Original Paper

Impact of KDIGO-Defined Acute Kidney Injury on Mortality after Percutaneous Coronary Intervention for Acute Myocardial Infarction

Vojko Kanic^a Gregor Kompara^a David Suran^a Robert Ekart^b
Sebastjan Bevc^{c, d} Radovan Hojs^{c, d}

^aDepartment of Cardiology and Angiology, University Medical Center Maribor, Maribor, Slovenia; ^bDepartment of Dialysis, University Medical Center Maribor, Maribor, Slovenia; ^cDepartment of Nephrology, University Medical Center Maribor, Maribor, Slovenia; ^dFaculty of Medicine, University of Maribor, Maribor, Slovenia

Keywords

Acute kidney injury · Myocardial infarction · Mortality · Percutaneous coronary intervention · KDIGO

Abstract

Background: There are limited data regarding the incidence and long-term impact of acute kidney injury (AKI) according to the KDIGO guidelines on the outcome in patients with myocardial infarction (MI) treated with percutaneous coronary intervention (PCI). The aim of the study was to evaluate the prevalence of AKI, as classified by the KDIGO criteria, and its association with long-term mortality. **Methods:** Data from 5,859 MI patients undergoing PCI at our institution were analyzed. We compared the group without and with AKI according to the KDIGO criteria in relation to long-term mortality. **Results:** AKI was documented in 499 (8.5%) patients. AKI stage 1 occurred in 6.2% of patients, AKI stage 2 in 0.9% of patients, and AKI stage 3 in 1.5% of patients. Patients with AKI had a higher long-term mortality (57.3 vs. 20.6%; $p < 0.0001$). The mortality was 50.3% in AKI stage 1, 56.9% in AKI stage 2, and 87.2% in AKI stage 3. The hazard ratios for all-cause mortality for AKI stages 1–3 were 1.77, 1.85, and 6.30 compared to patients with no AKI. Cardiogenic shock, bleeding, heart failure, age, renal dysfunction, diabetes, hyperlipidemia, ST-elevation MI, contrast volume/glomerular filtration ratio, P2Y12 receptor antagonists, and radial access were associated with the development of AKI. **Conclusion:** A slight increase in serum creatinine was associated with a progressive increase in long-term mortality in patients with AKI according to the KDIGO definition.

© 2018 S. Karger AG, Basel

Vojko Kanic
Department of Cardiology and Angiology, Division of Internal Medicine
University Medical Center Maribor
Ljubljanska ulica 5, SI-2000 Maribor (Slovenia)
E-Mail vojko.kanic@guest.arnes.si

Introduction

Patients undergoing invasive treatment of myocardial infarction (MI) are at high risk of acute kidney injury (AKI) [1, 2]. In this group, AKI is associated with contrast volume, hemodynamic impairment, inflammation, bleeding, and nephrotoxic agents [1, 3, 4]. However, the incidence of AKI reported varies considerably with the population evaluated and the definitions used [1, 6]. There are limited data regarding the incidence and long-term impact on the outcome of AKI according to the KDIGO guidelines in patients with MI treated with percutaneous coronary intervention (PCI) [5]. The “Kidney Disease: Improving Global Outcomes (KDIGO)” expanded the time frame for AKI detection from the previous 48–72 h to within 7 days [7]. We aimed to evaluate the prevalence of AKI, as classified by the KDIGO criteria, in MI patients treated with PCI, and its association with long-term all-cause mortality.

Methods

A retrospective, single-center observational study was performed at the University Medical Center Maribor, a tertiary referral hospital with a 24/7 primary PCI service. We reviewed 6,387 consecutive MI patients who were treated with PCI between January 2007 and December 2016. The definition of MI was based on current guidelines [8–10]. We excluded patients on dialysis (97 [1.5%]), patients without data on serum creatinine before or after PCI (149 [2.3%]), and/or patients who died in less than 7 days after admission (282 [4.4%]), since it was assumed that such patients would have had a fair chance of developing AKI within 7 days if they had survived, leaving 5,859 (91.7%) for further analysis. No thrombolysis was used.

