Global Incidence and Outcomes of Adult Patients With Acute Kidney Injury After Cardiac Surgery: A Systematic Review and Meta-Analysis

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Objectives: **To estimate the global incidence and outcomes of acute kidney injury (AKI) after cardiac surgery in adult patients.**

Design: **A systematic review and meta-analysis.**

Setting: **Cardiac surgery wards.**

Participants: **Adult patients after cardiac surgery**

Interventions: **None.**

Measurements and Main Results: **The authors searched PubMed, Web of Science, Cochrane Library, OVID, and EMBASE databases for all articles on cardiac surgery patients published during 2004 to 2014. Meta-analyses were conducted to generate pooled incidence, mortality, ICU length of stay, and length of hospital stay. The authors also described the variations according to study design, criteria of AKI, surgical methods, countries, continents, and their economies. After a primary and secondary screen, 91 observational studies with 320,086 patients were identified. The pooled incidence rates of AKI were 22.3% (95% confidence interval [CI], 19.8 to 25.1) in total and 13.6%, 3.8%, and 2.7% at stages 1, 2, and 3, respectively, whereas 2.3% of patients received renal replacement therapy. The pooled short-term and long-term mortality were 10.7% and 30%, respectively, and increased along with the severity of stages. The pooled unadjusted odds ratio for short-term and long-term mortality in patients with AKI relative to patients without AKI was 0.144 (95% CI, 0.108 to 0.192, $p < 0.001$) and 0.342 (95% CI 0.287-0.407, $p < 0.001$), respectively. The pooled average ICU length of stay and length of hospital stay in the AKI group were 5.4 and 15 days, respectively, while they were 2.2 and 10.5 days in the no-AKI group.**

Conclusions: **AKI is a great burden for patients undergoing cardiac surgery and can affect short-term and long-term prognoses of these patients.**

KEY WORDS: cardiac surgery, coronary artery bypass grafting, cardiopulmonary bypass, acute kidney injury

APPROXIMATELY 2 MILLION cardiac surgeries are performed around the world each year,[1] and acute kidney injury (AKI) is one of the most serious postoperative complications. Unlike septic and other AKI, ischemia-reperfusion injury is the main cause of AKI after cardiac surgery, and use of contrast media, cardiac dysfunction, old age, and mechanical ventilation exacerbate it. Although there are various mechanisms to prevent or treat AKI, including renal protective drugs[2] and continuous renal replacement therapy,[3] most of them have yielded limited success. Therefore, AKI remains a serious consequence for patients undergoing cardiac surgery. However, if renal injury could be anticipated, preoperative risk factors could be identified, and AKI with variable severity could be correlated with outcomes during the postoperative period, the clinician still would have opportunities to improve outcomes in patients with AKI. It was therefore useful to review the varied incidence and outcomes of AKI after cardiac surgery according to degree of severity and other factors.

For many years, varying definitions of AKI have appeared in the literature, making comparisons among studies difficult. When AKI was defined as requiring renal replacement therapy, the incidence of AKI after cardiac surgery usually was low, 1.6%[4]∼5.8%[5], but the hospital mortality was high, up to 50%[5]∼66.7%.[4] When AKI was defined as a 50% decrease in estimated glomerular filtration rate, the frequency of AKI ranged between 5%[6] and 10%[7]. However, the Risk, Injury, Failure, Loss and End-stage Kidney (RIFLE)[8] and the Acute Kidney Injury Network (AKIN)[9] classification and staging systems have advanced this field, allowing improved comparisons among study populations. Recently, the Kidney Disease Improving Global Outcomes (KDIGO)[10] Clinical Practice Guidelines for Acute Kidney Injury provided a welcome and timely synthesis of the 2 criteria regarding the management of AKI.

The publication of studies using the RIFLE, AKIN, or KDIGO classification and staging systems over the past decade provided a good opportunity to generate a common view on the incidence of AKI and its associated outcomes. This review was conducted to estimate the global incidence and outcomes of AKI after cardiac surgery in adult patients and to describe the variations according to study designs, criteria for AKI, surgical methods, countries, continents, and their economies. This effort hoped to raise awareness of AKI after cardiac surgery around the world and to provide a resource for public health policies and clinical trials.

METHODS

Database Search

The authors performed a computerized search to identify relevant published original studies (2004 to December 2014). The year 2004 was selected because it corresponded to the year in which the RIFLE criteria were first published. PubMed, Web of Science, Cochrane Library, OVID, and EMBASE databases were searched using medical subject headings (MeSH) or keywords. These words were "acute kidney failure," "acute kidney injury," "acute kidney dysfunction," "acute kidney insufficiency," "acute tubular necrosis," "acute renal failure," "acute renal injury," "acute renal dysfunction," "acute renal insufficiency" and "cardiothoracic surgery, coronary artery bypass

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grafting," "cardiovascular surgical procedures," "cardiac surgery," as well as "incidence," "mortality," "prevalence," and "epidemiology." This search was not limited to English language or by publication type. Table 1 shows the numbers of studies found.

