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Under-recognition of Acute Kidney Injury after Cardiac Surgery in the ICU Impedes Early Detection and Prevention

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Acute kidney injury · Adherence to guidelines · Acute kidney injury awareness · Acute kidney injury prevention · Acute kidney injury undercoding · Acute kidney injury under-recognition · Cardiac surgery-associated acute kidney injury · Kidney Disease: Improving Global Outcomes recommendations

Abstract

Background: Acute kidney injury (AKI) is associated with high morbidity and mortality; therefore, prevention is important. The aim of this study was to systematically assess AKI incidence after cardiac surgery as documented in clinical routine compared to the real incidence because AKI may be under-recognized in clinical practice. Further, its postoperative management was compared to Kidney Disease: Improving Global Outcomes (KDIGO) recommendations because recognition and adequate treatment represent the fundamental cornerstone in the prevention and management of AKI. ***Methods:*** This retrospective single-center study included $n = 100$ patients who underwent cardiac surgery with cardiopulmonary bypass. The coded incidence of postoperative AKI during intensive care unit stay after surgery was compared to the real AKI incidence. Furthermore, conformity of postoperative parameters with KDIGO recommendations for AKI prevention and management was reviewed. ***Results:*** We found a considerable discrepancy between coded and real incidence, and conformity with KDIGO recommendations was found to be relatively low. The coded incidence was significantly lower ($n = 12$ vs. $n = 52$, $p < 0.05$), representing a coding rate of 23.1%. Regarding postoperative management, 90% of all patients had at least 1 episode with mean arterial pressure <65 mm Hg within the first 72 h. Furthermore, regarding other preventive parameters (avoiding hyperglycemia, stopping angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, avoiding contrast media, and nephrotoxic drugs), only 10 patients (20.8%) in the non-AKI group and in 5 (9.6%) subjects in the AKI group had none of all the above potential AKI-promoting factors.

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Conclusions: AKI recognition in everyday clinical routine seems to be low, especially in lower AKI stages, and the current postoperative management still offers potential for optimization. Possibly, higher AKI awareness and stricter postoperative management could already achieve significant effects in prevention and treatment of AKI.

Introduction

Acute kidney injury (AKI) is of particular relevance in all fields of medicine, especially in critically ill patients because of its association with considerable mortality [1]. In such patients, incidences have been reported to range from 8 to 39%, in some cases even up to 67% [2, 3]. Mortality in critically ill patients with AKI ranges from 40 to 60% [4–6]. In cardiac surgery, mortality ranges between 1 and 5%, but as soon as replacement therapy (KRT) is required, mortality increases up to 25% [7]. In the last 50 years, the mortality of KRT-dependent intensive care unit (ICU) patients has hardly changed and remains at a very poor, high level [8, 9]. The incidence of AKI is increasing [10], possibly due to more invasive measures (e.g., surgery and interventions) but also due to an aging population with an increase in comorbidities.

The additional costs of AKI are substantial and not necessarily directly associated with its severity. Once AKI is manifested, increased resource consumption must be expected in the short as well as in the long term. Additional costs incurred at a median of approximately 2,600.00 USD per patient with AKI [11, 12]. In this context, a prolonged hospital or ICU stay certainly plays a significant role [3, 11–13].

Data on biomarker-guided intervention studies using urinary [TIMP-2]·[IGFBP7] demonstrated AKI incidence or severity reduction in surgical settings [14–16], whereas in internal medicine patients in the emergency department, such an intervention seems to have no significant effects [17]. Early AKI detection and prevention also seem to be useful from an economic point of view. Zarbock et al. [18] demonstrated that the length of stay (LoS) in ICUs and the need for KRT in patients undergoing cardiac surgery can be reduced if AKI is avoided.

The widely accepted Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for management of AKI describe expert opinion-based recommendations for interventions that, in addition to addressing the causative injury, describe a variety of measures to reverse or mitigate AKI or to prevent AKI in high-risk patients [19]. These recommendations are especially: (1) optimization of volume status and hemodynamics with adequate mean arterial pressure (MAP) (MAP ≥65 mm Hg), (2) stopping of nephrotoxic drugs, (3) avoidance of hyperglycemia, (4) avoidance of radiocontrast media, (5) functional hemodynamic monitoring, and, of course, (6) close monitoring of the serum creatinine and urine output.

However, reports have emerged that when comparing billing codes with serum creatinine-based AKI diagnoses, many AKIs are not even recognized in routine daily clinical practice, which makes the application of these measures not even possible in the first place [20]. Moreover, concerning the measures mentioned above, adherence to KDIGO recommendations in the clinical routine seems to be quite low, even if occurrence of AKI is recognized [21].

The aim of this study was to systematically assess AKI incidence after cardiac surgery as documented in clinical routine (billing codes) compared to the real incidence according to KDIGO definition, as well as its postoperative management toward AKI prevention or therapy. Recognition and adequate treatment represent the fundamental cornerstone in the prevention and management of AKI, way before establishment of costly urinary biomarker interventions, since this cornerstone is a precondition for the implementation of a successful biomarker-guided prevention program.