Patients were treated according to the guidelines for the management of MI [8, 9]. The PCI strategy and concomitant medication were at the discretion of the operator.

Renal protection with continuous infusion of saline (1 mL/kg/h during PCI and the next 12 h) was given. In patients with overt heart failure, the hydration rate was reduced at the discretion of the operator and/or attending physician. Patients who received P2Y₁₂ receptor inhibitors prior to or during hospitalization before, during, or after PCI, and were discharged with these drugs, were recognized as having received these drugs.

All-cause mortality was assessed over a mean period of 4.2 ± 3.0 years up to January 1, 2018. All medical records were obtained from the hospital information system to complete the data collection.

The initial serum creatinine at admission was used to determine the baseline renal function. Renal dysfunction was defined as an estimated glomerular filtration rate (eGFR) less than 60 mL/kg/1.73 m². The Modification of Diet in Renal Disease Study formula was used for calculations of eGFR [11]. Serum creatinine levels were determined on admission and after 24 and 48 h. After the first 48 h, serum creatinine levels were obtained at various time points, at the discretion of the treating physician.

AKI was determined using the KDIGO criteria, as follows [7]: stage 1 – a rise in serum creatinine by ≥ 0.3 mg/dL within 48 h, or an increase in serum creatinine of at least 1.5 times the baseline that is known or presumed to have occurred within the prior 7 days; stage 2 – more than a 2- to 2.9-fold increase in serum creatinine; stage 3 – more than a 3-fold increase in serum creatinine from the baseline or an increase in serum creatinine to >4.0 mg/dL.

The nonionic contrast agent iopamidol (concentration 370 mgI/mL – Iopamiro 370R, Bracco) was used in our laboratory. Information on the contrast volume used during PCI was available for 5,412 (90.7%) patients.

Anemia was defined as proposed by the World Health Organization: a serum hemoglobin level <130 g/L for men and <120 g/L for women [12]. The Bleeding Academic Research Consortium (BARC) bleeding criteria and BARC 3a bleeding (Hb drop of 30–50 g/L or any transfusion) were used [13]. Thrombolysis in Myocardial Infarction (TIMI) flow grades were used for coronary flow assessment [14].

Cardiogenic shock on admission was defined according to clinical and hemodynamic criteria, including hypotension (systolic blood pressure ≤ 90 mm Hg for ≥ 30 min or the need for supportive measures to maintain a systolic blood pressure of >90 mm Hg) and evidence of end-organ hypoperfusion.

Heart failure (excluding cardiogenic shock) was defined according to the clinical criteria (bilateral pulmonary rales, S₃ gallop, edema) and/or ejection fraction $<30\%$ and/or pulmonary edema on chest X-ray. The ventricular ejection fraction was assessed by bedside echocardiography in the first 48 h after admission.

Table 1. Basic demographic characteristics of patients with and without AKI

	AKI (n = 499)	No AKI (n = 5,360)	All patients (n = 5,859)	p value
Age, years ¹	69.8 (11.8)	63.8 (11.9)	64.3 (12.0)	<0.0001
Male gender, n (%) ²	313 (62.7)	3,750 (70.0)	4,063 (69.3)	0.001
STEMI, n (%) ²	305 (61.1)	3,001 (56.0)	3,306 (56.4)	0.003
Diabetes, n (%) ²	164 (32.9)	1,173 (21.9)	1,337 (22.8)	<0.0001
Hypertension, n (%) ²	283 (56.7)	3,179 (59.3)	3,462 (59.1)	0.27
Hyperlipidemia, n (%) ²	167 (33.5)	2,679 (49.8)	28,538 (48.4)	<0.0001
Cardiogenic shock, n (%)	70 (14.0)	108 (2.0)	178 (3.0)	<0.0001
Anemia, n (%) ¹	215 (43.1)	1,379 (25.7)	1,594 (27.2)	<0.0001
Renal dysfunction, n (%) ²	219 (43.9)	993 (18.5)	1,212 (20.7)	<0.0001
Creatinine, mg/dL ¹	1.25 (0.62)	0.98 (0.34)	1.00 (0.38)	<0.0001
Heart failure, n (%) ²	120 (24.0)	484 (9.0)	604 (10.3)	<0.0001

AKI, acute kidney injury; STEMI, ST-elevation myocardial infarction. ¹ Mean (standard deviation).
² Comparison made using the χ^2 test.

