

Long-term outcomes following vehicle trauma related acute kidney injury requiring renal replacement therapy: A nationwide population study

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Research article

Keywords: acute kidney injury, renal replacement therapy, end-stage kidney disease, trauma, NSARF

Posted Date: February 12th, 2020

DOI: <https://doi.org/10.21203/rs.2.23346/v1>

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Version of Record: A version of this preprint was published at Scientific Reports on November 25th, 2020.
See the published version at <https://doi.org/10.1038/s41598-020-77556-3>.

Abstract

Background Acute kidney injury (AKI) is a frequent complication of traumatic injury; however, long-term outcomes such as mortality and end-stage kidney disease (ESKD) have been rarely reported in this important patient population. We compared the long-term outcome of traumatic and non-traumatic AKI requiring renal replacement therapy (AKI-RRT).

Methods This nationwide cohort study used data from the Taiwan National Health Insurance Research Database. Vehicle-trauma patients developing AKI-RRT during hospitalization were identified, and matching non-traumatic AKI-RRT patients were identified between 2000 and 2010. The incidences of end-stage kidney disease (ESKD), 30-day, and long-term mortality were evaluated, and clinical and demographic associations with these outcomes were identified using Cox proportional hazards regression models.

Results 546 traumatic AKI-RRT patients, median age 47.6 years (interquartile range: 29.0-64.3) and 76.4% male, were identified. Compared to non-traumatic AKI-RRT, traumatic AKI-RRT patients had longer length of stay in hospital [median (IQR):15 (5-34) days vs 6 (3-11) days; $p < 0.001$]. After propensity matching with non-traumatic AKI-RRT cases with similar demographic and clinical characteristics. Traumatic AKI-RRT patients had lower rates of long-term mortality (adjusted hazard ratio (HR), 0.488; 95% CI, 0.405-0.588; $p < 0.001$), but similar rates of ESKD (HR, 1.075; 95% CI, 0.767–1.509; $p = 0.674$) and short-term risk of death (HR, 1.165; 95% CI, 0.920-1.476; $p = 0.205$) as non-traumatic AKI-RRT patients.

Conclusions Despite severe injuries, traumatic AKI-RRT patients had better long-term survival than non-traumatic AKI-RRT patients, but a similar risk of ESKD. Our results provide a better understanding of long-term outcomes after traumatic AKI-RRT.

Background

Acute kidney injury (AKI) has been studied in a wide range of populations and has been consistently associated with increased risk of future morbidity and mortality.[1, 2] The in-hospital mortality associated with AKI ranges from 9.1% to 21.9% in the United States,[3] and amounts to as high as 62% in the critical care setting in patients requiring renal replacement therapy (RRT).[4, 5]

Trauma is a leading cause of hospitalization worldwide, which mainly affects a young and previously healthy population both in the developed and developing world. The incidence of AKI among major traumatic injuries has been reported to be 6.0–36.8% [6, 7], and traumatic AKI has been associated with a mortality rate of 14.9–57.0% [7-10]. Overall around 5% of trauma patients admitted to the intensive care unit (ICU) require RRT [10]. In a recent systematic review the pooled incidence of AKI after trauma was 20.4% with an associated 3.6-fold increase in the relative risk of death, commonly reported associations of AKI after trauma include older age, higher severity of injury, volume of blood transfusion, abdominal site of injury and presence of comorbid disease including diabetes mellitus.[11] Prior studies of traumatic

AKI-RRT have focused mainly on short-term outcomes [12, 13] and detailed comparisons of outcomes between traumatic-AKI and AKI of differing etiologies that have not been made.

Given the paucity of studies concerning traumatic AKI-RRT, we sought to describe its epidemiology and associated short and long-term outcomes in a large epidemiological database.

Methods

Study design and setting:

National Health Insurance registration database (NHIRD)

The Taiwan National Health Insurance (NHI) program is mandatory and universal, offering comprehensive medical care coverage to more than 99% of the country's population of 23 million people. This nationwide compulsory healthcare program that covers outpatient visits, hospital admissions, prescriptions, interventional procedures, disease profiles, and vital statuses. Taiwan's NHI records are regularly inspected, and physicians are subject to statutory regulation.[13-18] The National Health Insurance Research Database (NHIRD) thus represents a comprehensive, high-quality record of healthcare episodes provided to the Taiwanese population.