Materials and Methods

Study Population

The present cohort consists of patients of the Robert-Bosch Hospital who underwent cardiac surgery. The target number of cases was $n = 100$. Only patients meeting the inclusion and exclusion criteria were included. Inclusion criteria were (1) intensive care treatment after cardiac surgery at the Robert-Bosch Hospital, (2) surgery with use of cardiopulmonary bypass (CPB), (3) available billing and clinical data at the Robert-Bosch Hospital, and (4) available daily record of the urine output and serum creatinine. Exclusion criteria were (1) insufficient available urine output and serum creatinine record, (2) pre-existing AKI or high-grade renal function impairment (estimated glomerular filtration rate <30 mL/min/1.73 m^2), (3) postoperative mechanical circulatory support using extracorporeal membrane oxygenation, left-ventricular assist device, or intra-aortic balloon pump, (4) death on the day of surgery, and (5) no available billing data or clinical data at the Robert-Bosch Hospital. Indication for cardiac surgery was mainly valve surgery since most isolated bypass grafts are performed without CPB at our hospital. Aortic valve surgery was 42% (12% in conjunction with coronary artery bypass graft [CABG]), mitral valve surgery was 40% (8% with CABG), combined aortic and mitral valve surgery was 5%, aortic surgery was 5%, and other cardiac surgery (e.g., Ross and Morrow) was 8% (1% with CABG).

Collected Data and Definitions

For primary data collection, n = 367 potential study participants had to be screened for the inclusion of n = 100 patients (see Fig. 1). All cardiovascular surgeries were consecutively screened over a period of 51 days, and patients were included according to inclusion and exclusion criteria until the target number of cases (n = 100) was reached (see Fig. 1). Primary data sources were the hospital information system and the digital archive. Data collected included baseline, clinical (e.g., medical history, comorbidities, etc.,), laboratory, and billing data. Hourly urine output and daily serum creatinine values were evaluated during ICU stay after surgery to detect real incidence of AKI. AKI was defined according to the KDIGO definition [19]. After discharge from the ICU, the AKI incidence could only be recorded based on serum creatinine since the urine output is not routinely recorded on normal wards. For this reason, the serum creatinine-based incidence after ICU discharge was not included in the overall analysis. In addition, medication, including potential nephrotoxic medication, application of contrast media before and after cardiac surgery, vital sign course, and visit entries and transferring/discharge letters were reviewed. Two-hourly averaged MAP was recorded within the first 3 days after surgery to detect hypotensive circulatory conditions. Hyperglycemia was defined according to Meersch et al. [14] with blood glucose level ≥150 mg/dL for >3 h. Nephrotoxic drugs were defined according to Naugton [22], with substances like angiotensin-converting enzyme inhibitors (ACEis)/angiotensin receptor blockers (ARBs) and diuretics listed as extra items. Administration of antibiotics beyond post/perioperative prophylaxis was considered as infectious disease. For estimation of cardiac surgery and renal risk, the EuroScore II and Cleveland Clinic Score were used [23, 24].

Statistical Analysis

For group comparisons of baseline characteristics, categorical variables were analyzed using Fisher exact and χ^2 tests and for continuous variables using the t test and Mann-Whitney test, respectively, for normally and non-normally distributed variables. Statistical analysis was performed using Prism 9 (Version 9.0.2, GraphPad Software Inc., San Diego, CA, USA).

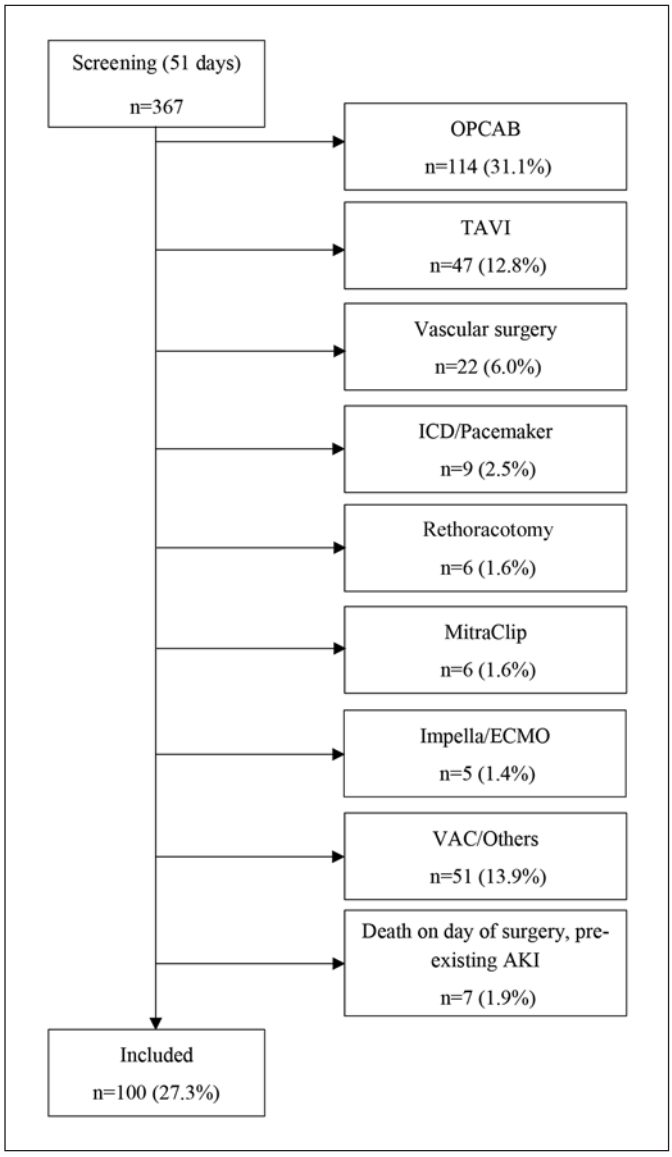

Fig. 1. Screening flow diagram of the study population according to in- and exclusion criteria to reach target number of cases (n = 100). ECMO, extracorporeal membrane oxygenation; ICD, implantable cardioverter defibrillator; OPCAB, off-pump coronary artery bypass; TAVI, transcatheter aortic valve implantation; VAC, vacuum-assisted closure therapy.