Study Selection

An initial eligibility screening of all retrieved titles and abstracts was conducted, and only studies reporting AKI after cardiac surgery were selected for further review. The following included criteria were used for final selection: (1) studies reporting the incidence or outcomes of AKI specifically after cardiac surgery, (2) studies showing clear definitions of AKI and its stages, using the criteria for RIFLE, AKIN, or KDIGO, and (3) studies enrolling more than 100 participants. The authors restricted their search to clinical studies performed in adult populations. Studies without explicit incidences and outcomes or experimental studies were excluded.

Data Extraction

Two reviewers (H.J.C. and C.R.Y.) independently examined the studies, and disagreement was resolved by discussion. Data extraction included country of origin, year of publication, study period, study design, sample size, patient characteristics (age and sex), surgery methods, definitions of AKI, the incidence of AKI and the associated outcomes, including short-term (in-hospital) mortality, long-term (1-5 years) mortality, renal recovery at discharge, ICU length of stay, and length of hospital stay. In this meta-analysis, the authors categorized the AKI definitions adopted in the individual studies by classifying them according to the RIFLE, AKIN, or KDIGO criteria, similar to a previous study.[11] Countries were grouped within continents and also divided into 4 categories according to the World Bank's classification of income of economies[12]: low; lower-middle; upper-middle; and high-income countries. Using the World Health Organization's world health statistics,[13] countries also were classified according to national total expenditure on health as a percentage of gross domestic product (GDP): $<5\%$, 5%-10%, and $>10\%$. The study selection, data extraction, and reporting of results were all based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.[14]

Quality Assessment

The quality of the cohort studies was assessed independently by pairs of 2 authors, using the Newcastle-Ottawa scale,[15]

Table 1. Characteristics of the 91 Studies Included in the Meta-Analysis

	All Studies	RIFLE Criteria	AKIN Criteria	KDIGO Criteria
No. of studies	91 (100)	51 (56)	34 (37)	6 (7)
No. of patients	3,517 (100-31,677)	3,243 (100-31,677)	4,315 (102-27,929)	1,328 (321-2,804)
Sample size	32,0086	165,402	146,718	7,966
Female (%)	31.7 (0.3-62.5)	24.1 (0.3-62.5)	34.6 (12.3-60.3)	36.5 (28.8-56.4)
Age of participants (y)	60.1 (44.0-88.2)	53.3 (44.0-88.2)	67.6 (53.0-84.3)	77.2 (63.7-82.0)
Study design				
Retrospective cohort	61 (67)	35 (38)	23 (25)	3 (3)
Prospective cohort	27 (30)	14 (15)	11 (12)	2 (2)
Others	3 (3)	2 (2)	0 (0)	1 (1)
Sample size				
$<1,000$	44 (48)	25 (27)	17 (19)	2 (2)
1,000-10,000	38 (42)	21 (23)	13 (14)	4 (4)
$>10,000$	9 (10)	5 (5)	4 (4)	0 (0)
Cardiac surgery				
CABG	22 (24)	11 (12)	11 (12)	0 (0)
Mixed with CABG	51 (56)	29 (32)	16 (18)	6 (7)
Other	18 (20)	11 (12)	7 (8)	0 (0)
Studies by continent				
Africa	1 (1)	1 (1)	0 (0)	0 (0)
Asia	17 (19)	7 (8)	9 (10)	1 (1)
Europe	37 (41)	22 (24)	14 (15)	1 (1)
North America	23 (25)	17 (19)	4 (4)	2 (2)
Oceania	10 (1)	2 (2)	8 (9)	0 (0)
South America	5 (5)	1 (1)	2 (2)	2 (2)
Multi-continents	1 (1)	1 (1)	0 (0)	0 (0)
Country income				
Lower middle income	1 (1)	1 (1)	0 (0)	0 (0)
Upper middle income	18 (20)	7 (8)	8 (9)	3 (3)
High income	71 (78)	42 (46)	26 (3)	3 (3)
Country total health expenditure (% of GDP)				
<5	1 (1)	1 (1)	0 (0)	0 (0)
5-10	48 (53)	25 (27)	19 (2)	4 (4)
>10	41 (45)	24 (26)	15 (16)	2 (2)

NOTE. Data are presented as the mean (range) or n (%).

Abbreviations: AKIN, acute kidney injury network; CABG, coronary artery bypass grafting; GDP, gross domestic product; KDIGO, Kidney Disease Improving Global Outcomes; RIFLE, Risk, Injury, Failure, Loss, and End-stage kidney.