Data on dates of death were provided by the Slovenian National Cause of Death Registry. The study was approved by the local ethics committee.

End Points

The end point was all-cause long-term mortality in both groups.

Statistical Methods

We counted the end point events that occurred during the follow-up period and compared their rates between the cohorts of patients with and without AKI. The cumulative incidence rates of the unadjusted long-term mortality were estimated by the Kaplan-Meier method (stratified to AKI stages) and compared by the log-rank test.

We used binary logistic regression to identify independent predictors of AKI. Binary logistic regression models were performed using the Enter mode. The models were adjusted for variables that were significantly different in bivariate analysis: age, gender, diabetes, hyperlipidemia, ST-elevation myocardial infarction (STEMI), PCI of the left main coronary artery, PCI of the right coronary artery, intra-aortic balloon pump insertion, radial access, cardiogenic shock on admission, eGFR, contrast volume/eGFR ratio, TIMI flow after PCI, anemia, bleeding, bivalirudin, P2Y12 receptor antagonists, heart failure, and AKI. These variables were also used in Cox regression analyses. Cox proportional hazards regression was used to compute the hazard ratios (HRs) as estimates of long-term mortality according to the AKI stages. The proportional hazard assumption was evaluated by calculating the correlations between Schoenfeld residuals for each covariate and the ranked failure times. All correlations were close to zero and the *p* values were above 0.05, which implies that the assumption was met. The differences between the groups in baseline clinical, angiographic, and procedural characteristics were compared using the independent samples *t* test or the Mann-Whitney *U* test for continuous variables, and the χ^2 test for categorical variables, as appropriate. Data were analyzed with SPSS 21.0 software for Windows (IBM Corp., Armonk, NY, USA). All *p* values were two-sided and values less than 0.05 were considered statistically significant.

Results

Out of 5,859 MI patients, 499 (8.5%) suffered AKI. AKI stage 1 occurred in 362 (6.2%) patients, AKI stage 2 in 51 (0.9%) patients, and AKI stage 3 in 86 (1.5%) patients. Patients with AKI were generally older, female, admitted for STEMI, had diabetes, anemia, and renal dysfunction on admission, and presented more often with cardiogenic shock. On the contrary,

Table 2. Procedural data of patients with and without AKI

	AKI (n = 499)	No AKI (n = 5,360)	All patients (n = 5,859)	p value
GPIIb/IIIa receptor antagonists, n (%) ²	250 (50.1)	2,518 (47.0)	2,768 (47.3)	0.19
Bivalirudin, n (%) ²	37 (7.4)	560 (10.4)	597 (10.2)	0.03
P2Y12 receptor antagonists, n (%) ²	419 (84.0)	4,939 (92.1)	5,358 (91.4)	<0.0001
PCI left main coronary artery, n (%) ²	30 (6.0)	141 (2.6)	171 (2.9)	<0.0001
PCI left anterior descending artery, n (%) ²	202 (40.5)	2,121 (39.6)	2,323 (39.7)	0.70
PCI circumflex artery, n (%) ²	117 (23.4)	1,163 (21.7)	1,280 (21.9)	0.36
PCI right coronary artery, n (%) ²	123 (24.6)	1,721 (32.1)	1,844 (31.5)	0.001
Radial access, n (%) ²	72 (14.4)	1,292 (24.1)	1,364 (23.3)	<0.0001
Intra-aortic balloon pump, n (%)	21 (4.2)	55 (1.0)	76 (1.3)	<0.0001
TIMI 0/1 flow after PCI, n (%) ²	48 (9.6)	286 (5.3)	334 (5.7)	<0.0001
Bleeding, n (%) ²	157 (31.5)	264 (4.9)	421 (7.2)	<0.0001
Contrast volume, mL ³	150.0 (110.0, 202.0)	150.0 (110.0, 205.0)	150.0 (110.0, 205.0)	0.93
Contrast volume/eGFR ratio ³	2.39 (1.52, 4.08)	1.85 (1.29, 2.73)	1.89 (1.30, 2.89)	<0.0001

AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction. ¹ Mean (standard deviation). ² Comparison made using the χ^2 test. ³ Median (25th, 75th percentile); comparison made using the Mann-Whitney test.