Results

Baseline Characteristics

In our cohort, the mean age was 68.2 years (95% confidence interval [CI]: 65.8–70.5), and 40% of patients were female. Subjects had a mean body mass index (BMI) of 26.6 kg/m^2 (95% CI: 25.8–27.4), which represents a mild preadipositas according to the definition of the World Health Organization. The median preoperative serum creatinine was 0.9 mg/dL (interquartile range [IQR]: 0.8–1.0) as pre-existing AKI was an exclusion criterion. The mean hospital stay was 14 days (95% CI: 12.8–15.9); thereof, patients had a mean stay on the ICU for 3 days (95% CI: 1.8–3.7). Regarding patient's comorbidities, most had arterial hypertension (73%) and about half had coronary artery disease (54%). Pre-existing chronic kidney disease (CKD) was evident in 46% of the patients; of these CKD patients, about half (21%) had CKD G3a (17%) or G3b (4%). Similarly, about half of the patients had chronic heart failure (CHF) (51%) but with only a small proportion of highly impaired left-ventricular ejection fraction (<35; 5%). In our cohort, 16% of the patients had acute infectious diseases with anti-infective therapy

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Table 1. Characteristics/outcomes between different AKI and non-AKI groups

n	Total 100	Non-AKI 48	AKI 52	*p* value[1]	Noncoded AKI 40	*p* value[1]	Coded AKI 12	*p* value[1]	*p* value[2]
Age, years (mean) 95% CI	68.2 65.8–70.5	66.6 63.2–70.0	69.6 66.3–72.8	0.21	69.3 65.8–73.4	0.29	70.2 62.3–77.0	0.33	0.87
Gender w, *n* (%)	40 (40.0)	18 (37.5)	22 (42.3)	0.69	17 (42.5)	0.67	5 (41.7)	0.99	0.99
Height, cm (mean) 95% CI	172 171–174	173 170–175	172 169–175	0.86	173 169–176	0.96	171 164–178	0.46	0.53
Weight, kg (mean) 95% CI	79.2 76.5–81.9	77.0 72.8–81.1	81.3 77.7–84.8	0.12	82.3 78.3–86.2	0.07	77.1 68.6–87.1	0.98	0.21
BMI, kg/m^2 (mean) 95% CI	26.6 25.8–27.4	25.7 24.6–26.8	27.4 26.3–28.6	0.03*	27.6 26.4–28.8	0.02*	26.8 23.1–30.5	0.41	0.58
Serum creat. pre-op, mg/dL (median) IQR	0.90 0.80–1.00	0.90 0.80–1.00	0.95 0.80–1.10	0.54	0.90 0.80–1.08	0.68	1.00 0.80–1.10	0.47	0.69
Dialysis (in-hospital), *n* (%)	7 (7.0)	0 (0.0)	7 (13.5)	0.01#	0 (0.0)	0.99	7 (58.3)	<0.0001#	<0.0001#
Death (in-hospital), *n* (%)	5 (5.0)	0 (0.0)	5 (9.6)	0.06	0 (0.0)	0.99	5 (41.7)	0.0001#	0.0003#
LoS, days (mean) 95% CI	14.3 12.8–15.9	13.7 11.5–15.8	15.0 12.6–17.3	0.41	13.6 11.6–15.6	0.99	23.3 11.4–27.6	0.01*	0.008*
ICU stay, days (mean) 95% CI	2.8 1.8–3.7	1.5 1.1–1.9	3.9 2.3–5.6	0.004*	2.2 1.4–3.0	0.12	9.2 3.7–16.0	<0.0001*	<0.0001*
% of ICU days of LoS, % (median) IQR	11.1 7.7–23.0	10.0 6.8–13.8	13.0 7.8–28.9	0.03*	11.0 7.1–23.2	0.42	42.0 21.8–96.9	0.0002*	<0.0001*
Revenue per day, € IQR	1,628 1,188–2,079	1,628 1,104–2,057	1,611 1,201–2,079	0.44	1,513 1,207–2,031	0.85	2,078 1,145–3,107	0.23	0.35
AKI stage 1, *n* (%)	31 (31.0)	0 (0.0)	31 (59.6)	<0.0001#	29 (72.5)	<0.0001#	2 (16.7)	0.04#	0.004#
AKI stage 2, *n* (%)	10 (10.0)	0 (0.0)	10 (19.2)	0.001#	10 (25.0)	0.0002#	0 (0.0)	0.99	0.09
AKI stage 3, *n* (%)	11 (11.0)	0 (0.0)	11 (21.2)	0.0006#	1 (2.5)	0.46	10 (83.3)	<0.0001#	<0.0001#
CPB, min (median) IQR	129 101–164	122 101–152	138 102–174	0.20	128 98–173	0.49	151 118–179	0.12	0.38
Aortic cross-clamp, min (median) IQR	85 70–100	83 72–100	91 68–104	0.69	90 66–100	0.85	92 70–111	0.78	0.78
Ventilation, h (Median) IQR	4.0 2.0–8.8	3.0 2.0–5.8	5.0 2.0–13.5	0.06	3.5 1.0–7.8	0.51	13.0 5.0–41.0	<0.0001*	0.003*
EuroScore II (median) IQR	2.57 1.45–6.24	1.76 1.15–5.37	3.43 1.79–7.71	0.02*	2.65 1.57–4.44	0.24	15.33 4.91–39.6	<0.0001*	<0.0001*
Cleveland clinic score (median) IQR	3 2–4	2 2–3	3 2–4	0.41	2 2–3	0.70	4 3–5	0.0005*	0.0007*
Infectious disease, *n* (%)	16 (16.0)	7 (14.6)	9 (17.3)	0.79	3 (7.5)	0.34	6 (50.0)	0.02#	0.003#
Art. hypertension, *n* (%)	67 (67.0)	35 (72.9)	32 (61.5)	0.29	21 (52.5)	0.07	11 (91.7)	0.26	0.02#
Diabetes mellitus, *n* (%)	14 (14.0)	4 (8.3)	10 (19.2)	0.15	7 (17.5)	0.22	3 (25.0)	0.14	0.68
Coronary artery disease, *n* (%)	54 (54.0)	23 (47.9)	31 (59.6)	0.32	23 (57.5)	0.40	8 (66.7)	0.34	0.74
Peripheral art. occlusive disease, *n* (%)	6 (6.0)	1 (2.1)	5 (9.6)	0.21	2 (5.0)	0.59	3 (25.0)	0.02#	0.07
CKD, *n* (%)	46 (46.0)	18 (37.5)	28 (53.8)	0.11	22 (55.0)	0.13	6 (50.0)	0.52	0.99
CKD G3, *n* (%)	21 (21.0)	6 (12.5)	15 (28.9)	0.05	11 (27.5)	0.11	4 (33.3)	0.10	0.73
CHF, *n* (%)	51 (51.0)	23 (47.9)	28 (53.8)	0.69	18 (45.0)	0.83	10 (83.3)	0.05	0.02#
LV-EF <35%, *n* (%)	5 (5.0)	3 (6.3)	2 (3.9)	0.67	0 (0.0)	0.25	2 (16.7)	0.26	0.05

