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The Risk and Burden of Acute Kidney Injury in elderly with Dementia

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Abstract

Background:

Advanced age is the strongest shared risk factor for both dementia and acute kidney injury (AKI). Previous studies have found that patients with AKI have an increased risk of developing dementia.Whether dementia itself independently predisposes to AKI remains unknown. This study aimed to investigate the association between pre-existing dementia and the incidence of AKI in elderly patients.

Methods:

We conducted a comprehensive analysis of the electronic health record repository at Guangdong Provincial People's Hospital, focusing on inpatient episodes involving patients aged 65 years and older who were admitted between January 1, 2012, and December 31, 2016. We employed both univariate and multivariable logistic regression models to examine the association between dementia, as defined by *International Classification of Diseases codes*, and AKI, as defined according to the Kidney Disease: Improving Global Outcomes creatinine criteria. Furthermore, patients were stratified into dementia and non-dementia cohorts and matched using a 1:1 propensity score matching (PSM) approach, employing a caliper of 0.1 standard deviations, to facilitate a more rigorous examination of the association between dementia and AKI. Stratified analyses were conducted based on age, sex, and different comorbidity statuses. At last, we compared the length of stay, hospitalization costs, and in-hospital mortality rates between the groups.

Results:

AKI was observed in 2,977 episodes, accounting for 5.5% of the cases. Following PSM, the incidence of AKI was 10.6% in patients with dementia compared to 7.1% in the control group (odds ratio [OR] 1.56, 95% CI 1.24–1.96). After adjusting for variables such as dementia, age, sex, hypertension, myocardial infarction, congestive heart failure, cardiovascular disease, chronic pulmonary disease, diabetes with or without complications, moderate to severe renal disease, moderate to severe liver disease, any tumor, and metastatic solid tumor, multivariable regression analysis identified dementia as an independent risk factor for AKI (OR 1.90, 95% CI 1.61–2.24). This association remained consistent across subgroups, including individuals aged 75 years or older, different genders, and those with or without hypertension. Episodes involving both AKI and dementia were associated with the longest LOS, the highest costs, and the greatest in-hospital mortality rates (all $P < 0.001$).

Conclusions:

In a cohort of 65,122 elderly admissions, dementia emerges as a strong and independent predictor of AKI. The occurrence of AKI in conjunction with dementia is associated with the most detrimental resource utilization and survival outcomes, highlighting the critical need for the development and implementation of targeted nephroprotective strategies for this vulnerable population.

Introduction

Acute kidney injury (AKI) is a clinical syndrome characterized by a rapid decline in renal function, leading to the accumulation of nitrogenous waste products and disturbances in fluid, electrolyte, and acid-base balance[1, 2]. AKI is associated with high global incidence and mortality rates, significantly prolongs hospital stays, increases healthcare costs, and is linked to the progression of chronic kidney disease, elevated risk of cardiovascular events, and reduced long-term survival[3].

Several risk factors for AKI are well-established, including advanced age, pre-existing chronic kidney disease, diabetes, hypertension, heart failure, sepsis, and exposure to nephrotoxic agents[4]. Among these, the elderly population is particularly vulnerable to AKI due to age-related decline in renal function, high prevalence of comorbidities, and polypharmacy[5]. Consequently, older adults exhibit a higher incidence of AKI and face a greater risk of adverse outcomes[6]. Identifiable high-risk populations in this demographic is therefore crucial for developing effective prevention and management strategies to improve clinical results.

Emerging evidence suggests potential bidirectional relationships between neurodegenerative disorders and kidney dysfunction[7]. Shared pathophysiological mechanisms, including chronic inflammatory states, endothelial dysfunction, and oxidative stress, may contribute to both cerebral and renal tissue injury[8]. Several cohort studies have demonstrated that patients who experience AKI are at increased long-term risk of developing dementia, suggesting that kidney-induced systemic effects may accelerate neurodegenerative processes[9, 10]. Conversely, neurodegenerative conditions may predispose patients to AKI through multiple pathways, including impaired thirst perception, autonomic dysfunction, and altered medication metabolism[11]. However, the specific role of neurodegenerative disorders as risk factors for AKI has not been adequately investigated.