Selection of Participants:

We enrolled patients aged ≥ 18 years who were admitted because of major trauma and developed AKI-RRT during their index admission as recognized by RRT-related procedure codes and survived to hospital discharge. All diagnoses, including trauma-related injuries and baseline comorbidities, were obtained by the codes of International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). Those that were related to vehicle-related accidents, defined as any of ICD-9-CM E-Code E800 to E844 included in the diagnosis codes, were aggregated to individuals and were enrolled as study subjects.[15] When more than one accident was encountered by a single person, only the first event was counted for analysis. We identified baseline comorbidities from at least three outpatient visits or one inpatient claim within a one-year antecedent to the index admission with first dialysis. This rule was constructed based on a relatively strict criterion and was well validated with good predictive power.[13-16, 19]

Dialysis patients who underwent renal transplantation, vascular access creation, or peritoneal-dialysis catheter implantation for chronic dialysis and those who had received chronic dialysis prior to the index admissions were excluded. To compare the long-term outcomes of interest, we constructed a comparator group of non-traumatic AKI-RRT patients matched to traumatic AKI-RRT patients in a 3:1 ratio based on age, gender, and propensity scores. (Supplemental Table 1)

As all personal information is de-identified in the research database to protect privacy, no informed consent was required, and this study was deemed exempt from a full ethical review by the institutional review board of the National Taiwan University Hospital (201212021RINC).

Outcomes:

Our primary outcome was long-term all-cause mortality after hospital discharge. The secondary outcomes were 30-day all-cause mortality and de novo end-stage kidney disease (ESKD) defined as the requirement of dialysis for at least three months after hospital discharge. We used a selection period of 90 days to define ESKD because all patients receiving dialysis for more than 90 days in Taiwan can apply to the NHI for catastrophic illness registration cards.[20] Each patient was monitored from the date of discharge and was censored at either death, dialysis, or the end of the study (December 31, 2010), whichever occurred first.

Research variables

We recorded the disease severity and patient condition during index hospitalization. Disease severity and patient condition are estimated by the ICU procedure and complications with acute pulmonary (prolonged mechanical ventilation, re-intubation, acute respiratory distress syndrome, pleural effusion, and chest tube insertion), cardiovascular [hemopericardium, hypovolemic shock, cardiac arrest, heart block, atrial fibrillation, extracorporeal membrane oxygenation (ECMO) and intra-aortic balloon pumping (IABP)] and infectious (pneumonia, urinary tract infection and severe sepsis) and other (delirium, stroke and gastrointestinal bleeding) disorders.[21]

The Charlson comorbidity index [22] was computed using baseline comorbidities. Additional adjustments in these models included control for direct effects from age, gender, and comorbidities that are listed in Table 1.

Analysis

Baseline characteristics were described as the percentages for categorical variables and median with interquartile range (IQR) for continuous variables. Differences between the trauma and non-trauma related groups were compared by the independent t -test or χ^2 test where appropriate.

To estimate each patient's propensity score for traumatic AKI-RRT, we fitted a separate multivariable logistic regression model with the factors predicting vehicle trauma as admitting diagnosis in patients with AKI-RRT during index hospitalization.[23] (further seen in supplementary Table 1). The caliper distance is 0.25 and subjects are matched without replacement in this propensity score matching. The estimated propensity score was also added to adjusting the Cox regression model as a single covariate for controlling selection bias. Multivariable logistic regression models before and after propensity-scored matching were applied to estimate odds ratio (OR) of study outcomes after adjusting all the confounders predicting trauma (supplementary Table 1).

The significance levels for entry and stay were set to 0.15 to be conservative. Then, with the aid of substantive knowledge, the best candidate final logistic model was identified manually by dropping the

covariates with p value > 0.05 one at a time until all regression coefficients were significantly different from 0.

All the analyses were conducted with R software, version 2.8.1 (Free Software Foundation, Inc., Boston, MA, USA); competing-risk analysis was performed using Stata/MP version 12 (Stata Corporation). A two-sided p -value < 0.05 was considered to be statistically significant.