Overview of baseline, clinical, and outcome data depending on the presence of acute kidney injury in total, noncoded, or coded AKI compared with the non-AKI group. AKI, acute kidney injury; art., arterial; BMI, body mass index; CHF, chronic heart failure; CKD, chronic kidney disease; CPB, cardiopulmonary bypass; cm, centimeter; creat., creatinine; €, Euro; ICU, intensive care unit; IQR, interquartile range; kg, kilogram; LV-EF, left-ventricular ejection fraction; *n*, sample size; LoS, length of stay; PiCCO, pulse-contour cardiac output; w, women; 95% CI, 95% confidence interval. * $p < 0.05$ (*t* test or Mann-Whitney test for normally or non-normally distributed variables, respectively). # $p < 0.05$ (Fisher's exact test or χ^2 test for normally or non-normally distributed variables, respectively). [1] *p* value versus non-AKI. [2] *p* value versus noncoded AKI.

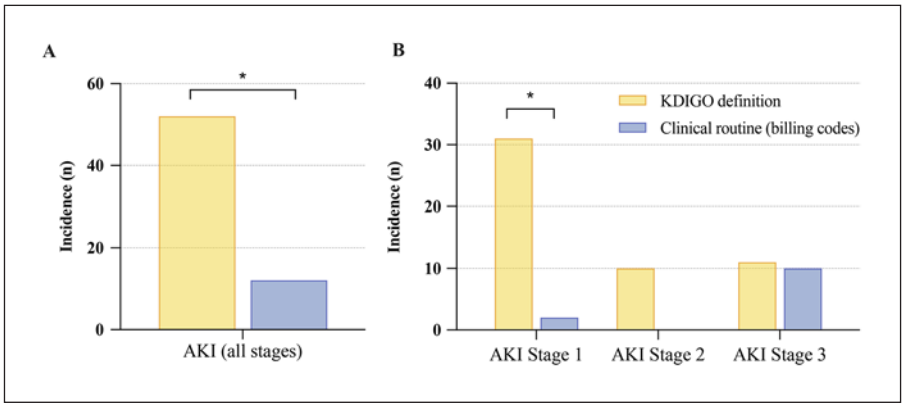

Fig. 2. Comparison of the incidence (*n*) of actually identified AKI according to the KDIGO definition and AKI coded in clinical routine after cardiac surgery. All AKI stages (**A**), broken down by AKI stage (**B**). AKI, acute kidney injury; KDIGO, Kidney Disease: Improving Global Outcomes. *$p < 0.05$.

beyond the routine perioperative prophylaxis. The proportion of peripheral arterial occlusive disease was low (6%). Median preoperative risk scores were 2.57 (IQR: 1.45–6.24) for EuroScore II and 3 (IQR: 2–4) for Cleveland Clinic Score.

Intraoperatively, patients had a median CPB time of approximately 2 h (129 min) (IQR: 101–164) and an aortic cross-clamp of 1.5 h (85 min) (IQR: 70–100). Postoperatively, the median duration of ventilation was 4 h (IQR: 2.0–8.8). For further details, concerning baseline parameters see Table 1.

Incidence of AKI according to the International Definition versus Coded AKI

Of $n = 100$ patients, $n = 52$ (52%) developed AKI during ICU stay after surgery according to the international definition of KDIGO [19]. The distribution of AKI stages was as follows: 31 patients developed stage 1 (59.6%), 10 had stage 2 (19.2%), and 11 had stage 3 (21.2%). In contrast, however, the actually coded incidence of all AKI stages was only $n = 12$ (12%). This corresponds to a coding rate of only 23.1% of the real incidence ($p < 0.0001$) in the present cohort (see Table 2 and Fig. 2).