Table 3. Predictors of AKI

	OR	CI	p value
Male sex	0.90	0.71–1.13	0.37
Age	1.03	1.02–1.04	<0.0001
Diabetes	1.42	1.12–1.79	0.004
Hyperlipidemia	1.40	1.11–1.76	0.005
Anemia	1.14	0.90–1.44	0.27
Bleeding	4.10	3.10–5.42	<0.0001
TIMI flow 0/1 after PCI	1.29	0.88–1.90	0.19
ST-elevation myocardial infarction	1.29	1.02–1.63	0.032
PCI left main coronary artery	1.02	0.62–1.70	0.93
PCI right coronary artery	0.83	0.65–1.07	0.15
Intra-aortic balloon pump	1.13	0.59–2.23	0.71
Radial access	0.70	0.53–0.94	0.016
Renal dysfunction	1.38	1.06–1.80	0.018
Contrast volume/eGFR ratio	1.11	1.05–1.17	<0.0001
Cardiogenic shock	4.37	2.88–6.61	<0.0001
P2Y12 receptor antagonists	0.70	0.51–0.97	0.034
Bivalirudin	0.76	0.51–1.12	0.16
Heart failure	2.15	1.65–2.82	<0.0001

CI, confidence interval; eGFR, estimated glomerular filtration rate; OR, odds ratio; PCI, percutaneous coronary intervention; renal dysfunction, eGFR <60 mL/min/1.73 m²; TIMI, Thrombolysis in Myocardial Infarction.

they had less hyperlipidemia, while radial access, bivalirudin, and P2Y12 receptor antagonists were less frequently used. Intra-aortic balloon pumps were used more often, and PCI of the left main coronary artery was performed more frequently, but TIMI flow after PCI was lower. The right coronary artery was less affected. They bled more, the contrast volume/eGFR ratio was higher in these patients, and they developed more heart failure. Tables 1 and 2 show the basic clinical and procedural characteristics of patients enrolled in the study.

Fig. 1. The cumulative unadjusted (a) and adjusted (b) mortality for patients with myocardial infarction on the basis of the KDIGO severity classification. AKI, acute kidney injury.

Predictors of AKI

Cardiogenic shock, bleeding, age, heart failure, renal dysfunction, diabetes, hyperlipidemia, STEMI, and contrast volume/eGFR ratio predicted the development of AKI. Patients with radial access and those who received P2Y12 receptor antagonists suffered less AKI (Table 3).

Mortality

Over a mean period of 4.2 ± 3.0 years, 1,389 (23.7%) patients died. Patients with AKI according to the KDIGO criteria had a higher mortality than patients without AKI (286 [57.3%] patients with AKI died compared to 1,103 [20.6%] patients without AKI; $p < 0.0001$). Of the 362 patients with AKI stage 1, 182 (50.3%) died. In patients with AKI stage 2, 29 (56.9%), and in patients with AKI stage 3, 75 (87.2%) died, respectively. Figure 1a shows the unadjusted and Figure 1b the adjusted long-term mortality according to the AKI stages. The hazard ratio for all-cause mortality for AKI patients was 2.09 (95% CI: 1.80–2.43; $p < 0.0001$). The hazard ratio for AKI stage 1 patients was 1.77 (95% CI: 1.49–2.11; $p < 0.0001$), 1.85 (95% CI: 1.21–2.83; $p = 0.005$) for AKI stage 2, and 6.30 (95% CI: 4.68–8.48; $p < 0.0001$) for AKI stage 3 compared to patients with no AKI. Other predictors of long-term mortality are listed in Table 4.

