Meta-Analysis

Clinical Characteristics and Outcomes of Community-Acquired versus Hospital-Acquired Acute Kidney Injury: A Meta-Analysis

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Keywords

Acute kidney injury · Community-acquired · Hospital-acquired · Clinical characteristics

Abstract

Background: The different clinical characteristics of community-acquired acute kidney injury (CA-AKI) versus hospital-acquired AKI (HA-AKI) have remained inconclusive, and thus, a meta-analysis was conducted to summarize and quantify the clinical significance distinguishing the 2 types of AKI. **Methods:** We identified observational studies reporting the clinical characteristics and prognosis of HA-AKI and CA-AKI. ORs and mean differences (MDs) were extracted for each outcome and the results aggregated. The primary outcome was defined as the mortality rate; renal recovery, oliguria incidence, dialysis, intensive care unit (ICU) requirement, and length of hospital stay were secondary outcomes. **Results:** Fifteen eligible studies involving 46,157 patients (22,791 CA-AKI patients and 23,366 HA-AKI patients) were included. Mortality was significantly lower in CA-AKI than in HA-AKI patients, with an OR of 0.43 (95% CI 0.35–0.53). The incidence of oliguria and need for ICU were also lower in CA-AKI patients (OR 0.58, 95% CI 0.38–0.88; OR 0.24, 95% CI 0.14–0.40, respectively). CA-AKI patients had a shorter hospital stay (MD –9.42, 95% CI –13.73 to –5.12). The renal recovery rate and dialysis need between CA- and HA-AKI were similar (OR 1.27, 95% CI 0.53–3.02; OR 1.05, 95% CI 0.82–1.34, respectively). **Conclusions:** CA-AKI showed better clinical manifestations with a lower incidence of oliguria, reduced risk of ICU treatment, and shorter hospital stay. Mortality associated with CA-AKI was lower compared with HA-AKI, indicating a better prognosis. The rate of renal recovery and need for dialysis showed no significant difference between the 2 groups.

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Introduction

Acute kidney injury (AKI) is a syndrome characterized by a rapid loss of kidney function and clinically diagnosed by the accumulation of nitrogenous metabolites (urea and creatinine), decreased urine output, or both [1–6]. It was first recognized during the air raids over London decades ago and is still a major contributor to poor patient outcomes, currently occurring in approximately 13.3 million people per year [7, 8].

Hospital-acquired AKI (HA-AKI) has long been a research focus, especially in the intensive care unit (ICU) [9]. In 1991, Kaufman et al. [10] reported patients who had presented acutely increased serum urea and creatinine levels at admission to hospital and initiate the diagnosis of community-acquired AKI (CA-AKI). With improving diagnostic and therapeutic modalities and the rapidly aging population worldwide, the incidence of AKI has been reported to be rising, and CA-AKI seems to dominate [11]. Nevertheless, confirmed epidemiological data for AKI are scarce, and the available data vary among regions and countries [12]. Loo and Zainal [13] reported 2 AKI patients per 1,000 admissions based on data from a single hospital in Malaysia. Studies conducted in southern Saudi Arabia and North India reported an AKI incidence upon hospitalization of approximately 0.6% [14, 15]. A systematic review of large cohort studies provided an AKI world incidence estimate of 1 in 5 adults and 1 in 3 children during hospital care [16]. In Taiwan, the incidences of CA-AKI and HA-AKI were separately calculated as 17.25 and 8.14 per 1,000 admissions, and the annual rate of CA-AKI was increasing, while that of HA-AKI was maintained [17]. A large cross-sectional study conducted in China indicated that CA-AKI patients made up 54.4% of all hospitalized AKI patients [18].

The differences in clinical characteristics between CA-AKI and HA-AKI patients are controversial. Similar long-term sequelae of CA-AKI and HA-AKI patients, such as renal disease progression and mortality, have been reported, while higher mortality has been observed for CA-AKI patients [19, 20]. Xu et al. [5] reported that the dialysis requirement rate for CA-AKI was 4.5%, which was significantly higher than that for HA-AKI of 3.5% ($p < 0.001$). Hsu et al. [17] reported the opposite result, with a dialysis rate of 2.06% for HA-AKI compared with 1.45% for CA-AKI ($p < 0.001$). Thus, it has become necessary to conduct a study that compares the characteristics of CA- and HA-AKI to show the complete landscape of their difference. Moreover, the application of different criteria in published studies for the diagnosis of AKI complicate data comparisons [16, 21, 22]. Thus, here we attempted to surmount the above-mentioned possible obstacles to summarize and provide comprehensive and convincing evidence.