In 4 (33.3%) of the coded AKI, an incorrect stage was documented. Severe AKIs (stage 3) are coded with the highest reliability (90.9%), whereas AKI stage 2 was documented with the lowest reliability (0.0%). Thus, in this cohort, a pronounced undercoding and, to a lesser extent, miscoding could be noticed.

Serum creatinine-based AKI incidence in the normal ward after ICU discharge was $n = 35$ (35%); of those, $n = 21$ (21%) had already an AKI episode during ICU stay, whereas $n = 14$ (14%) had their first AKI episode in the normal ward. Of the latter, all had AKI stage 1.

Table 2. Discrepancy of real and coded AKI incidence

AKI stage	AKI incidence, *n*	Coded AKI, *n*	KDIGO, %
Stage 1	31	2	6.5
Stage 2	10	0	0.0
Stage 3	11	10	90.9
Total	52	12	23.1

Comparison of actually identified acute kidney injury according to the KDIGO classification of 2012 and acute kidney injury coded in clinical routine. AKI, acute kidney injury; KDIGO, Kidney Disease: Improving Global Outcomes.

Cohort Comparisons

For comparisons of patient's characteristics, our cohort was divided into different (sub-) groups (see Table 1): AKI and non-AKI group and the AKI-subgroup "noncoded" and "coded" as described in the previous section. Various group comparisons were made: on the one hand, all AKI-groups (including subgroups) with the non-AKI group (p value with the note digit "[1]" in Table 1), and on the other hand, the AKI subgroups among themselves (p value with the note digit "[2]" in Table 1).

Not surprisingly, dialysis requirement and in-hospital death were higher in the AKI group. Patients with AKI had significantly longer ICU stays ($p = 0.004$) and a significantly higher percentage of ICU days of total hospital stay ($p = 0.03$). Furthermore, the AKI group had higher risk scores and ventilation time in the ICU. Significant differences between AKI and non-AKI group were primarily driven by the "coded" subgroup, with the exception of BMI. In coded AKI also, peripheral arterial occlusive disease and infectious diseases had a significant higher prevalence as pre-existing conditions (both $p = 0.02$). Noncoded AKI did not differ significantly in baseline

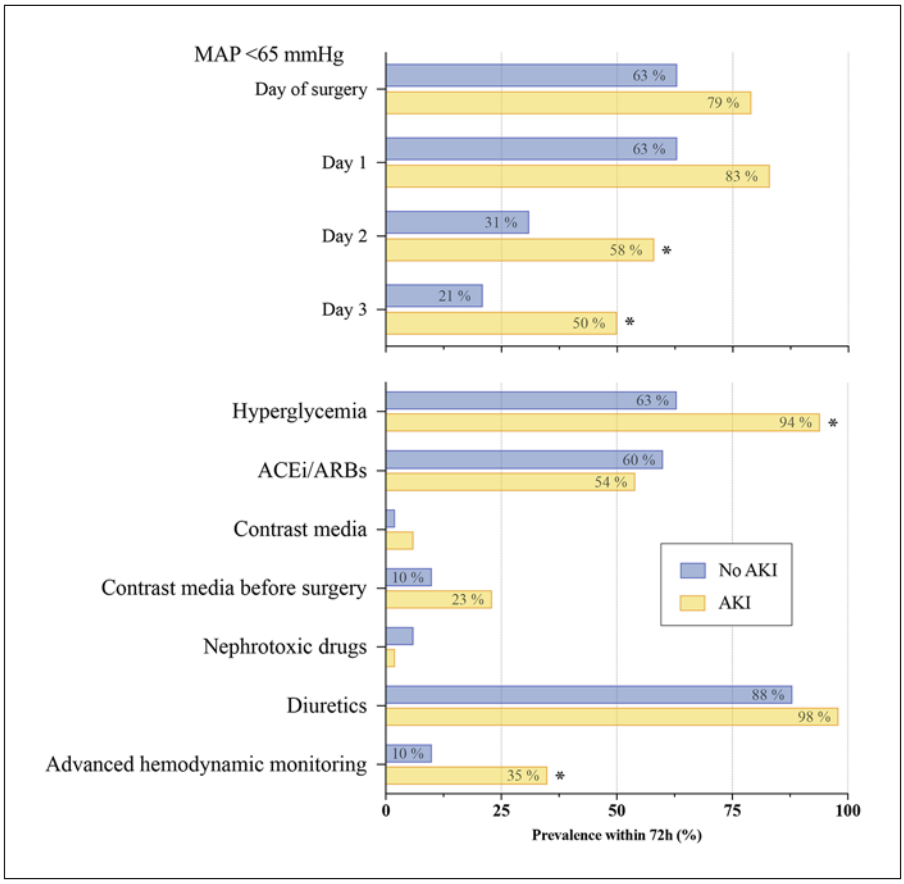

Fig. 3. Prevalence of parameters (%) within 72 h after cardiac surgery, mentioned in KDIGO recommendations to be optimized to prevent/treat AKI. Definitions: MAP <65 mm Hg: at least 1 episode over 2 h. Hyperglycemia: blood glucose level ≥150 mg/dL >3 consecutive hours. *$p < 0.05$. ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin receptor blocker; KDIGO, Kidney Disease: Improving Global Outcomes; MAP, mean arterial pressure.

characteristics, comorbidities, surgical parameters, and risk scores from non-AKI, with the exception of BMI, which was significant higher in the noncoded group ($p = 0.02$; see Table 1).