Discussion

Data on the long-term association of AKI according to the KDIGO guidelines in patients with MI are limited [5]. In our long-term follow-up study, we validated the KDIGO AKI criteria in unselected patients with MI treated with PCI. We followed patients for up to 10 years, with a mean of 4.2 years. We found that 8.5% of patients suffered AKI according to the KDIGO definition and that they had a 2.09 times greater long-term risk of dying than patients without

Table 4. Predictors of long-term mortality

	HR	CI	p value
Male sex	1.35	1.19–1.53	<0.0001
Age	1.06	1.05–1.07	<0.0001
Diabetes	1.55	1.37–1.75	<0.0001
Hyperlipidemia	1.37	1.22–1.55	<0.0001
Anemia	1.37	1.22–1.55	<0.0001
Bleeding	1.70	1.43–2.01	<0.0001
TIMI flow 0/1 after PCI	1.39	1.14–1.89	0.001
ST-elevation myocardial infarction	1.10	0.97–1.24	0.13
PCI left main coronary artery	1.02	0.77–1.36	0.88
PCI right coronary artery	0.87	0.76–0.99	0.04
Intra-aortic balloon pump	1.57	1.08–2.34	0.016
Radial access	0.92	0.77–1.10	0.38
eGFR	0.995	0.992–0.998	<0.0001
Contrast volume/eGFR ratio	1.01	0.99–1.04	0.26
Acute kidney injury	2.09	1.80–2.43	<0.0001
Cardiogenic shock	2.65	2.07–3.39	<0.0001
P2Y12 receptor antagonists	0.82	0.69–0.98	<0.0001
Bivalirudin	0.80	0.64–1.02	0.069
Heart failure	1.75	1.51–2.03	<0.0001

CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction.

AKI, which is consistent with previous reports [2, 15]. The main finding is that even AKI stage 1 almost doubled the long-term risk. A graded increase in the severity of AKI according to the KDIGO definition is associated with a progressively increased risk of long-term mortality in these patients. The prevalence of AKI was lower than in similar trials, probably because less contrast was used and good hydration was maintained in our study to prevent AKI [16]. Unfortunately, comparison is difficult due to the different study populations and different definitions of AKI and comparisons must be made in light of these differences. Beside patient characteristics, procedural data and outcome characteristics were included in the multi-variable regression model to elucidate the risk factors predicting AKI. As previously found, cardiogenic shock on admission, diabetes, hypertension, renal dysfunction, STEMI, heart failure [2, 5, 15, 17, 18], and contrast volume/eGFR ratio predicted AKI [5, 19]. In fact, this ratio seems to have a greater potential to discriminate between the patients who are at higher risk of AKI than the contrast volume alone since it includes 2 parameters (contrast volume and eGFR) that both predispose to AKI [19, 20]. The contrast volume/eGFR ratio also predicted long-term mortality. Besides sex and bivalirudin, for which the data are inconsistent, all other predictors of long-term mortality in our study (listed in Table 4) are well established [8, 9].

Bleeding after PCI more frequently complicated hospitalization in patients with AKI (unadjusted OR: 8.95; 95% CI: 7.06–11.09; $p < 0.0001$) and also predicted AKI, as previously seen [16, 18, 21, 22].

Patients who did not receive P2Y12 receptor antagonists suffered more AKI. P2Y12 receptor antagonists were also an independent predictor of AKI. Some experimental animal data show that P2Y12 inhibition prevents glomerular injury and protects both glomerular and peritubular capillaries, but data on P2Y12 inhibition and AKI in patients are lacking [23]. Moreover, patients who did not receive P2Y12 receptor antagonists were sicker (older, with more STEMI, a higher prevalence of cardiogenic shock, diabetes, renal dysfunction and anemia, more IABP were implanted, they bled more, received more IIb/IIIa receptor antago-

nists, they had less radial access, lower TIMI flow after PCI, and higher contrast/eGFR ratios). The role of P2Y12 receptor antagonists in AKI is strongly confounded by the clinical characteristics and still needs to be determined. Radial access was shown to be protective for AKI, which is consistent with previous reports [16].