The present meta-analysis aims to comprehensively quantify and classify the differences in CA- and HA-AKI patients both in demography, the degree of need for clinical care, and prognosis, especially in mortality and renal recovery, which will be helpful for evidence-based clinical decision-making.

Methods

We conducted a comprehensive search of the medical literature using PubMed, EMBASE, Cochrane, and Web of Science from their inception to January 2019. The PubMed search terms (both as medical subject headings and free text terms) were as follows: (CA-AKI) and (HA-AKI). We additionally searched the reference lists of the original reports, reviews, guidelines, and meta-analyses retrieved through the electronic searches. Only publications in English were retrieved.

We selected the studies in 2 steps. First, 2 review authors (L.H. and J.X.) independently screened the titles and abstracts. Second, the full texts of potentially eligible studies were retrieved and assessed independently by the same 2 authors. The pre-specified eligibility criteria were as follows: (1) observational studies, either retrospective or prospective studies; (2) mentioned both CA-AKI and HA-AKI patients; (3) made comparisons between CA and HA-AKI patients; (4) mentioned clinical characteristics, particularly mortality. Studies using other observational methods were eligible as long as there were comparable data related to both CA and HA-AKI patients. We excluded studies with the following properties: (1) case report; (2) studies focusing on pediatric patients; (3) mono-drug-induced AKI. We identified 2 articles that used the same patient samples, and we included the 1 with the most relevant information [23, 24]. Any disagreement between review authors was resolved by consensus, adjusted with the support of a third review author (C.X.).

Data Extraction

Two authors (L.H. and M.R.) extracted all data independently into a predesigned data collection form (Microsoft Office Excel 2010; Microsoft Corp, Redmond, WA, USA). A third review author (Z.M.) checked all the extracted data. The following data were extracted for each study: study design; geographical setting of the study; follow-up year; sample size; patient characteristics (age; proportions of male and female patients; and AKI stages); detailed relevant medical management; duration of hospital stay; and number of patients along with detailed information about the clinical characteristics and prognosis. We defined our primary outcome as the mortality of CA and HA-AKI patients. As renal recovery compromises the prognosis of AKI patients, it was combined as a secondary outcome; oliguria occurrence, dialysis need, ICU specialized care, and length of hospital stay were also analyzed as secondary outcomes. We attempted to contact the original investigators to obtain further information if necessary.

Assessment of the Risk of Bias

Assessment of the risk of bias was performed independently by 2 review authors (J.K. and C.X.), with disagreements resolved by discussion. Risks of bias ratings for each study were evaluated according to the quality domains in the Cochrane risk of bias tool Nosgen-ranking. Risk of bias for each domain was rated as high (seriously weakens confidence in the results), unclear, or low (unlikely to seriously alter the results).

Data Synthesis and Statistical Analysis

For retrospective studies, heterogeneity among studies was evaluated by calculating the I^2 statistic and chi-square test (assessing the p value). If the p value was <0.10 and I^2 exceeded 50%, we considered the heterogeneity substantial. We used the random effects model to combine data with substantial heterogeneity among studies. We summarized dichotomous data for patient properties as the OR. Continuous data were pooled as the mean difference (MD) with 95% CIs. We conducted pre-specified subgroup analyses according to the baseline properties and prognosis of the subjects. Sensitivity analyses were carried out by excluding outliers and studies with a small sample size to test the stability of our results.

Review Manager version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012) was used to generate forest and funnel plots. The funnel plots were assessed for evidence of asymmetry and other small study effects. We also assessed the publication bias via Egger's test. We followed the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines in reporting our findings.

Results

The search strategy initially identified 137 records, of which 48 were potentially relevant to our meta-analysis, for which the full texts were retrieved for further evaluation (Fig. 1). Of these, 32 were excluded according to the inclusion/exclusion criteria, leaving a total of 16 eligible articles. Two articles described results from the same research with different focuses, and thus we adopted the more relevant of the 2. Finally, all included studies comprised 46,157 patients for the quantitative synthesis and meta-analysis.

