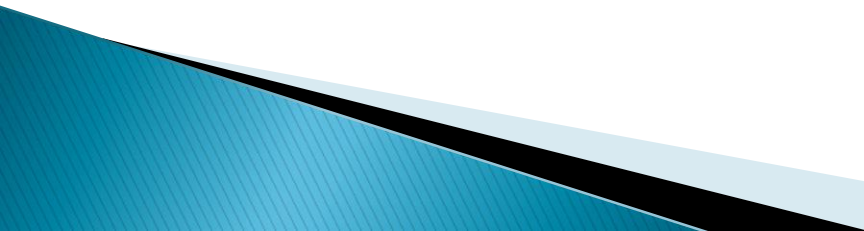
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HUYNH ET AL.

I / INRODUCTION

- Anemia commonly accompanies acute coronary syndromes (ACS) and is associated with poorer outcomes.
- Anemia accounts for 12% to 25% of the total cohort of patients that present to hospital with acute coronary syndrome (ACS).
- Numerous studies have shown that anemia is associated with poorer outcomes and those presenting with ACS and baseline anemia have a significantly increased risk of early and late mortality
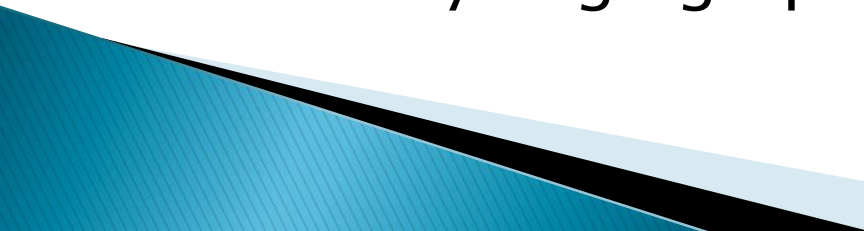
I / INRODUCTION

- The aims of this study were to identify the differences in care offered to anemic vs non-anemic ACS patients and to examine the associations between anemia and inhospital outcomes in an Australian ACS population

II / METHODS

- This analysis of the CONCORDANCE database included 8665 ACS patients presenting to 41 Australian hospitals. Baseline characteristics, management, and outcomes were compared between patients with anemia (Hb $\leq$ 130 for males, Hb $\leq$ 120 g/L for females) and non-anemia.

II / METHODS

2.1 | Study population

- Derived from the CONCORDANCE registry which is an ongoing Australian observational study which describes the management and outcomes of ACS patients.

- The CONCORDANCE study involves more than 40 Australian public hospitals which service metropolitan, rural, and remote locations.

- Enrolling hospitals were distributed between metropolitan (64%) and rural (36%) locations.

- The majority of these hospitals (79%) had on site coronary angiographic facilities
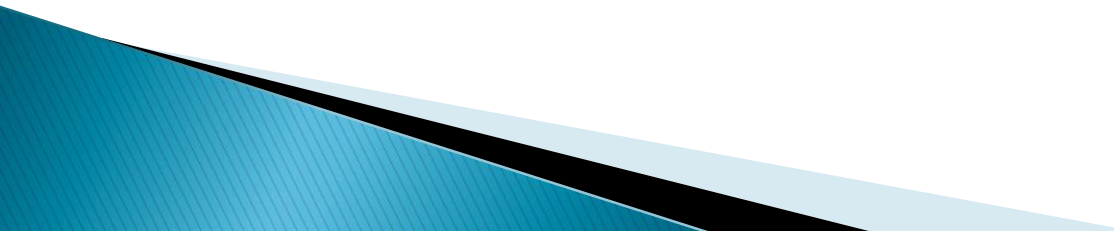
II / METHODS

Inclusion criteria:

Age of 18 years or grater at the admitted with a diagnosis of ACS, together with significant electrocardiographic changes, elevated cardiac biomarkers, a history of newly documented coronary artery disease, or two features of high risk ACS

II / METHODS

- This analysis included ACS patients from the period 2009 to 2015.
- The cohort was dichotomized into anemic and non-anemic groups based on the World Health Organization classification of anemia: admission Hb $\leq$ 120 g/L for females and Hb $\leq$ 130 g/L for males.

II / METHODS

2.2 | Outcomes

▸ In-hospital outcomes of the anemic and non-anemic patients were compared.