Results

Temporal change in in-hospital mortality

Among 123,470 hospitalized AKI-RRT patients in the past decade, we identified 546 vehicle-traumatic AKI-RRT patients who survived to index discharge (Figure 1). The annual number of trauma cases decreased gradually; however, the proportions of traumatic AKI-RRT patients tended to increase over time, especially in the elderly group (aged ≥ 65 years) (Figure 2). In our cohort, young patients (aged ≤ 44 years) were less likely to be admitted because of trauma; however, they had the highest incidence of traumatic AKI-RRT (Figure 2) during hospitalization. On the other hand, soft tissue injury from trauma had the lowest incidence of AKI-RRT (Figure 3).

Patient characteristics before and after propensity score matching

Compared to patients with other causes of AKI-RRT, vehicle-traumatic AKI-RRT patients were younger [median IQR: 47.6 (29.0-64.3) vs 65.9 (53.7-74.5), $p < 0.001$] and more of them were male (77.1% vs 54.2%, $p < 0.001$). Vehicle-traumatic AKI-RRT patients also had a lower rate of cerebrovascular disease, COPD, diabetes, liver disease, and advanced chronic kidney disease (CKD). More pulmonary and cardiac complications occurred in AKI-RRT patients than non-traumatic AKI-RRT patients during hospitalization. Among them, 517 traumatic AKI-RRT patients were successfully matched with 1,551 non-traumatic AKI-RRT patients. (Table 1).

Outcomes in patients with AKI-RRT after discharge

After propensity score matching, the follow-up period was 2.98 years. The 30-day mortality was similar between two groups (18.4% vs 15.9%, $p = 0.207$). Although the baseline comorbidities and acute medical problems before index hospitalization were similar in both groups after matching, vehicle-traumatic AKI-RRT patients had a longer length of stay in hospital [median IQR 15 (5-35) vs 12 (5-28) days, $p = 0.007$]. The long-term incidence of ESKD was similar between groups (10.6% vs 13.4%, $p = 0.832$) (Table 1).

The risk of developing ESKD (HR, 1.075, $p = 0.674$) and 30-day mortality after discharge (HR, 1.165, $p = 0.205$) among the vehicle-traumatic AKI-RRT patients relative to non-traumatic AKI-RRT were similar. However, vehicle-traumatic AKI-RRT patients had a lower risk of long-term mortality than non-traumatic group (adjust HR: 0.488, $p < 0.001$) (Table 2). Furthermore, this lower mortality rate after vehicle-traumatic AKI-RRT persisted after adjusting for age, gender and Charlson score Cox proportional analysis. ($p < 0.001$) (Figure 3)

Discussion

Our study is, to our knowledge, the first to describe the short-term and long-term outcomes of vehicle-traumatic AKI-RRT patients from a large national database. Our study demonstrated that vehicle-traumatic AKI-RRT patients had lower long-term mortality than non-traumatic AKI-RRT patients. However, incident ESKD and short-term mortality were similar between vehicle-traumatic and non-traumatic AKI-RRT patients.

The trend of traumatic AKI-RRT

In an observational study in the United States, the incidence of AKI-RRT increased at an average of 10% per year from 2000 to 2009.[9] In the NHIRD, we found that the proportions of patients with AKI-RRT among vehicle-traumatic patients also increased throughout the years. The older the patients, the higher annual number of trauma cases was found; however, the oldest traumatic group had the lowest incidence of AKI-RRT (Figure 2). These results may indicate that young people had higher severity of trauma and the consequent risk of AKI-RRT. There seemed to be no difference in body distribution of injury on the incident vehicle-traumatic AKI-RRT except for the lowest incidence of soft tissue injury related AKI-RRT.