Study Characteristics

Table 1 shows the characteristics of the included studies. Subjects in 15 studies were all AKI patients. Seven studies [16–18, 20–23] were based on data from mono-centers, while the rest were based on multicenters. Among all 46,157 AKI patients, 22,791 were confirmed as community-acquired. The definitions of CA and HA-AKI were clearly described in all the included studies. Regarding the AKI definitions, Loo and Zainal [13], Obialo et al. [25], Al-Homrany [14], and Wang et al. [24] required serum creatinine (SCr) >2 mg/dL. The KDIGO criteria [21, 26] were applied in 6 studies [5, 12, 18, 27–29], RIFLE [30] was applied in 4 studies [15, 18, 19, 23], and Sesso et al. [31] defined AKI as a SCr level >1.4 mg/dL (124 mol/L) for men or >1.3 mg/dL (115 mol/L) for women. Mortality was compared in 14 studies [5, 13, 14, 17–20, 24, 25, 27–29, 31, 32], among which 11 studies compared in-hospital mortality; Wonnacott et al. [28] compared in-hospital and 14-month mortality; Sawhney et al. [27] provided 30-day, 1-year, and 5-year mortality; and Holmes et al. [29] compared 90-day mortality. To reduce bias due to data extraction, we collected the 30-day mortality data from Sawhney et al. [27] and the overall mortality from Wonnacott et al. [28]. Nine studies [12, 14, 17, 20, 24, 27–29, 32] compared renal recovery, but the criteria differed among all the included studies. Nevertheless, a decline in SCr to almost the normal level was at least required for renal recovery. Sawhney et al. [27] and Mehta et al. [12] classified partial and full recovery. Thus, we took the sum of the 2 kinds of recovery data to reduce bias in the prognosis analysis in our study. Three studies [24, 25, 31] compared oliguria, and 11 studies [5, 13, 14, 17, 20, 24, 25, 28, 29, 31, 32] compared dialysis rate. Eight studies [5, 13, 20, 24, 25, 27, 28, 32] calculated the ICU hospitalization period, and 9 studies [5, 13, 17, 20, 24, 25, 28, 29, 32] compared the length of hospital stay.

Evidence from the Included Studies

Mortality

Fourteen studies involving 42,204 patients were pooled. As shown in Figure 2, mortality was significantly lower in the CA-AKI than in HA-AKI patients (OR 0.43, 95% CI 0.35–0.53, $p < 0.00001$, $I^2 = 90\%$). Exclusion of studies with a small sample size ($n = 100$) did not change the effect size nor the degree of heterogeneity (OR 0.43, 95% CI 0.35–0.54, $I^2 = 91\%$, $p < 0.00001$). Subgroup analyses of different AKI definitions provided consistent results with the overall analysis (SCr >2 mg/dL: OR 0.26, 95% CI 0.18–0.37, $p < 0.00001$, $I^2 = 0\%$; KDIGO: OR 0.48, 95% CI 0.36–0.63, $p < 0.00001$, $I^2 = 92\%$; RIFLE: OR 0.51, 95% CI 0.26–0.99, $p = 0.05$, $I^2 = 94\%$; Sesso et al. [31]: OR 0.36, 95% CI 0.23–0.56, $p < 0.00001$). Schissler et al. [32] reported detailed data for mortality in different RIFLE stages, and we then conducted a subgroup analysis. The results showed that in stages of “Risk,” “Injury,” and “Failure,” respectively, CA-AKI patients had a lower mortality than HA-AKI patients (RIFLE R: OR 0.16, 95% CI 0.06–0.46, $p = 0.0006$; RIFLE I: OR 0.29, 95% CI 0.12–0.69, $p = 0.005$; RIFLE F: OR 0.21, 95% CI 0.07–0.61, $p = 0.004$). We did not identify publication bias based on Egger’s test ($p = 0.868$).

Fig. 1. Flow chart of the included studies. HA-AKI, hospital-acquired acute kidney injury; CA-AKI, community-acquired acute kidney injury.