Dementia, as a prevalent neurodegenerative disorder in the elderly, is increasing in incidence amid global population aging[12]. Patients with dementia often experience cognitive impairment, reduced self-care ability, and communication barriers, which can lead to dehydration, medication errors, and poor infection control—all established risk factors for AKI. The neuropathological changes in dementia may further exacerbate these risks through direct effects on fluid regulation homeostasis and drug clearance. However, evidence regarding the association between dementia and AKI remains limited, and it is still uncertain whether dementia independently increases the risk of AKI.

This study aimed to investigate the epidemiology of AKI in older patients with dementia, examine the relationship between pre-existing dementia and the occurrence of AKI, and assess the impact of comorbid AKI and dementia on clinical outcomes and healthcare resource utilization. The findings may help identify high-risk populations and inform integrated care strategies for elderly patients with multiple chronic conditions.

Materials and Methods

Study design and data sources

This study utilized data from a single geriatric center, which was part of the larger, multi - center China Collaborative Study on Acute Kidney Injury (CCS - AKI) (ClinicalTrials.gov Identifier: NCT03061786. Registration Date: 02/15/2017). The CCS-AKI retrospectively recruited hospitalized patients from 12 tertiary and 3 secondary hospitals in China between January 2010 and December 2016, sourcing data from the electronic clinical data of various hospitals. The parent CCS-AKI study applied the following exclusion criteria: 1) inability to ascertain in-hospital outcomes; 2) inability to establish a definitive diagnosis; 3) absence of at least two serum creatinine measurements within a 7-day period; 4) history of kidney transplantation; 5) diagnosis of chronic kidney disease at stage 5; 6) estimated glomerular filtration rate (eGFR) less than 15 ml/min/1.73 m^2; 7) initiation of dialysis prior to the diagnosis of AKI; 8) peak serum creatinine concentration below 53 μmol/L; and 9) hospital stay duration of less than 2 days. Following initial data cleaning, 561,137 out of a total of 3,970,702 hospital admissions were deemed suitable for inclusion in adult AKI research[13].The present study included only one hospital from the CCS-AKI network because it was the sole provincial-level center with standardized dementia diagnoses and available pre-admission serum creatinine records.

Research Ethics

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Guangdong Provincial People's Hospital (Approval No. GDREC.2016327H). The requirement for informed consent was waived due to the retrospective design and the de-identification of all patient data prior to analysis.

Definitions

In line with international standards, older adults were defined as those aged ≥ 65 years and were further categorized into three subgroups: 65–74, 75–84, and ≥ 85 years [14].

As the optimal eGFR formula for older adults remains debated, eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [15].

AKI was defined according to the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, which specify an increase in serum creatinine by ≥ 26.5 μmol/L within 48 hours, or an increase in serum creatinine to ≥ 1.5 times the baseline value (i.e., a 50% increase above baseline) within the preceding 7 days [1, 13]. The lowest serum creatinine level recorded during hospitalization served as the baseline measurement. Community-Acquired AKI (CA-AKI) was characterized by serum creatinine levels at admission that were 1.5 times greater than the minimum serum creatinine levels observed during hospitalization. Patients who developed AKI but did not fulfill the criteria for CA-AKI were classified as having Hospital-Acquired AKI (HA-AKI) [16, 17].

Comorbidities were classified and scored according to the Charlson Comorbidity Index (CCI), based on our previous validation study in the Chinese population[18]. Dementia was identified through discharge diagnosis using the International Classification of Diseases (ICD) code: F00, F01, F02, F03; F051, G30; G311.

Statistical Analysis

Continuous variables adhering to a normal distribution were reported as means ± standard deviation. For intergroup comparisons of these variables, analysis of variance (ANOVA) was employed. Continuous variables not conforming to a normal distribution were represented as medians with interquartile ranges [25th percentile (Q25) and 75th percentile (Q75)]. The rank sum test was utilized for intergroup comparisons of these non-normally distributed variables. Categorical data were presented as counts and percentages [n (%)] and were analyzed using the chi-square (χ^2) test. Variables found to be statistically significant ($P < 0.05$) in univariate logistic regression and clinically significant were included in a multivariate analysis to calculate the odds ratio (OR) and 95% confidence interval (95% CI). A two-tailed P-value of less than 0.05 was considered indicative of statistical significance.