Conformity with KDIGO Recommendations

Conformity with KDIGO recommendations was evaluated with parameters, of which most were applied in the previous studies [14, 21] and mentioned in the introduction (item 1–6). To evaluate "(1) optimization of volume status and hemodynamics," we reviewed the documented MAP. An episode with an average MAP of <65 mm Hg over 2 h was considered to be an inadequate hemodynamic condition. Interestingly, 90% of all patients had at least 1 episode within the first 72 h after surgery. Thereof, 70% of patients had such an episode on the day of surgery with decreasing frequency over the following days (see Fig. 3 and Table 3). The percentage of all MAP values <65 mm Hg was significantly higher in the AKI group on the day of surgery than in the non-AKI group (30% vs. 18%, $p = 0.008$), and the incidence of episodes with MAP <65 mm Hg between AKI and non-AKI groups were clearer on postoperative day 2 and 3 with significantly higher rates in the AKI group (day 2: 19% vs. 9%, $p = 0.02$ and day 3: 15% vs. 5%, $p = 0.007$).

For evaluation of "(2) stopping of nephrotoxic drugs," in our study, potential nephrotoxic agents were broken down into ACEis/ARBs, "true" nephrotoxic drugs (e.g., gentamicin and vancomycin), and diuretics. In 55% of patients, ACEis/ARBs were administered during the first 72 h after cardiac surgery, with no significant differences noted between groups. The rate of "true" nephrotoxic drugs was low (4%). Almost all patients received diuretics (89%).

Regarding "(3) avoidance of hyperglycemia" and "(4) avoidance of radiocontrast media," hyperglycemia over at least 3 h occurred in 75% of patients, with significant higher rates in the AKI group (87% vs. 63%, $p = 0.01$), during the first 72 h after surgery. The number of patients receiving contrast media after surgery was low (4%), thereof, the coded group received significantly more contrast media than the noncoded group (25% vs. 0%, $p = 0.01$). Sixteen percentage of patients had contrast media within 72 h before surgery with no differences between groups (see Fig. 3).

Table 3. Postoperative management

n	Total 100	Non-AKI 48	AKI 52	*p* value[1]	Noncoded AKI 40	*p* value[1]	Coded AKI 12	*p* value[1]	*p* value[2]
MAP <65 mm Hg, *n*[§] (%)	90 (90.0)	42 (87.5)	48 (92.3)	0.51	36 (90.0)	0.75	12 (100.0)	0.33	0.56
Day of surgery	68 (68.0)	30 (62.5)	38 (73.1)	0.29	29 (72.5)	0.37	9 (75.0)	0.51	0.99
Percentage of all MAP values	23.9	17.5	29.9	0.008*	27.3	0.03*	39.2	0.02*	0.31
Day 1	70 (70.0)	30 (62.5)	40 (76.9)	0.13	31 (77.5)	0.17	9 (75.0)	0.51	0.99
Percentage of all MAP values	23.8	20.7	26.6	0.17	26.1	0.20	28.5	0.38	0.86
Day 2	43 (43.0)	15 (31.3)	28 (53.9)	0.03#	17 (42.5)	0.37	11 (91.7)	0.0002#	0.003#
Percentage of all MAP values	14.1	9.1	18.8	0.02*	15.1	0.20	30.4	0.0001*	0.01*
Day 3	34 (34.0)	10 (20.8)	24 (46.2)	0.01#	13 (32.5)	0.23	11 (91.7)	<0.0001#	0.0005#
Percentage of all MAP values	10.0	5.1	14.5	0.007*	10.6	0.17	26.6	<0.0001*	0.003*
Hyperglycemia[$], *n* (%)	75 (75.0)	30 (62.5)	45 (86.5)	0.01#	35 (87.5)	0.01#	10 (83.3)	0.30	0.66
ACEis/ARBs, *n* (%)	55 (55.0)	29 (60.4)	26 (50.0)	0.32	22 (55.0)	0.67	4 (33.3)	0.11	0.32
Contrast media, *n* (%)	4 (4.0.)	1 (2.1)	3 (5.8)	0.62	0 (0.0)	0.99	3 (25.0)	0.02#	0.01#
Contrast media before surgery, *n* (%)	16 (16.0)	5 (10.4)	11 (21.2)	0.18	7 (17.5)	0.37	4 (33.3)	0.07	0.25
Nephrotoxic drugs, *n* (%)	4 (4.0)	3 (6.3)	1 (1.9)	0.35	0 (0.0)	0.25	1 (8.3)	0.99	0.23
Diuretics, *n* (%)	89 (89.0)	42 (87.5)	47 (90.4)	0.75	35 (87.5)	0.99	12 (100.0)	0.33	0.58
Advanced hemodynamic monitoring[+], *n* (%)	22 (22.0)	5 (10.4)	17 (32.7)	0.008#	8 (20.0)	0.24	9 (75.0)	0.007#	0.0008#
Subclavian dialysis catheter, *n* (%)	3/7 (42.0)	0 (0.0)	3 (5.8)	0.24	0 (0.0)	0.99	3 (25.0)	0.006#	0.01#

Postoperative management of cardiac surgery patients within 72 h after surgery with CPB. ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin receptor blocker; MAP, mean arterial pressure; *n*, sample size; CPB, cardiopulmonary bypass. [§] With at least 1 episode of an average MAP <65 mm Hg over 2 h. [$] Blood glucose level ≥150 mg/dL >3 consecutive hours. [+] PiCCO-catheter. * $p < 0.05$ (*t* test or Mann-Whitney test for normally and non-normally distributed variables, respectively). # $p < 0.05$ (Fisher's exact test). [1] *p* value versus non-AKI. [2] *p* value versus noncoded AKI.