Table 1. Characteristics of included studies

Study	Group	Setting	Study design	Follow-up	Patients	Patients	Mean age	Male/ female, <i>n</i>	AKI definition	AKI stage risk	AKI stage injury	AKI stage failure	Mortality	Renal recovery	Oliguria	Length of stay	Dialysis ICU	
Loo and Zainal [13], 1995	CA-AKI	Single center	Retrospective cohort study	1986–1990	164	113	51.1±16.4	NA	SCR ≥177 μmol/L (2 mg/dL) occurring during hospital stay with a previously normal SCr (62–124 μmol/L); 2-fold rise in scr occurring during hospitalization with previous SCr >177 μmol/L	NA	NA	NA	23	NA	NA	28.5±30.2	20	12
	HA-AKI					51	46.8±18.9	NA		NA	NA	NA	20	NA	NA	30.5±23.6	10	19
Obialo et al. [25], 2000	CA-AKI	Single center	Retrospective cohort study	1994–1996	100	79	53.1±9.8	54/25	A rise in SCr level of at least 44.2 μmol/L (0.5 mg/dL) and 176.8 μmol/L (2.0 mg/dL) or greater during hospitalization; and admission creatinine level of 176.8 μmol/L (2.0 mg/dL) or greater when no prior history of renal disease was available	NA	NA	NA	26	NA	28	12±11	6	5
	HA-AKI					21	58.3±20.4	13/8		NA	NA	NA	13	NA	13	26±28	3	12
Al-Homrany [14], 2003	CA-AKI	Single center	Prospective study	January 1999– December 2000	150	57	55.1±22.78	36/21	Oliguria (urine volume ≤400 mL/day) for at least 48 h or as a rise in SCr level of >50% and ≥2 mg/dL	NA	NA	NA	12	37	NA	NA	14	NA
	HA-AKI					93	61.25±22.18	52/41		NA	NA	NA	48	35	NA	NA	18	NA
Sesso et al. [31], 2004	CA-AKI	Single center	Prospective study	1999–2002	325	171	71±8	93/78	An increase in serum creatinine level of at least 0.5 mg/dL (44 μmol/L); creatinine level >1.4 mg/dL (124 μmol/L) for men or > 1.3 mg/dL (115 μmol/L) for women	NA	NA	NA	73	NA	77	NA	86	NA
	HA-AKI					154	72±8	87/67		NA	NA	NA	104	NA	80	NA	62	NA
Wang et al. [24], 2007	CA-AKI	Single center	Retrospective cohort study	1994–2003	205	122	51.1±20.3	NA	A rise within hours or days in SCr level to 176 μmol/L (2.0 mg/dL) or above if no prior history of renal dysfunction was available, or by more than a 50% increase in creatinine if baseline was above 132 μmol/L (1.5 mg/dL)	NA	NA	NA	28	82	67	25.3±13.7	51	6
	HA-AKI					83	61.5±16.3	NA		NA	NA	NA	52	17	59	51.4±40.8	39	46
Daher et al. [19], 2012	CA-AKI	Single center	Retrospective cohort study	2008	491	270	62.7±21.6	160/110	RIFLE	NA	NA	NA	62	NA	NA	NA	NA	NA
	HA-AKI					221	NA	44/177		NA	NA	NA	42	NA	NA	NA	NA	NA
Schisler et al. [32], 2013	CA-AKI	Single center	Retrospective cohort study	1995–2007	422	335	67.8±12.2	NA	RIFLE	125	104	106	38	248	NA	8.9	18	119
	HA-AKI					87	69.5±11.1	NA		34	35	18	31	74	NA	15.8	9	53

Table 1 (continued)

Study	Group	Setting	Study design	Follow-up	Patients	Patients	Mean age	Male/female, n	AKI definition	AKI stage risk	AKI stage injury	AKI stage failure	Mortality	Renal recovery	Oliguria	Length of stay	Dialysis ICU
Der-Mesropian et al. [20], 2014	CA-AKI	Multi-center	Retrospective cohort study	2004–2005	718	560	71.6±11.8	545/15	RIFLE	126	189	245	110	248	NA	11.4	20
	HA-AKI																
Wonnacott et al. [28], 2014	CA-AKI	Two district general hospitals	Retrospective cohort study	2011–2012	1,020	686	74.4±15.4	342/344	KDIGO	291	210	185	302 (14-month)	376	NA	7 (3–16)	24
	HA-AKI																
Xu et al. [5], 2015	CA-AKI	Multi-center	Retrospective cohort study	2013–2013	14,985	4,562	57.8±18.8	2,682/1,880	KDIGO	1,720	1,218	1,624	214	NA	NA	16 (10, 25)	205
	HA-AKI																
Wang et al. [18], 2015	CA-AKI	Multi-center	Cross-sectional study	2013	7,475	4,068	NA	NA	KDIGO	NA	NA	NA	295	NA	NA	NA	NA
	HA-AKI																
Sawhney et al. [27], 2016	CA-AKI	Single center	Retrospective cohort study		4,550	1,771	NA	764/407	KDIGO	1,312	287	172	230	963	NA	NA	148
	HA-AKI																
Mehta et al. [12], 2016	CA-AKI	Multi-center	Cross-sectional study	September 29–December 7, 2014	3,953	2,337	NA	NA	KDIGO	NA	NA	NA	NA	764	NA	NA	NA
	HA-AKI																
Hsu et al. [17], 2016	CA-AKI	Multi-center	Retrospective cohort study	January 1, 2010–December 31, 2014	9,391	6,287	68.02±15.33	3,688/2,599	RIFLE	1,174	1,237	3,876	1,639	2,531	NA	21.25±22.35	91
	HA-AKI																
Holmes et al. [29], 2004	CA-AKI	Multi-center	Prospective cohort study	November 2013–April 2016	2,208	1,373	64.2±15.8	763/610	KDIGO	714	298	361	484	775	NA	12.1±9.4	95
	HA-AKI																