ESKD and long-term mortality in patients with traumatic AKI-RRT

AKI in traumatic patients is a common complication and associated with significantly higher 30-day and 1-year mortality than traumatic patients without AKI.[12] Although trauma-related risk factors for kidney injury (e.g., direct lesions to the kidneys, shock, ischemia-reperfusion, rhabdomyolysis, exposure to nephrotoxic substances, abdominal compartment syndrome, hemorrhagic shock and sepsis), The rate of long term incident ESKD in patients after AKI-RRT in our study did not significantly differ vehicle-trauma and non-trauma populations. However, compared to non-traumatic AKI-RRT patients, traumatic patients had lower risk of long-term mortality after survival in our cohort. The above results may indicate that the etiology of AKI-RRT may be associated with long-term mortality. On the other hand, the risk of ESKD existed if renal damage happened regardless of trauma or non-trauma.

One of the few other studies examining long term-outcomes after traumatic AKI examined 40 soldiers who survived traumatic AKI-RRT in that study there was a lower incidence of ESKD (2.5% vs 10.6%) and a lower long-term mortality (2.5% vs 25%) rate over a median follow-up of 2.7 years than in our cohort.[24] These differences might be attributed to low incidence rates, younger age (26 ± 6 years), and fewer baseline comorbidities in the military study. [24]

Follow-up strategy in patients of AKI-RRT

AKI-RRT has been shown to be associated with an increased incidence of ESKD, mortality,[25] coronary events,[13] stroke,[26] and bone fracture[14] among those who survived to hospital discharge. Although guidelines published by Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline recommend that survivors of AKI be followed up by a nephrologist within 90 days,[27] reports in the literature suggest only a small proportion of patients after severe AKI are followed-up by a nephrologist after survival discharge.[28-30] Given their young age, relative lack of comorbidity, and still significant risk of developing ESKD, AKI-RRT is a neglected population where focused medical follow-up could address the progression of CKD and development of other complications over a long expected lifespan. These results further provide the outcome information for patient care and rational health resource allocation.

Limitations

Our study has certain limitations. Firstly, as all observational studies, we could not exclude the possibility of residual confounding. To decrease the effect of potential confounding factors, we developed a 3:1 propensity score. We were able to construct a comparison cohort with balanced covariates between the two groups. Second, with all administrative databases, detailed in-hospital parameters, and laboratory results were not available in our cohort. Therefore, we could not examine whether classifying patients into different severity scoring systems, such as the Injury Severity Score and Acute Physiology and Chronic Health Evaluation score. The severity of trauma and illness has been found to be associated with AKI, [8, 31] and thus could be potential predictors of clinical outcome. Third, we did not analyze the effect of duration and modality of RRT which may be the predictors of disease severity and the confounding factors of long-term outcomes in our study. To attenuate the effect of the limitations, we did adjust by Charlson comorbidity index (pre-admission comorbidities) and in-hospital acute comorbidities, including pulmonary and hemodynamic complications, to evaluate the disease severity of each patient in our database.

Conclusion

In our study, we found that the vehicle-traumatic AKI-RRT patients had better long-term survival than non-traumatic counterparts with AKI-RRT. However, there were similar outcomes of ESKD and short-term mortality. Our findings are pertinent to civilian populations with similar demographics and may inform care in real-world practice.

Abbreviations

AKI: Acute kidney injury; CKD: chronic kidney disease; ECMO: extracorporeal membrane oxygenation; ESKD: end-stage kidney disease; IABP: intra-aortic balloon pumping; ICD-9-CM: International Classification of Diseases, 9th Revision, Clinical Modification; ICU: intensive care unit; IQR: interquartile range; KDIGO:

Kidney Disease: Improving Global Outcomes; NHI: National Health Insurance; NHIRD: National Health Insurance registration database; OR: odds ratio; RRT: renal replacement therapy.

Declarations

Ethics approval and consent to participate

National Taiwan University Hospital (201212021RINC)

Consent for publication

Yes

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was supported by Taiwan National Science Council [101-2314-B-002-085-MY3, 102-2314-B-002-140-MY2, 104-2314-B-002-125-MY3, 106-2314-B-002 -166 -MY3,107-2314-B-002-026-MY3], National Health Research Institutes [PH-102-SP-09)], National Taiwan University Hospital [106-FTN20, 106-P02, UN106-014, 106-S3582, 105-P05, VN105-04, 105-S3061, 107-S3809, 107-T02] and Ministry of Science and Technology (MOST) of the Republic of China (Taiwan) [grant number, MOST 106-2321-B-182-002]

Authors' contributions

Chan, Wu and Prowle authored the article and made final editorial decisions. Chan and Wu contributed to the study design and data collection and analysis. All authors contributed to article development and revision.