The presence of a pulse-contour cardiac output-catheter, commonly used in our institution, was counted as "(5) functional hemodynamic monitoring." This form of extended hemodynamic monitoring was applied in 22%, with use occurring significantly more often in the AKI group (33% vs. 10%, $p = 0.008$). Regarding all nonhemodynamic parameters together (hyperglycemia, ACEis/ARBs, contrast media after surgery, and nephrotoxic drugs, excluding diuretics), only 10 patients (20.8%) in the non-AKI group and $n = 5$ (9.6%) in the AKI group were free of all the above factors. In addition, 3 of the 7 patients requiring KRT during their hospitalization had a dialysis catheter in the subclavian vein, which should be avoided whenever possible following the KDIGO recommendations.

Discussion

To our knowledge, this is the first analysis evaluating the coded-AKI incidence compared to the KDIGO-defined incidence including urine output criteria in conjunction with analysis of postoperative conformity with KDIGO recommendations. In our cohort, we could demonstrate 2 important issues: (1) we found a considerable discrepancy between coded and real incidence of AKI and (2) the conformity with KDIGO recommendations regarding AKI prevention was found to be relatively low.

The observed pronounced discrepancy between the real AKI incidence and coded incidence could have several consequences, medical as well as economic ones. Such undercoding, probably representing under-recognition, has recently been described in the literature: Khadzhynov et al. [20] demonstrated in a large retrospective study that in only 27.8% of cases with laboratory-confirmed AKI, an AKI diagnosis (ICD-10-GM code: N17) was coded. In this study, however, only serum creatinine-based AKIs were evaluated since not all wards (especially nonmonitored wards) recorded the urine output on an hourly basis. The percentage of coded AKI in our cohort (23.1%) was about within the similar range as the study by Khadzhynov et al. [20], with the difference that the urine output was included in our cohort and their analysis comprised not exclusively surgical patients. This could explain the slightly lower percentage in our analysis.

A low-coded incidence may indeed indicate low recognition of AKI because coding is usually based on diagnoses in discharge/transfer letters, visit entries, and medical records. The recognition of AKI is a fundamental cor-

nerstone for all further measures to prevent and treat AKI. Thus, appropriate interventions can only be successfully implemented if there is an adequate AKI awareness.

For many years, AKI was dismissed as harmless, and renal function deterioration was not declared relevant for further prognosis. At least low AKI stages (especially stage 1) were not considered clinically relevant until recently. But in the past 2 decades, however, studies have shown that serum creatinine increases of 0.3–0.4 mg/dL, corresponding to AKI stage 1, already raising the mortality risk by a factor of 1.7-fold [25]. Thus, it became clear that even AKI stage 1 is associated with an impaired prognosis and should be recognized and prevented. In our cohort, especially lower AKI stages were undercoded, with a rate of uncoded AKI stage 1 of 93.9%.

Furthermore, whether AKI is coded or noncoded appears to have also prognostic implications: Wilson et al. [26] described in a cohort adjusted for case severity that noncoded AKI was associated with increased mortality. This reinforces the medical necessity of recording all AKI according to the current definition in order to avert negative prognostic consequences for the patient by underrecognition or undercoding.

Beyond the medical consequences, undercoding may also have significant economic implications: it has been demonstrated that even a slight deterioration in serum creatinine (e.g., +0.3 to +0.4) leads to considerable cost increases, even in a population which most likely received no KRT (which is commonly known to be associated with significant additional costs) [25, 27]. However, this higher resource consumption is not taken into account in the German Diagnosis Related Groups (DRG)-reimbursement system by means of a flat charge after cardiac surgery since the additional diagnosis of AKI does not generate additional revenue.

Regarding our cohort, AKI patients had a significantly higher ICU LoS and a higher proportion of ICU days of total length of hospital stay. This is consistent with the previous literature where AKI was associated with increased resource expenditures [25]. A longer hospital and ICU stay seems to be the decisive factor here as the revenue per day in hospital does not differ significantly.

There are clear differences between noncoded and coded AKI in the collectives, which have already been evident to some extent in the overall comparison of AKI versus non-AKI: there are highly significant differences for ICU LoS, hospital LoS, need for dialysis, and mortality. This is not surprising as the coded group had a significantly higher prevalence of AKI stage 3 (83.3% vs. 2.5%), which is known to be associated with a worse outcome [28].

In our cohort, postoperative management was considered strictly from a renal perspective according to KDIGO recommendations and not from a cardiac surgery point of view. These KDIGO recommendations include measures for preventing or managing AKI [19]. These measures can certainly not be applied to all patients for reasons of personnel and time, but they should also be applied to high-risk patients without manifest AKI [19]. It has been demonstrated that application of KDIGO measures to high-risk surgical patients reduces AKI incidence or AKI severity [14, 29, 30]. In our cohort, we recognized that conformity to KDIGO recommendations was not optimal as parameters which promote AKI are relatively high: 90% of all patients had at least one 2-h-episode with MAP <65 mmHg within the first 72 h after surgery postoperative and significant higher rates of such episodes on day 2 and 3 in the AKI group. Hereby, we prove that higher rates of episodes with MAP <65 mm Hg are associated with AKI. Furthermore, regarding all other preventive parameters together (avoiding hyperglycemia, stopping ACEis/ARBs, avoiding contrast media, and nephrotoxic drugs), only 10 patients (20.8%) in the non-AKI group and 5 (9.6%) subjects in the AKI group had none of all the above factors.