▸ These outcomes included: congestive cardiac failure, cardiogenic shock, acute renal failure, re-infarction, cardiac arrest, major bleed, and in-hospital mortality.
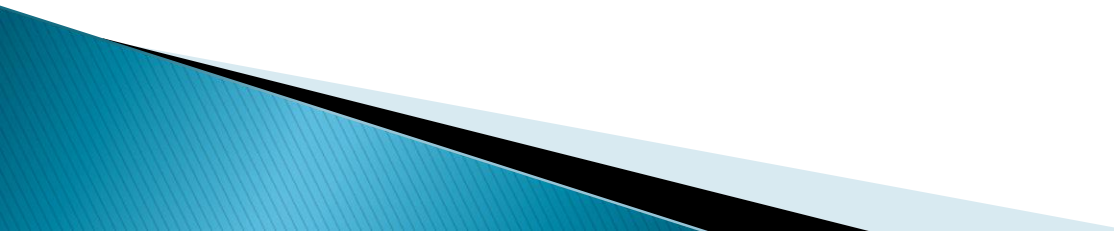
II / METHODS

2.3 | Statistical analyses

▸ Multivariable logistic generalized estimating equation (GEE) regression models adjusting for hospital clustering effect and patient clinical characteristics (GRACE score21 categories, STEMI vs not, diabetes, and previous myocardial infarction) were used to investigate the independent contribution of anemia to in-hospital mortality.

▸ Adjusted probability of death was modeled with hemoglobin as a continuous variable using the multivariable GEE model, and the probability of death with an increase of hemoglobin by 1 g/L was graphically represented.

III/ RESULTS

3.1 | Baseline characteristics

- Our anemic patients were older (72 years vs 63 years, $P < .0001$)

- Comorbidities including previous myocardial infarction (MI), chronic renal failure, diabetes, hypertension, and dyslipidaemia were more prevalent when compared to the non-anemic group.

- They had more frequently been investigated for coronary artery disease prior to their admission.

III/ RESULTS

TABLE 1 Baseline characteristics of anemia vs non-anemia

Variable	Anemia (n = 1880) n (%) Hb ≤ 120 (females)|Hb ≤ 130 (males)		Non-anemia (n = 6785), n (%) Hb > 120 (females)|Hb > 130 (males)		P value
Age (years)	72.3 ± 12.6		62.8 ± 13.0		<.0001
Sex	F: 641 (34)	M: 1239 (66)	F: 1855 (27)	M: 4930 (73)	<.0001
Diagnosis	STEMI: 394 (21)	NSTEMI: 1032 (55)	STEMI: 2344 (35)	NSTEMI:3147 (46)	<.0001
Previous MI	836 (44)		1737 (26)		<.0001
Previous angiogram	966 (51)		2064 (30)		<.0001
Previous PCI	541 (29)		1262 (19)		<.0001
Previous CABG	384 (20)		612 (9)		<.0001
Chronic renal failure	473 (25)		279 (4)		<.0001
Diabetes	848 (45)		1537 (23)		<.0001
Hypertension	1477 (79)		3914 (58)		<.0001
Dyslipidaemia	1278 (68)		3615 (53)		<.0001

Abbreviations: CABG, coronary artery by-pass graft; MI, myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST elevation myocardial infarction.

III/   RESULTS

3.2 | In-hospital management
(Table 2a):

- Anemic patients presenting with STEMI were less likely to be emergently reperfused with either thrombolytic therapy (22% vs 33%, $P < .0001$) or primary PCI (45% vs 51%, $P = .033$).
- When a coronary stent was deployed during primary PCI, drug eluting stents (DES) were used less in the anemic cohort ($P = .016$)

(Table 2b):

- For all ACS patients (which includes STEMI non-STEMI and unstable angina), anemic patients less frequently received coronary angiography (63% vs 86%, $P < .0001$) and PCI (30% vs 52%, $P < .0001$).
- If a stent was deployed, drug eluting stents (50% vs 58%, $P < .0001$) were less likely to be utilized .

III/ RESULTS

TABLE 2 (a) Thrombolytic therapy and primary PCI in anemic and non-anemic cohort in STEMI only

Variable	Anemia (n = 394), n (%) Hb ≤ 120 (females) |Hb ≤ 130 (males)	Non-anemia (n = 2344), n (%) Hb > 120 (females) |Hb > 130 (males)	P value
Thrombolytic therapy	87 (22)	778 (33)	<.0001
Primary PCI	179 (45)	1201 (51)	.0330
BMS[a]	88 (49)	504 (42)	.0695
DES[a]	80 (45)	652 (54)	.0164

(b) Interventions in anemic vs non-anemic cohort presenting with ACS (includes NSTEMI and STEMI)

Variable	Anemia (n = 1880), n (%) Hb ≤ 120 (females)|Hb ≤ 130 (males)	Non-anemia (n = 6785), n (%) Hb > 120 (females) |Hb > 130 (males)	P value
Angiography	1191 (63)	5804 (86)	<.0001
PCI	573 (30)	3542 (52)	<.0001
BMS[b]	252 (44)	1356 (38)	.0095
DES[b]	284 (50)	2068 (58)	<.0001
CABG	150 (8)	595 (9)	.2792

[a]Denominator: primary PCI patients.