To minimize confounding, we employed a 1:1 nearest-neighbor propensity-score matching (PSM) utilizing a stringent caliper of 0.1 standard deviations of the logit-transformed propensity score[19]. The propensity score was estimated non-parametrically using logistic regression, modeling the probability of dementia based on the following baseline covariates: age, sex, hypertension, myocardial infarction, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, diabetes mellitus, diabetes mellitus with chronic complications, moderate to severe renal disease, moderate to severe liver disease, any tumor and metastatic solid tumor, based on previously recognized AKI-associated factors.[20]. Matching was done without replacement, and balance was evaluated before and after matching using standardized mean differences (SMDs), with an SMD ≤ 0.1 signifying adequate balance.[21]

All analyses were performed using R software (version 4.5.1). A two-tailed P value ≤ 0.05 was considered statistically significant.

Results

Patient characteristics

Among the 65,122 hospital admissions, a total of 54,319 met the study inclusion criteria (Figure 1). Among these included admissions, 2,977 (5.4%) had AKI, including 1,618 (2.9%) with CA-AKI and 1,359 (2.5%) with HA-AKI. Dementia was documented in 1,845 admissions (3.4%). Admissions with AKI demonstrated a higher prevalence of comorbidities, including congestive heart failure, cerebrovascular disease, dementia, chronic pulmonary disease, moderate to severe renal disease, moderate to severe liver disease, and metastatic solid tumors ($P < 0.05$), whereas a lower percentage of hypertension, compared with those without AKI (Table 1).

Table 1. Baseline Characteristics of Study Population Stratified by AKI Status

Variable	Total (n =54,319)	Non-AKI (n = 51,342)	AKI (n=2,977)	P-value
Age, mean (SD)	75±8	75±8	76±8	<0.001
Age_group, (%)				<0.001
65-74 years	27,222	25,848 (95.0)	1,374 (5.0)	
75-84 years	19,182	18,167 (94.7)	1,015 (5.3)	
85 years or above	7,915	7,327 (92.6)	588 (7.4)	
Gender, n(%)				<0.001
Male	35,826	33,98 (94.9)	1,84 (5.1)	
Female	18,493	17,360 (93.9)	1,133 (6.1)	
eGFR groups, n(%)				<0.001
90 mL/min/1.73m² or above	14,467	13,006 (89.9)	1,461 (10.1)	
60-89 mL/min/1.73m²	27,566	26,654 (96.7)	912 (3.3)	
30-59 mL/min/1.73m²	10,467	9,986 (95.4)	481 (4.6)	
15-29 mL/min/1.73 m²	1,819	1,696 (93.2)	123 (6.8)	
eGFR [Median (IQR)]	81 (62, 91)	80 (62, 90)	90 (68, 102)	<0.001
Comorbidities, n(%)				
High blood pressure	29,053	27,557 (53.7)	1,496 (50.3)	<0.001
Myocardial infarction	4,151	3,924 (7.6)	227 (7.6)	1.000
Congestive heart failure	1,494	1,312 (2.6)	182 (6.1)	<0.001
Cerebrovascular disease	12,873	12,023 (23.4)	850 (28.6)	<0.001
Dementia	1,845	1,649 (3.2)	196 (6.6)	<0.001
Chronic pulmonary disease	8,341	7,815 (15.2)	526 (17.7)	<0.001
Diabetes mellitus without chronic complications	13,265	12,534 (24.4)	731 (24.6)	0.878

Variable	Total (n =54,319)	Non-AKI (n = 51,342)	AKI (n=2,977)	P-value
Diabetes mellitus with chronic complications	2,029	1,910 (3.7)	119 (4.0)	0.468
Moderate/severe renal disease	3,652	3,221 (6.3)	431 (14.5)	<0.001
Moderate/severe liver disease	1,086	914 (1.8)	172 (5.8)	<0.001
Any Tumor	10,885	10,265 (20.0)	620 (20.8)	0.280
Metastatic Solid Tumor	3,723	3,481 (6.8)	242 (8.1)	0.005

Abbreviations: AKI, acute kidney injury; eGFR, estimated glomerular filtration rate.