Scr, serum creatinine; NA, not applicable; ICU, intensive care unit; AKI, acute kidney injury; HA-AKI, hospital-acquired AKI; CA-AKI, community-acquired AKI.

Fig. 2. Forest plot of mortality between CA- and HA-AKI patients. HA-AKI, hospital-acquired acute kidney injury; CA-AKI, community-acquired acute kidney injury; SCr, serum creatinine.

Renal Recovery

Overall, 9 studies involving 22,617 patients were pooled. As shown in Figure 3, CA-AKI patients tended to show a similar renal recovery to HA-AKI patients (OR 1.27, 95% CI 0.53–3.02, $I^2 = 99\%$, $p = 0.59$). Exclusion of studies with a small sample size ($n = 150$) did not change the effect size nor the degree of heterogeneity (OR 1.14, 95% CI 0.46–2.86, $I^2 = 99\%$, $p = 0.78$). The subgroup analysis of different AKI definitions provided inconsistent results. The studies that required SCr over 2 mg/dL as the AKI definition showed significantly better renal recovery of CA-AKI compared with HA-AKI patients (OR 4.97, 95% CI 1.95–12.66, $I^2 = 74\%$, $p = 0.0008$). The studies that applied the KDIGO or RIFLE criteria showed no difference in renal recovery between CA- and HA-AKI patients (KDIGO: OR 0.69, 95% CI 0.22–2.14, $I^2 = 99\%$, $p = 0.52$; RIFLE: OR 1.22, 95% CI 0.35–4.30, $I^2 = 98\%$, $p = 0.76$). No publication bias was detected based on Egger's test ($p = 0.214$).

Fig. 3. Forest plot of renal recovery between CA- and HA-AKI patients. HA-AKI, hospital-acquired acute kidney injury; CA-AKI, community-acquired acute kidney injury; SCr, serum creatinine.

Oliguria

Three studies involving 630 patients were pooled for oliguria. In the overall analysis, CA-AKI patients showed a significantly lower rate of oliguria occurrence than HA-AKI patients (OR 0.58, 95% CI 0.38–0.88, $I^2 = 28\%$, $p = 0.01$). Subgroup analyses of AKI definitions showed that Sesso et al. [31] reported no differences in the oliguria rate between CA- and HA-AKI patients (OR 0.76, 95% CI 0.49–1.17, $p = 0.27$). The other 2 studies, which required SCr >2 mg/dL, showed consistent result with the overall analysis (OR 0.45, 95% CI 0.27–0.75, $I^2 = 0\%$, $p = 0.002$). Figure 4 illustrates the details. No publication bias was identified based on Egger's test ($p = 0.275$).

Dialysis

Eleven studies involving 28,834 patients were pooled for dialysis. Our analysis indicated that both groups of AKI patients were similarly in the need of dialysis treatment (OR 1.05, 95% CI 0.82–1.34, $I^2 = 60\%$, $p = 0.70$; Fig. 5). Exclusion of studies with a small sample size ($n = 100$) did not change the effect size or the degree of heterogeneity (OR 1.07, 95% CI 0.83–1.37, $I^2 = 62\%$, $p = 0.60$). In the subgroup analysis of AKI definitions, studies that applied the KDIGO criteria showed a significantly higher need of dialysis for CA-AKI patients, which is exactly the opposite of the result obtained in studies using RIFLE (KDIGO: OR 1.35, 95% CI 1.16–1.57, $I^2 = 0\%$, $p < 0.0001$; RIFLE: OR 0.67, 95% CI 0.50–0.89, $I^2 = 0\%$, $p = 0.006$). Studies

Fig. 4. Forest plot of the oliguria rate between CA- and HA-AKI patients. HA-AKI, hospital-acquired acute kidney injury; CA-AKI, community-acquired acute kidney injury; SCr, serum creatinine.

that required SCr >2 mg/dL and Sesso et al. [31] both showed consistent results with the overall analysis (SCr >2 mg/dL: OR 0.90, 95% CI 0.61–1.33, $I^2 = 0\%$, $p = 0.60$; Sesso et al. [31]: OR 1.50, 95% CI 0.97–2.33, $p = 0.07$). Egger’s test did not show a publication bias ($p = 0.381$).