[b]Denominator: PCI.

Abbreviations: BMS, bare metal stent; CABG, coronary artery bypass graft; DES, drug eluting stent; PCI, percutaneous coronary intervention.

III/   RESULTS

(Table 3):

- Anemic patients were less likely to be prescribed parenteral anticoagulation in the form of heparin or low molecular weight heparin (82% vs 88%, $P < .0001$) and overall received less antiplatelet therapy and in particular were less likely to be escalated to the more potent P2Y12 inhibitors prasugrel (2% vs 5%, $P < .0001$) and ticagrelor (11% vs 20%, $P < .0001$).

- They were less likely to receive intravenous glycoprotein IIb/IIIa inhibitors (6% vs 15%, $P < .0001$)

III/   RESULTS

3.2 | In-hospital management
(Table 4):

Anemic patients presenting with ACS had more complex hospital stays marked by a higher frequency of in-hospital events: These included higher rates of :

- cardiogenic shock (5% vs 2%, $P < .0001$)
- recurrent ischemia (13% vs 8%, $P < .0001$)
- re-infarction (4% vs 2%, $P < .0006$)
- major bleeds (13% vs 7%, $P < .0001$)
- death from all causes (7% vs 3%, $P < .0001$)

III/ RESULTS

TABLE 3 In-hospital management with anticoagulation and antiplatelet agents

Variable	Anemia (n = 1880), n (%) Hb ≤ 120 (females)| Hb ≤ 130 (males)	Non-anemia (n = 6785), n (%) Hb > 120 (females)| Hb > 130 (males)	P value
Parenteral anticoagulation[a]	1536 (82)	5986 (88)	<.0001
Aspirin	1740 (93)	6564 (97)	<.0001
Aspirin and clopidogrel	1317 (70)	4828 (71)	.3511
Aspirin and prasugrel	34 (2)	351 (5)	<.0001
Aspirin and ticagrelor	208 (11)	1345 (20)	<.0001
Glycoprotein IIb/ IIIa antagonist	121 (6)	1013 (15)	<.0001

[a]Heparin or low molecular weight heparin.

III/   RESULTS

(Figure 1).

▸ Anemia was also an independent predictor of mortality when adjusted for GRACE risk score, ACS diagnosis, diabetes, and previous MI with an adjusted OR for death of 1.62 (95% CI, 1.16–2.25) compared to patients without anemia.

▸ There was an inverse relationship between admission hemoglobin and the adjusted probability of death