Acknowledgments:

The study was partly based on data provided by the National Health Insurance Administration, Ministry of Health and Welfare, Taiwan. The interpretation and conclusions shown in this paper do not represent those of the National Health Insurance Administration, Ministry of Health and Welfare, National Health Research Institutes, or National Taiwan University Hospital. We also express our sincere gratitude to all staff of the Taiwan Clinical Trial Consortium, TCTC.

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Tables

Table 1: Clinical characteristics after propensity score matching (NHIR database)

	Before matching			After matching		
	Non-trauma group (n = 122,924)	Trauma group (n = 546)	p-Value	Non-trauma group (n = 1,551)	Trauma group (n = 517)	p-Value
ortality	66595 (54.2%)	421 (77.1%)	<0.001	1183 (76.3%)	395 (76.4%)	0.952
ortality (IQR)	65.9 (53.7-74.5)	47.6 (29.0-64.3)	<0.001	48.7 (34.2-64.9)	48.7 (31.5-65.3)	0.469
Major Comorbidities						
Major morbidity index (IQR)	0 (0-0)	0 (0-1)	<0.001	0 (0-1)	0(0-1)	0.075
Myocardial infarction	988 (0.8%)	3 (0.6%)	0.51	10 (0.6%)	3 (0.6%)	0.872
Heart failure	5410 (4.4%)	22 (4.0%)	0.67	80 (5.1%)	22 (4.3%)	0.412
Cerebrovascular disease	9742 (7.9%)	13 (2.4%)	<0.001	41 (2.6%)	13 (2.5%)	0.874
	1384 (1.1%)	1 (0.2%)	0.04	6 (0.4%)	1 (0.2%)	0.512
Chronic obstructive pulmonary disease	12042 (9.8%)	30 (5.5%)	<0.001	90 (5.8%)	30 (5.8%)	0.999
	12025 (9.8%)	28 (5.1%)	<0.001	99 (6.4%)	28 (5.4%)	0.428
	42643 (34.7%)	77 (14.1%)	<0.001	209 (13.4%)	77 (14.9%)	0.419
	7229 (5.9%)	24 (4.4%)	0.14	91 (5.8%)	24 (4.6%)	0.293
	92238 (75.0%)	130 (23.8%)	<0.001	388 (24.9%)	130 (25.2%)	0.953
	51628 (42.0%)	41 (7.51%)	<0.001	119 (7.6%)	41 (7.9%)	0.849
Minor Comorbidities						
Complications						
	10506 (8.6%)	416 (76.2%)	<0.001	1184 (76.0%)	387 (74.9%)	0.494
	5989 (4.9%)	228 (41.8%)	<0.001	688 (44.2%)	217 (42.0%)	0.344
	509 (0.4%)	7 (1.3%)	0.002	35 (2.3%)	7 (1.4%)	0.208
	376 (0.3%)	3 (0.6%)	0.30	11 (0.7%)	3 (0.6%)	0.753
	1041 (0.9%)	111 (20.3%)	<0.001	247 (15.9%)	90 (17.4%)	0.429
Other complications						
	668 (0.5%)	12 (2.2%)	<0.001	32 (2.1%)	10 (1.9%)	0.856
	147 (0.1%)	17 (3.1%)	<0.001	44 (2.8%)	12 (2.3%)	0.532
Infections						
	2346 (1.9%)	5 (0.9%)	0.09	14 (0.9%)	5 (1.0%)	0.894
	2984 (2.4%)	4 (0.7%)	0.01	19 (1.2%)	4 (0.8%)	0.397
	6041 (4.9%)	72 (13.2%)	<0.001	243 (15.6%)	68 (13.2%)	0.166
	6 (3-11)	15 (5-34)	<0.001	12 (5-28)	15 (5-35)	0.007
	2490 (2.0%)	99 (18.1%)	<0.001	248 (15.9%)	95 (18.4%)	0.207
	73777 (60.0%)	134 (24.5%)	<0.001	729 (46.8%)	129 (25.0%)	<0.001
	32445 (26.4%)	45 (8.2%)	<0.001	208 (13.4%)	55 (10.6%)	0.892

Abbreviation: ECMO, extracorporeal membrane oxygenation; ESKD, end stage kidney disease; IQR, interquartile range.