The result of our study may be relevant for the treatment of patients with MI in everyday practice. A slight increase in serum creatinine (>0.3 mg/dL) almost doubles the long-term mortality risk in these patients. Therefore, we must obtain the serum creatinine value at hospital admission. We can easily define the patients who are prone to develop AKI (eGFR < 60 mL/min/1.73 m², hemodynamic impairment, STEMI, diabetes, hypertension, hyperlipidemia, elderly) [1, 3–5] and instigate early nephroprotective strategies (low contrast volume, crystalloid infusions, measures to ensure optimal hemodynamics, discontinuation of nephrotoxic drugs, adjustment of anti-thrombotic drugs, radial access), which might provide a significant long-term benefit [5, 7, 16, 24, 25]. In cases of AKI, the consultation with a nephrologist would be beneficial for these patients.

Limitations

We did not follow the data on possible normalization of serum creatinine. This was an observational single-center study. Our data encompassed all-cause mortality only. Data on complications of PCI were not available for a sufficient number of patients to be considered in the evaluation. Data on medication (ACE inhibitors, ARB, statins), hyperuricemia, and glucose were not collected. Calculations of eGFR were based on creatinine at presentation, which may not have been in a steady state, and thus may not be a true estimate of patients' baseline kidney function. For the calculations of eGFR, we used the MDRD equation, whose accuracy and reliability decreases with extreme eGFR values.

Conclusion

Even a slight increase in serum creatinine (>0.3 mg/dL) is important in MI patients undergoing PCI. A graded increase in the severity of AKI according to the KDIGO definition is associated with a progressively increased risk of long-term mortality in these patients.

Acknowledgment

The authors would like to thank Alojz Tapajner, BSc, from the Faculty of Medicine, University of Maribor, for help with statistical analyses.

Disclosure Statement

The authors declare that there is no conflict of interest.

Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

- 1 Marenzi G, Cosentino N, Moltrasio M, Rubino M, Crimi G, Buratti S, et al. Acute Kidney Injury Definition and In-Hospital Mortality in Patients Undergoing Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction. *J Am Heart Assoc*. 2016 Jul;5(7):e003522.