III/ RESULTS

TABLE 4 In-hospital events in the anemic and non-anemic cohort

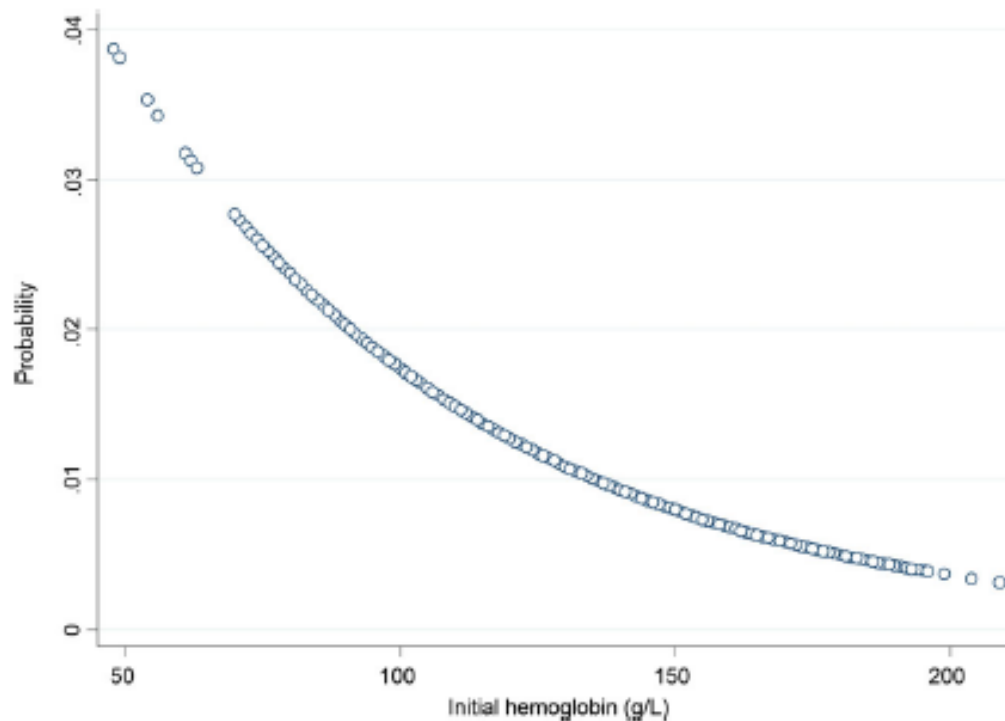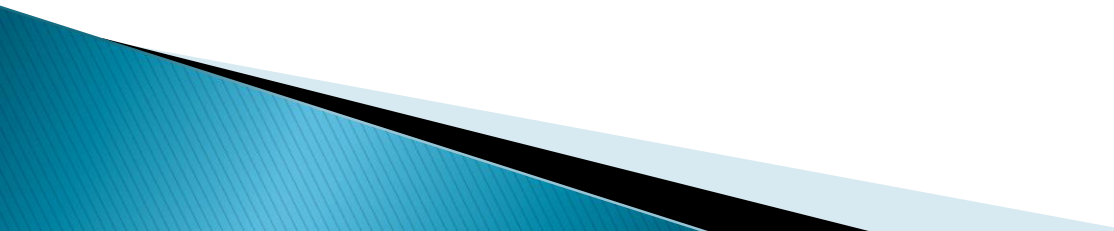| Variable	Anemia (n = 1880), n (%) Hb ≤ 120 (females) |Hb ≤ 130 (males)	Non-anemia (n = 6785), n (%) Hb > 120 (females) |Hb > 130 (males)	P value
Congestive heart failure	278 (15)	450 (7)	<.0001
Cardiogenic shock	91 (5)	167 (2)	<.0001
Acute renal failure	251 (13)	237 (4)	<.0001
Recurrent ischemia	240 (13)	572 (8)	<.0001
Re-infarction	73 (4)	165 (2)	0.0006
Cardiac arrest	84 (5)	217 (3)	0.0074
Atrial fibrillation	281 (15)	576 (9)	<.0001
Major bleed	247 (13)	473 (7)	<.0001
Death	124 (7)	180 (3)	<.0001

III/ RESULT

FIGURE 1 Adjusted odds of death and hemoglobin
†Adjusted for hospital clustering effect, grace risk score, diagnosis
(STEMI vs other), diabetes, and previous myocardial infarction

IV / DISCUSSION

- In our study anemic patients were significantly older with more cardiovascular risk factors and comorbidities. They were less likely prescribed coronary intervention and medical therapies including antithrombotic agents that have been shown to have prognostic benefit in ACS.

- Our anemic patients had more complicated hospital stays with higher rates of cardiogenic shock, re-infarction, and major bleeds. Inhospital mortality in the anemic population was 60% higher after adjustment for comorbidities.

IV / DISCUSSION

Poor prognosis ?

IV / DISCUSSION

- Studies which examine the impact of anemia on patients with ACS treated by primary PCI have found that anemia was a powerful marker of poor prognosis.

IV / DISCUSSION

ACUTE CORONARY SYNDROME

Impact of Early Invasive Approach on Outcomes of Patients With Acute Coronary Syndrome and Baseline Anemia: Analysis From the ACSIS Registry

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ILAN GOLDENBERG, MD,[5,6] ATERET FARCAS, MSc,[6] EUGENIA NIKOLSKY, MD PhD,[2,7]
and FOR THE ACSIS INVESTIGATORS

Early coronary angiography and PCI in an anemic STEMI cohort was associated with improved clinical outcomes and a comparable incidence of bleeding with the anemic cohort who did not undergo PCI.