Propensity Matching

From 52,474 admissions without a dementia diagnosis, 1,840 admissions with a dementia diagnosis were matched as controls utilizing 1:1 PSM. Upon PSM, the primary clinical variables demonstrated an SMD of less than 0.1, signifying adequate balance across the comparison groups (Supplementary Table 1 and Supplementary Figure 1). Even after PSM adjustment, the prevalence of AKI was still significantly elevated in patients with dementia compared with non-dementia admissions (10.6% vs. 7.1%, P < 0.001). Sensitivity analyses using different caliper widths (0.05, 0.1, and 0.2) and adjustment for propensity score yielded consistent results (OR range 1.54–1.56), confirming the robustness of the main findings (Supplementary Table 2).

Multivariate logistic regression analysis of risk factors for AKI

Multivariate logistic regression analysis further showed that dementia was independently associated with AKI after adjusting for demographics and comorbidities (OR 1.90, 95% CI 1.61-2.24 in the fully adjusted model). This association persisted across all three models (unadjusted, age-sex adjusted, and fully adjusted), with ORs ranging from 1.81 to 2.12 (all *P* < 0.001) (Table 2).

Table 2. Association Between Pre-existing Dementia and AKI: Results from Multivariable Logistic Regression

Variable	OR	95% CI	*P* value
Model 1			
Dementia	2.12	1.82-2.47	<0.001
Model 2			
Dementia	1.81	1.54-2.13	<0.001
Age groups			
65 - 74 years	Reference		
75 - 84 years	1.03	0.95-1.12	0.475
≥ 85 years	1.37	1.23-1.52	<0.001
Gender			
Male	Reference		
Female	1.22	1.13-1.31	<0.001
Model 3			
Dementia	1.90	1.61-2.24	<0.001
Age groups			
65 - 74 years	Reference		
75 - 84 years	1.00	0.92-1.09	0.941
≥ 85 years	1.19	1.06-1.34	0.004
Gender			
Male	Reference		
Female	1.26	1.16-1.36	<0.001
Congestive heart failure	2.49	2.10-2.92	<0.001
Cerebrovascular disease	1.13	1.03-1.24	0.008
Chronic pulmonary disease	1.09	0.99-1.21	0.087
Moderate/severe renal disease	2.38	2.12-2.65	<0.001
Moderate/severe liver disease	3.38	2.85-4.00	<0.001
Metastatic Solid Tumor	1.42	1.24-1.63	<0.001

Abbreviations: AKI, acute kidney injury; OR, odds ratio; CI, confidence interval.

Subgroup analyses

Subgroup analyses confirmed a consistent association between dementia and AKI across gender and hypertension status. The association was strongest in patients aged 75-84 years (OR 2.88, 95% CI 2.19-3.74) and remained significant in those aged ≥85 years (OR 1.63, 95% CI 1.30-2.02) (Table 3).

Table 3. Association Between Pre-existing Dementia and AKI Across Subgroups

	OR	95% CI	P value
[a] Age stratification			
64-74years	1.12	0.49-2.19	0.771
75-84years	2.88	2.19-3.74	<0.001
85 years or above	1.63	1.30-2.02	<0.001
[b] Gender			
male	2.05	1.67-2.50	<0.001
female	1.65	1.22-2.20	<0.001
With or without hypertension			
[c] With hypertension	1.61	1.18-2.16	0.002
[d] Without hypertension	2.03	1.66-2.47	<0.001

Abbreviations: AKI, acute kidney injury

[a] Adjusted for gender, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, moderate/severe renal disease, and moderate/severe liver disease, metastatic solid tumor.

[b] Adjusted for age stratification, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, moderate/severe renal disease, moderate/severe liver disease, and metastatic solid tumor.

[c] Adjusted for age stratification, gender, hypertension, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, moderate/severe renal disease, moderate/severe liver disease, and metastatic solid tumor.

[d] Adjusted for age stratification, gender, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, moderate/severe renal disease, moderate/severe liver disease, and metastatic solid tumor.

Medical burdens of dementia and AKI

Admissions with both AKI and dementia experienced the longest hospital stays (median, 57.5 days), highest costs (median, ¥348,000), and highest in-hospital mortality (31.6%), followed by those with AKI

alone (26.0 days; ¥117,000; 16.6%), dementia alone (17.0 days; ¥56,000; 2.7%), and neither condition (10.0 days; ¥32,000; 1.6%) (all P < 0.05) (Table 4).