ICU Risk

In total, 8 studies involving 22,164 patients were pooled. As shown in Figure 6, ICU need was significantly lower in CA-AKI patients (OR 0.24, 95% CI 0.14–0.40, $I^2 = 96\%$, $p < 0.00001$). Exclusion of studies with a small sample size did not change the effect size or the degree of heterogeneity (OR 0.27, 95% CI 0.16–0.47, $I^2 = 96\%$, $p < 0.00001$). Subgroup analysis of different AKI definitions showed consistent results with the overall analysis (SCr >2 mg/dL: OR 0.08, 95% CI 0.03–0.23, $I^2 = 72\%$, $p < 0.00001$; KDIGO: OR 0.40, 95% CI 0.18–0.89, $I^2 = 98\%$, $p = 0.02$; RIFLE: OR 0.32, 95% CI 0.24–0.44, $I^2 = 0\%$, $p < 0.00001$). The study by Schissler et al. [32] showed that for patients at stage of “Failure” classified by RIFLE criteria, CA-AKI patients were in higher need of ICU (OR 31.85, 95% CI 1.87–542.24, $p = 0.002$). In contrast, for patients at the other 2 stages of “Risk” and “Injury”, CA-AKI patients were less inclined to require the ICU (RIFLE R: OR 0.28, 95% CI 0.13–0.62, $p = 0.002$; RIFLE I: OR 0.33, 95% CI 0.15–0.73, $p = 0.006$). No publication bias was observed ($p = 0.059$).

Length of Hospital Stay

Altogether, 9 studies provided data for the length of hospital stay. Figure 7 shows a significantly shorter hospitalization period for CA-AKI patients (MD –9.42, 95% CI –13.73 to –5.12, $I^2 = 98\%$, $p < 0.0001$). No publication bias was also observed ($p = 0.077$). Exclusion of studies with a small sample size ($n = 100$) did not change the effect size or the degree of heterogeneity (OR –9.11, 95% CI –13.56 to –4.67, $I^2 = 98\%$, $p < 0.001$). For the subgroup analysis of different AKI definitions, studies that applied the KDIGO or RIFLE criteria showed consistent results with the overall analysis (KDIGO: MD –5.27, 95% CI –9.15 to –1.40, $p = 0.008$, $I^2 = 97\%$; RIFLE: MD –11.13, 95% CI –15.92 to –6.34, $p < 0.00001$, $I^2 = 87\%$). Studies that required SCr >2 mg/dL showed no significant difference in length of hospitalization stay between CA- and HA-AKI

Fig. 5. Forest plot of the need for dialysis between CA- and HA-AKI patients. HA-AKI, hospital-acquired acute kidney injury; CA-AKI, community-acquired acute kidney injury; SCr, serum creatinine.

patients (MD -13.97 , 95% CI -29.16 to 1.22 , $I^2 = 86\%$, $p = 0.07$). The study by Schissler et al. [32] showed that for patients at stage of “Risk” classified by RIFLE criteria, CA- and HA-AKI patients had a similar length of hospital stay (OR -1.80 , 95% CI -3.94 to 0.34 , $p = 0.10$). In contrast, for patients at the other 2 stages of “Injury” and “Failure,” CA-AKI patients tended to have a shorter hospital stay than HA-AKI patients (RIFLE I: OR -7.00 , 95% CI -12.43 to -1.57 , $p = 0.01$; RIFLE F: OR -18.30 , 95% CI -30.83 to -5.77 , $p = 0.004$).

Risk of Bias

Risk of bias ratings for each study were assessed with the Nosgen-ranking tool. All the studies were observational, including ten retrospective cohort, 3 prospective, and 2 cross-sectional studies. Considering the similar data content calculated in the 2 cross-sectional studies, they were regarded as cohort studies when assessing bias. The included studies collected statistics from hospitals covering large local populations and equipped with well-

Fig. 6. Forest plot of ICU treatment between CA- and HA-AKI patients. HA-AKI, hospital-acquired acute kidney injury; CA-AKI, community-acquired acute kidney injury; SCr, serum creatinine.