This means that from a renal perspective, especially the cohort with AKI but also the non-AKI group received suboptimal kidney care. Low conformity with guidelines is by far not a problem of an individual center and becomes clear when looking into the existing literature. This is in accordance to an observational multicenter study by Küllmar et al. [21]. In their study, they showed that in 12 European centers, compliance with KDIGO recommendations is low in routine clinical practice. In only 5.3% of patients, postoperative management was entirely compliant with all parameters of the bundle [21]. On an average, patients received approximately 50% of the supportive measures recommended by KDIGO. However, the observation of low compliance with guidelines can also be made in other fields of intensive care medicine. In general, compliance rates with guidelines ranges with a percentage from almost zero to two-thirds in an intensive care setting, with a decrease in adherence as the number of measures increases [31]. Even for very important intensive care topics such as sepsis management, there does not appear to be good guideline adherence [31], and also on matters relevant to cardiac surgery, such as perioperative antibiotic prophylaxis, low guideline adherence was described [32, 33]. In contrast, it has

been shown that compliance with AKI care bundles is associated with better outcomes, for example, reduced AKI progression or case fatality [34].

Certainly, strict adherence to KDIGO recommendations is not completely free of risk. For example, overly ambitious glycemic control in critically ill patients can also lead to potentially dangerous hypoglycemia [35]. Likewise, thrombotic or infectious complications of additionally installed advanced hemodynamic monitoring may occur. It is also possible that concerns about postoperative bleeding in our collective may have led to suboptimal MAP levels on the day of surgery.

Nevertheless, there is certainly room for some optimization in the postoperative management of cardiac surgery patients to prevent AKI. Possible measures could include team training, AKI alerts in conjunction with treatment bundles, or identification of high-risk patients with biomarkers, in order to also achieve increased AKI awareness.

However, our study has some limitations. Due to its retrospective design, we cannot prove causality. Furthermore, we cannot definitively distinguish whether AKI is a cause or consequence of severe disease after cardiac surgery. In addition, as a single-center study, we cannot generalize the results, although the latter is consistent with the multicenter study by Küllmar et al [21].

Conclusions

In conclusion, from a medical and economic perspective, there is still a great need for the optimization of AKI as little progress has been made in terms of therapy and prevention for quite some time. New biomarker-based intervention trials offer hope in cardiac surgery as they describe AKI incidence reduction. However, it also became clear that AKI recognition in everyday clinical routine seems to be low, especially in lower AKI stages, and the current postoperative management still offers room for optimization. Possibly, higher AKI awareness and stricter postoperative management could already achieve significant effects in prevention and treatment of AKI beyond biomarkers.

Certainly, in ICU settings with a constantly high workload, some intensivists will retort there may be subjectively more important acute problems than observation of small renal changes. In addition, it is sometimes difficult to notice even slight serum creatinine fluctuations or even a slight decrease in the urine output in clinical routine. Nevertheless, a preventive approach in an intensive care setting seems much more worthwhile than constantly chasing problems. AKI alerts and biomarkers could certainly help to focus attention on renal changes despite many other intensive care tasks.

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Statement of Ethics

The study was reviewed and approved by the Ethics Committee of the University of Tübingen. Due to its retrospective design with appropriate criteria, no written informed consent was necessary (project number: 104/2020BO2).

Conflict of Interest Statement

Mark Dominik Alscher obtained lecture honoraria from Abbott and Roche. Martin Kimmel received lecture honoraria from Abbott, Roche, and Astute Medical. Markus Ketteler, Moritz Schanz, Oliver Schöffski, Severin Schricker, Tina Oberacker,Nora Göbel and Ulrich F. W. Franke have no conflicts of interest to declare.

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Author Contributions

Moritz Schanz, Oliver Schöffski, Martin Kimmel, Tina Oberacker, Nora Göbel, Ulrich F. W. Franke, Mark Dominik Alscher, Markus Ketteler, and Severin Schricker designed the study protocol, monitored data collection for the whole trial, cleaned and analyzed the data, and edited and discussed the article. Moritz Schanz, Nora Göbel, and Severin Schricker collected the data. Moritz Schanz, Martin Kimmel, Markus Ketteler, Severin Schricker, and Tina Oberacker cleaned and analyzed data and discussed results; monitored data collection, the data collection for the whole trial, the draft, and the statistical analysis; and edited and discussed the article. Moritz Schanz, Oliver Schöffski, Markus Ketteler, Mark Dominik Alscher, Markus Ketteler, Nora Göbel, and Ulrich F. W. Franke guided the research, designed the study protocol, and monitored the design of data collection tools. Moritz Schanz, Tina Oberacker, and Severin Schricker drafted the manuscript. All con-

tributors were substantially involved in the conception or design of the work, the acquisition, analysis, or interpretation of the data for the work; all the authors critically revised the intellectual content and the drafted manuscript, approved the final version of this draft, and are accountable for the aspects of the work.

Neither this manuscript nor substantial parts of it are under consideration for publication elsewhere, have been published, or made available elsewhere in a manner that could be construed as a prior or duplicate publication of the same content. The results presented in this article have not been published previously in whole or part, except in an abstract form.

Data Availability Statement

The data underlying this article will be shared on reasonable request to the corresponding author after internal board review.

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