Table 4. Length of Stay, Hospitalization Costs, and In-Hospital Mortality by AKI and Dementia Status

	AKI+Dementia+, n = 196	**AKI+ Dementia-, n = 2,781**	**AKI- Dementia+, n = 1,649**	**AKI- Dementia-, n = 49,693**
Length of stay (days)	57.5 (26.8-120.2)	26.0 (16.0-41.0)	17.0 (12.0-28.0)	10.0 (6.0-15.0)
Costs (×10³ CNY)	348.0(111.2-690.2)	117.0(62.0-215.0)	56.0 (32.0-108.0)	32.0 (14.0-61.0)
In-Hospital Mortality Rates n(%)	6 (31.6)	46 (16.6)	4 (2.7)	80 (1.6)

Abbreviations: AKI, acute kidney injury; CNY, Chinese Yuan;

Data are presented as median (interquartile range)

Discussion

This retrospective cohort study investigated the association between pre-existing dementia and AKI in a large elderly population. Our findings demonstrate that dementia is independently associated with an increased risk of AKI, a finding that remained robust in multivariable adjustment and sensitivity analyses. Moreover, the coexistence of dementia and AKI was linked to the longest hospital stays, highest costs, and greatest in-hospital mortality, highlighting a distinct and substantial clinical burden.

The independent association between dementia and AKI may be explained by multiple intersecting pathways. Dementia can contribute to prerenal, intrarenal, and postrenal AKI through dehydration (due to impaired thirst perception) [22], polypharmacy and drug-induced injury, autonomic dysfunction, and delayed recognition of urinary obstruction. In China, where home-based care is common for dementia patients, the management of complex medication regimens in non-clinical settings may introduce risks such as inadvertent misuse, which could further elevate the susceptibility to AKI [23,24]. Notably, the use of atypical antipsychotics (e.g., quetiapine, risperidone, olanzapine) for neuropsychiatric symptoms may precipitate hypotension, urinary retention, or rhabdomyolysis, thereby inducing AKI[25]. Our finding that AKI incidence remained higher in dementia patients suggests that beyond environmental factors, intrinsic pathophysiological changes, comorbidities, and medication exposure substantially contribute to AKI development. Shared mechanisms such as chronic inflammation and endothelial dysfunction likely further link cerebral and renal injury[26]

Although hypertension was more prevalent in the non-AKI group in univariate analysis, multivariable models adjusting sequentially for demographics, dementia, and comorbidities (including hypertension)

confirmed that dementia remained a significant, independent predictor of AKI. This highlights the importance of incorporating cognitive status into AKI risk assessment beyond traditional somatic comorbidities. The robustness of this association was further supported by propensity-score matching and subgroup analyses. Interestingly, hypertension did not attenuate the relationship, suggesting that the dementia-AKI pathway may operate independently of vascular injury alone.

From a clinical perspective, these findings underscore the need to recognize dementia as a key risk factor for AKI in the elderly. Routine cognitive screening, careful fluid and medication management, and close renal monitoring could help mitigate risk in this vulnerable population. The substantial burden associated with comorbid dementia and AKI calls for integrated, multidisciplinary care models.

Several limitations should be acknowledged. The single-center, retrospective design may limit generalizability and preclude causal inference. Dementia was identified via ICD codes, without quantitative severity assessment, which may underestimate milder cases and preclude dose-response analysis. Although we adjusted for major comorbidities, residual confounding—particularly by unmeasured medication exposure—cannot be excluded. Furthermore, using the lowest inpatient serum creatinine as the baseline, while practical and highly sensitive, may overestimate AKI incidence by misclassifying reversible creatinine elevations as true renal injury. This potential overdiagnosis should be considered when interpreting our findings. Future prospective studies incorporating detailed cognitive and pharmacological data, as well as using pre-admission outpatient creatinine measurements or a stable baseline derived from multiple previous values, are needed to confirm and further elucidate these associations.

In conclusion, this study identifies dementia as an independent risk factor for AKI in the elderly, contributing to a substantial disease burden. These findings underscore the need for an integrated clinical approach to the management of patients with both conditions.

Declarations

Statement of Ethics

The study protocol has been approved by the research institutes committee on human research.

Disclosure Statement

The authors have no conflict of interest to report.