Fig. 7. Forest plot of length of hospital stay between CA- and HA-AKI patients. HA-AKI, hospital-acquired acute kidney injury; CA-AKI, community-acquired acute kidney injury; SCr, serum creatinine.

Fig. 8. Risk of bias graph for the included studies.

applied electronic medical systems that documented patients' detailed information. We considered the selection bias to be low risk but the comparability to be high risk. Regarding outcomes, all the included studies provided complete and adequate hospitalization information, and therefore we assessed the outcome bias as low risk. The details are presented in Figures 8 and 9.

Discussion

With the advances in the research and recognition of AKI, CA-AKI has aroused similar attention and importance as HA-AKI. This meta-analysis provides evidence for the different clinical characteristics and prognosis between CA and HA-AKI patients. In our study, we included 1 study consisting of data collected worldwide [12]; 5 studies conducted in Asia [5, 13, 17, 18, 33]; another 5 studies in America [19, 20, 25, 31, 32], including 1 specializing in the African-American population [25]; 3 studies in the United Kingdom [27–29]; and 1 study in Saudi Arabia [14]. Overall, our study managed to cover a broad population. For each outcome, the results did not show a significant change after we excluded the relatively smaller samples. Considering the different AKI definitions applied by the included studies, we conducted subgroup analyses to reveal potential disagreements among different AKI definitions in terms of performance. A subgroup analysis for separate stages of AKI was also conducted if data were available.

Our study supported a relatively worse prognosis for HA-AKI patients. The mortality of HA-AKI patients was higher. In the subgroup analysis of various AKI definitions, the results remained in accordance with the overall analysis of mortality. In addition, HA-AKI patients showed more severe clinical manifestations, with a higher oliguria rate, greater demand for the ICU, as well as a longer hospitalized stay. Although in the subgroup analysis of the study by Schissler et al. [32], CA-AKI patients in RIFLE's "Failure" stage needed more ICU admissions than HA-AKI patients in the same stage, this result has a much weaker statistical value, given its wider 95% CI and the fact that it stems from only one study. For renal recovery, oliguria, and length of hospital stay, inconsistency was drawn by using different diagnostic criteria. Two studies requiring SCr over 2 mg/dL showed significantly better renal recovery of CA-AKI compared with HA-AKI patients, while the other studies using the RIFLE or KDIGO

	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts
Al-Homrany 2003	+	+	+	?	+	+	+	+
Daher 2012	+	+	+	+	+	+	+	+
Der Mesropian 2014	+	+	+	+	+	+	+	+
Holmes 2018	+	+	+	+	+	+	+	+
Hsu 2016	+	+	+	+	+	+	+	+
Loo 1995	?	+	+	+	+	+	+	+
Mehta 2016	+	+	+	+	+	+	+	+
Obialo 2000	+	+	+	+	+	+	+	+
Sawhney 2016	+	+	+	+	+	+	+	+
Schissler 2013	+	+	+	+	+	+	+	+
Sesso 2004	+	+	+	?	+	+	+	+
Wang 2007	+	+	+	+	+	+	+	+
Wang 2015	+	+	+	+	+	+	+	+
Wonnacott 2014	?	+	+	+	+	+	+	+
Xu 2015	+	+	+	+	+	+	+	+

Fig. 9. Risk of bias summary for the included studies.

criteria showed no difference. Sesso et al. [31] alone reported no difference in oliguria rate between CA- and HA-AKI patients, while the other 2 studies using SCr >2 mg/dL showed a significantly lower rate of oliguria occurrence in CA-AKI. As the recognition of AKI develops, the definition of AKI becomes more specific and sensitive. The subsequent criteria such as the RIFLE or KDIGO perform better in a consensus of identifying AKI occurrence as well as clinical characteristics than the previously used ones.