- 2 James MT, Samuel SM, Manning MA, Tonelli M, Ghali WA, Faris P, et al. Contrast-induced acute kidney injury and risk of adverse clinical outcomes after coronary angiography: a systematic review and meta-analysis. *Circ Cardiovasc Interv*. 2013 Feb;6(1):37–43.
- 3 Azzalini L, Spagnoli V, Ly HQ. Contrast-Induced Nephropathy: From Pathophysiology to Preventive Strategies. *Can J Cardiol*. 2016 Feb;32(2):247–55.
- 4 Shacham Y, Steinvil A, Arbel Y. Acute kidney injury among ST elevation myocardial infarction patients treated by primary percutaneous coronary intervention: a multifactorial entity. *J Nephrol*. 2016 Apr;29(2):169–74.
- 5 Margolis G, Gal-Oz A, Letourneau-Shesaf S, Khoury S, Keren G, Shacham Y. Acute kidney injury based on the KDIGO criteria among ST elevation myocardial infarction patients treated by primary percutaneous intervention. *J Nephrol*. 2018 Jun;31(3):423–8.
- 6 Koeze J, Keus F, Dieperink W, van der Horst IC, Zijlstra JG, van Meurs M. Incidence, timing and outcome of AKI in critically ill patients varies with the definition used and the addition of urine output criteria. *BMC Nephrol*. 2017 Feb;18(1):70.
- 7 Kellum JA, Lamire J, Aspelin P, et al. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl*. 2012;2:1–138.
- 8 Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al.; ESC Scientific Document Group. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2016 Jan;37(3):267–315.
- 9 Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J*. 2018 Jan 7;39(2):119–77.
- 10 Thygesen K, Alpert JS, Simoons ML, Chaitman BR, White HD, et al.; Writing Group on the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction; ESC Committee for Practice Guidelines (CPG). Third universal definition of myocardial infarction. *Eur Heart J*. 2012 Oct;33(20):2551–67.
- 11 Nutritional anaemias. Report of a WHO scientific group. Haemoglobin Concentrations for the Diagnosis of Anaemia and Assessment of Severity VMNIS. Geneva: World Health Organization; 1968.
- 12 Levey AS, Coresh J, Greene T, Marsh J, Stevens LA, Kusek JW, et al.; Chronic Kidney Disease Epidemiology Collaboration. Expressing the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate with standardized serum creatinine values. *Clin Chem*. 2007 Apr;53(4):766–72.
- 13 Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. *Circulation*. 2011 Jun;123(23):2736–47.
- 14 White CW. Simplicity's virtue scorned. Precision comes to TIMI flow grading and the results are ...surprising. *Circulation*. 1996 Mar;93(5):853–6.
- 15 Pickering JW, Blunt IR, Than MP. Acute Kidney Injury and mortality prognosis in Acute Coronary Syndrome patients: A meta-analysis. *Nephrology (Carlton)*. 2018 Mar;23(3):237–46.
- 16 Andò G, Cortese B, Russo F, Rothenbühler M, Frigoli E, Gargiulo G, et al.; MATRIX Investigators. Acute Kidney Injury After Radial or Femoral Access for Invasive Acute Coronary Syndrome Management: AKI-MATRIX. *J Am Coll Cardiol*. 2017 May;69(21):2592–603.
- 17 Marenzi G, Cosentino N, Bartorelli AL. Acute kidney injury in patients with acute coronary syndromes. *Heart*. 2015 Nov;101(22):1778–85.
- 18 Marenzi G, Cabiati A, Bertoli SV, Assanelli E, Marana I, De Metrio M, et al. Incidence and relevance of acute kidney injury in patients hospitalized with acute coronary syndromes. *Am J Cardiol*. 2013 Mar;111(6):816–22.
- 19 Celik O, Ozturk D, Akin F, Ayca B, Yalcin AA, Erturk M, et al. Association Between Contrast Media Volume-Glomerular Filtration Rate Ratio and Contrast-Induced Acute Kidney Injury After Primary Percutaneous Coronary Intervention. *Angiology*. 2015 Jul;66(6):519–24.
- 20 Mager A, Vaknin Assa H, Lev EI, Bental T, Assali A, Kornowski R. The ratio of contrast volume to glomerular filtration rate predicts outcomes after percutaneous coronary intervention for ST-segment elevation acute myocardial infarction. *Catheter Cardiovasc Interv*. 2011 Aug;78(2):198–201.
- 21 Andò G, Cortese B, Frigoli E, Gagnor A, Garducci S, Briguori C, et al.; MATRIX investigators. Acute kidney injury after percutaneous coronary intervention: rationale of the AKI-MATRIX (acute kidney injury-minimizing adverse hemorrhagic events by TRansradial access site and systemic implementation of angioX) sub-study. *Catheter Cardiovasc Interv*. 2015 Nov;86(5):950–7.
- 22 Andò G, Costa F, Trio O, Oreto G, Valgimigli M. Impact of vascular access on acute kidney injury after percutaneous coronary intervention. *Cardiovasc Revasc Med*. 2016 Jul-Aug;17(5):333–8.
- 23 Schwarzenberger C, Sradnick J, Lerea KM, Goligorsky MS, Nieswandt B, Hugo CP, et al. Platelets are relevant mediators of renal injury induced by primary endothelial lesions. *Am J Physiol Renal Physiol*. 2015 Jun;308(11):F1238–46.
- 24 Marenzi G, Cosentino N, Guastoni C. How to balance risks and benefits in the management of CKD patients with coronary artery disease. *J Nephrol*. 2015 Aug;28(4):403–13.
- 25 Marenzi G, Assanelli E, Campodonico J, De Metrio M, Lauri G, Marana I, et al. Acute kidney injury in ST-segment elevation acute myocardial infarction complicated by cardiogenic shock at admission. *Crit Care Med*. 2010 Feb;38(2):438–44.