Table 2. Incidence and risks for outcome of interest in AKI patients with renal replacement therapy during hospitalization, between vesicle-traumatic patients and their matches.

Events	Person-Years	Incidence Rate per 1000 Person-Years		Events	Person-Years	Incidence Rate per 1000 Person-Years	Crude		Adjust*	
							Hazard Ratio (95% CI)	p	Hazard Ratio (95% CI)	p
Trauma			Non-trauma			Trauma vs Non-trauma				
45	3614.99	12.45		132	11068.44	11.93	1.039 (0.741-1.457)	0.825	1.075 (0.767-1.509)	0.674
95	36.94	2571.74		248	111.68	2220.63	1.154 (0.911-1.462)	0.234	1.165 (0.920-1.476)	0.205
129	2453.31	52.58		769	5946.12	129.33	0.434 (0.360-0.523)	<0.001	0.488 (0.405-0.588)	<0.001

Abbreviations: ESKD, end-stage kidney disease; CI, confidence interval.

* The multivariate Cox regression model selected covariates from all variables in Table1 by a stepwise procedure.

Figures

Figure 1 Flow chart of the participants

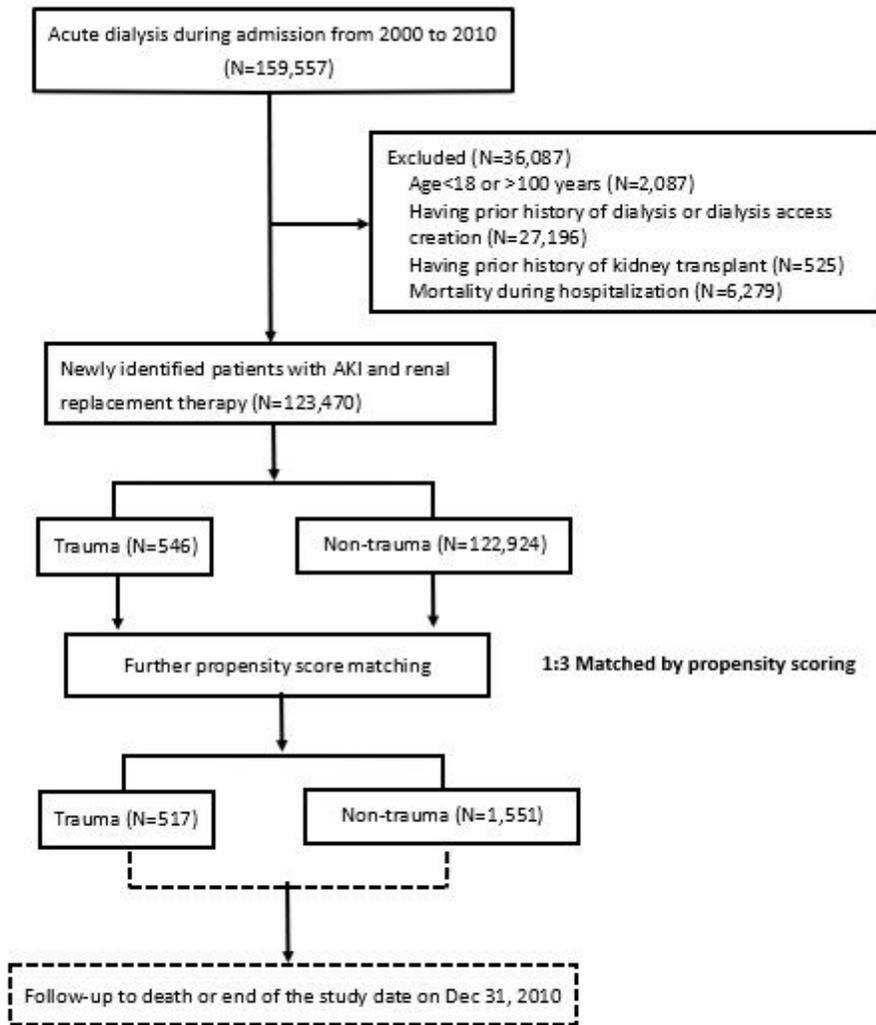


Figure 1

Flow chart of the participants

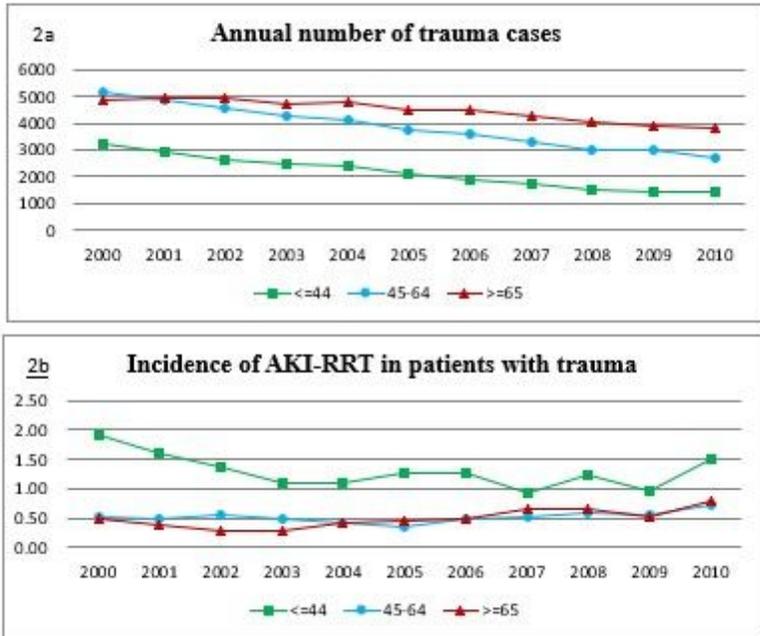


Figure 2

Temporal patterns of annual number of trauma cases (2a) and incidence of vesicle-traumatic AKI-RRT (2b) stratified by age groups. (Figure 2b p for trend, age \leq 44: 0.073, 45 < age <65: 0.183, age \geq 65: 0.004)

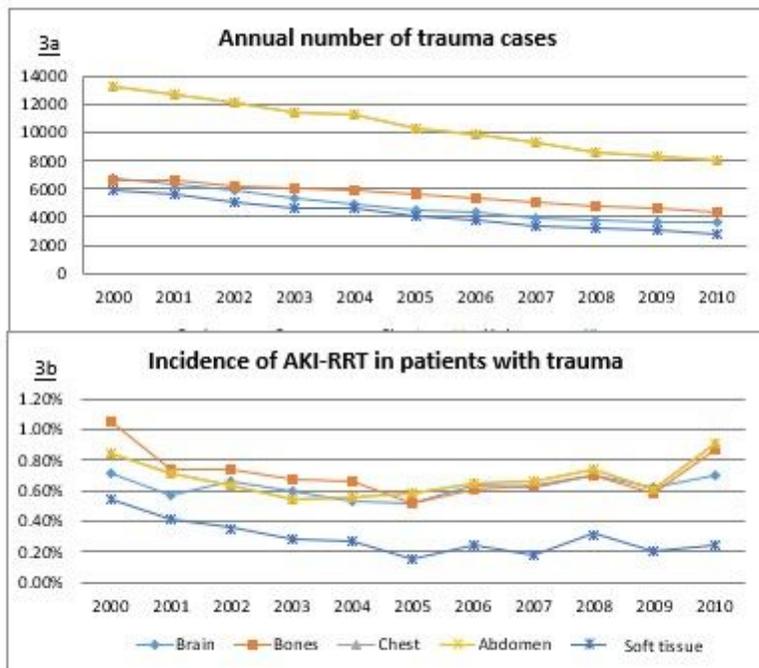


Figure 3

Temporal patterns of annual number of trauma cases (3a) and incidence of traumatic AKI-RRT (3b) stratified by injured body part. (Figure 3b p for trend, brain: 0.697, bones: 0.186, chest: 0.484, abdomen: 0.484, Skin: 0.024)

Supplementary Files

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