An exceptional inconsistent result between the RIFLE and KDIGO criteria was presented in dialysis. In studies using the KDIGO criteria, CA-AKI was associated with a higher need for dialysis compared with HA-AKI, but were with a lower need in studies using the RIFLE criteria. It can be attributed to the later publish of the KDIGO criteria [26] than the RIFLE criteria [30]. The therapeutic efficacy of dialysis, especially continuous renal replacement therapy (RRT), was first applied and emphasized in the treatment of HA-AKI patients in ICU [34]. With the accumulation of evidence from numerous clinical researches, dialysis becomes more and more widely used in the rescue of all kinds of AKI patients, including CA-AKI. Different from HA-AKI patients, who may appear in every department in the hospital, most CA-AKI patients are admitted to the nephrology department and treated by nephrologists. These patients are usually better recognized and have more access to dialysis. This might contribute to the higher rate of appliance of dialysis in CA-AKI patients in the KDIGO subgroup than the RIFLE subgroup. However, we noticed that no significant difference in renal recovery was found between KDIGO and RIFLE subgroups. Factors associated with renal recovery and patients prognosis after an AKI episode are complicated, including inherent risk factors (e.g., age, CKD status, or comorbidities such as diabetes), modifiable patients factors (e.g., anemia, sepsis, or number of organ failure), and process of care (e.g., hemodialysis dose and modality, or nephrotoxic drug exposure) [35]. Hemodialysis provides definitive benefits to recovery, but the optimal dialysis dose, modality, and initiation time were still under debate. There was even less evidence in peritoneal dialysis [36, 37]. The RENAL study [38] and the ATN study [39] showed that an improvement in patient survival or renal recovery could not be achieved by increasing the intensity of RRT. Moreover, a recent meta-analysis [40] and a large-scale randomized controlled trial (RCT) [41] revealed no added benefit of early initiation of RRT for patients with AKI. Therefore, despite the inconsistency of dialysis risk between CA-AKI and HA-AKI, dialysis may not sufficiently affect the recovery rate of AKI patients. More well-designed RCTs with sufficient follow-up are necessary to evaluate the recovery of AKI patients between CA- and HA-AKI.

Another systematic review and meta-analysis, conducted by Inokuchi et al. [42], also examined the difference between CA and HA-AKI patients in terms of patient characteristics, in-hospital mortality, and hospital length of stay. Eight eligible observational studies with 17,939 patients were enrolled. We acquired similar results for comparisons of in-hospital mortality and length of hospital stay. Furthermore, our study included a larger number of studies and also covered a larger population, which may provide more convincing advice for the clinicians. Moreover, clinical characteristics were covered in more detail, such as renal recovery, oliguria rate, dialysis need, and ICU risk. We believe these details will help to form a comprehensive understanding of the discrepancies of the 2 types of AKI.

There are several limitations to our study. First, we combined studies with certain degrees of heterogeneity. Retrospective studies encompassed the majority, and 3 prospective observational studies were included [14, 29, 31]. The inconsistency among different definitions of AKI and renal recovery also contributed to the variations of our results. The difference among different hospitals, age and gender distribution, ethnicities screened, and sampling error may all contribute to the high heterogeneity. Thus, more sensitive and precise kidney monitoring may allow better detection. Second, the total sample size was moderate. Third, sampling bias may exist due to the limited studies in this meta-analysis, and more studies are required to verify our results in the future.

Conclusions and Implications for Future Research

Significant differences exist in the clinical characteristics between CA and HA-AKI. CA-AKI patients showed less severe clinical manifestations and a better prognosis in comparison to HA-AKI patients. Indicators such as mortality, oliguria incidence, ICU need, and length of hospital stay all showed better results for CA-AKI patients. Concerning renal recovery, CA and HA-AKI patients showed no significant difference. The optimal timing and dosage of dialysis to improve prognosis of AKI patients need further evidence and debate. The subgroup analysis of AKI definitions indicated that the KDIGO and RIFLE criteria were nearly consistent in assessing AKI clinical conditions and predicting prognosis. However, the distinct results for dialysis between these 2 might be partly due to the later publish of KDIGO criteria than RIFLE criteria. More studies, particularly multicenter RCTs, are required to illustrate potential differences in the renal recovery of CA- and HA-AKI patients as well as in the performance of diverse AKI definitions.

Statement of Ethics

The authors have no ethical conflicts to declare.

Disclosure Statement

The authors declare no conflict of interest.

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Author Contributions

Z.M.: acts as guarantor for the validity of the study report. Z.M. and J.X.: study concept and design. L.H. and C.X.: acquisition of data. M.R. and J.K.: extraction of data. J.X. and C.X.: checking of data. C.X. and L.H.: analysis and interpretation of data. L.H.: drafting of the manuscript. Z.M. and C.M.: critical revision of the manuscript for important intellectual content.

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