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Author Contributions

XLL, YHC: Design of the research and supervising the work; YHW, WL, ZZ: Acquisition of data, statistical analysis ; YHW, Drafting the manuscript; YHC, LS, XLL: Critical revision of the manuscript for important intellectual content.

Declaration of conflicts of interest:

The authors report no conflicts of interest.

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Figures

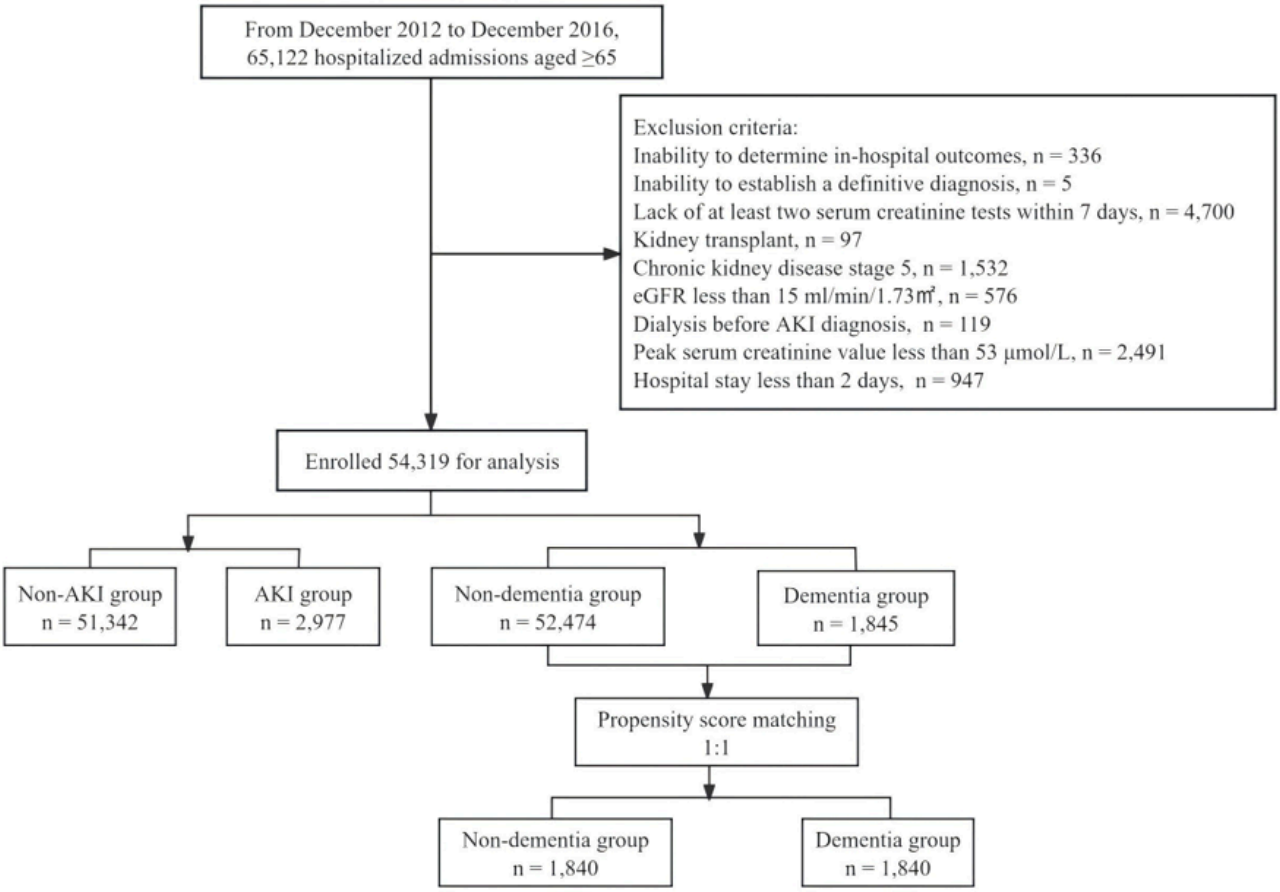


Figure 1

Flow Chart of Patients

Abbreviations : AKI, acute kidney injury; eGFR, estimated glomerular filtration rate.

Supplementary Files

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- supplementaryTable1.docx
- SupplementaryFigure1.pdf
- SupplementatyTable2.docx