IV / DISCUSSION

Association of Anemia With Outcomes Among ST-Segment–Elevation Myocardial Infarction Patients Receiving Primary Percutaneous Coronary Intervention

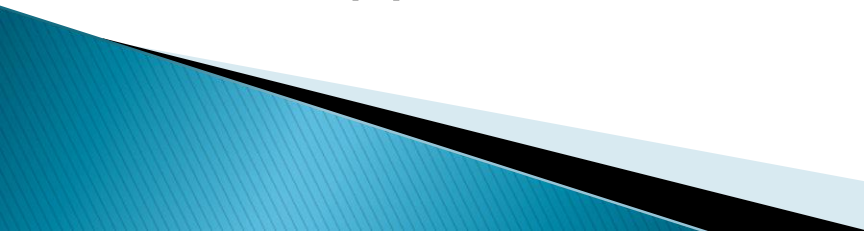Moghaddam et al; Anemia in STEMI Patients Receiving Primary PCI

Timely primary PCI in anemic STEMI patients had no increase in mortality but a penalty of major bleeding when compared to STEMI patients without anemia.

IV / DISCUSSION

- There is general agreement that the management of ACS patients should incorporate anemia into the overall PCI strategy but there are no guidelines directly addressing this common clinical dilemma.
- Whilst no causal relationships have been identified between anemia and poor prognosis, being aware of these associations allows clinicians to understand risk and exercise caution when managing anemic STEMI patients

IV / DISCUSSION

- Anemic patients in our cohort received less thrombolysis, anticoagulation, and antiplatelet therapy. When dual antiplatelet agents were prescribed, patients were less likely to receive more potent PY212 inhibitors. This likely reflects the unequivocal associations of these therapies with increased bleeding, and the fact that anemic patients have been routinely excluded from trials of these agents meaning there are limited randomized data to guide decisions.
- We also found that anemic patients received less drugeluting stents when a stent was deployed— perhaps a physician decision related to the requirement for longer duration dual antiplatelet therapy with DES.

Guidelines ?

IV / DISCUSSION

- Guidelines recommend consistent approaches to patients at high bleeding risk of whom those with anemia form a subset.
- The **2016 National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand (CSANZ)** recommends applying a "priority low-bleeding" strategy which includes the use of reversible and short acting antithrombotic agents, minimization of the number of agents used and substitution rather than addition of agents when necessary (Grade B recommendation, Evidence Level II).
- **The European Cardiac Society (ESC) guidelines** suggest additional strategies including avoidance of overdosing and applying renal adjustments to medications.
- **The American Heart Association (AHA)** suggest that weight-based calculations should be used for anticoagulants and antiplatelets (Level II Evidence).
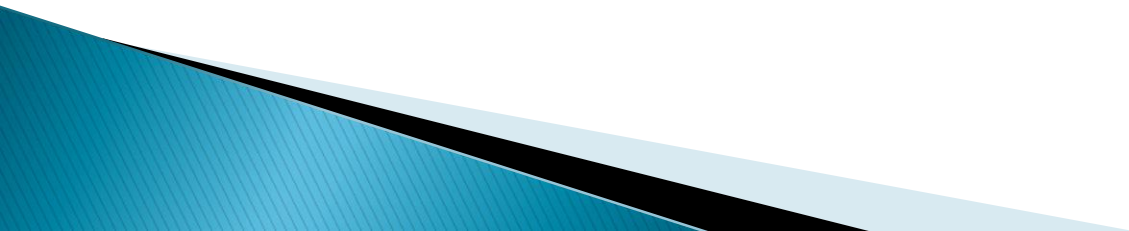
IV / DISCUSSION

Mortality ?

IV / DISCUSSION

▸ The mortality relationship with anemic patients presenting with ACS shown in this study is consistent with that reported in the literature

▸ **Sabatine et al** examined the 30 day cardiovascular mortality in patients with STEMI categorized by 1 g/dL hemoglobin increments and found a J-shaped relationship with increased mortality at hemoglobins below 140 g/L and above 170 g/L.

▸ **A more recent British retrospective study** confirmed both the optimal hemoglobin range and the J shaped relationship with 30-day mortality in 71 223 patients presenting with anemia and ACS.

▸ **In our smaller population** we too found a close association between hemoglobin and mortality after adjustment for comorbidities. The relationship was curvilinear because the number of patients with hemoglobins over 17 was small but was otherwise consistent with previous studies.

V/ CONCLUSION

V/   CONCLUSION

▸ Anemic patients presenting with ACS have poorer outcomes. They receive less evidenced based medical therapies which we postulate contributes to their overall worse outcomes.

▸ We would suggest that this cohort requires further focused study to determine whether more active treatment in the acute phase of their presentation will improve outcomes.