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Original Research

Long-term renal outcomes in patients with traumatic renal injury after nephrectomy: A nationwide cohort study

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A R T I C L E I N F O

Keywords:
Trauma
Traumatic renal injury
Nephrectomy
Renal outcome
Dialysis

A B S T R A C T

Background: The long-term renal outcomes of patients who underwent nephrectomy for traumatic renal injury (TRI) have rarely been reported. Therefore, we investigated the impact of nephrectomy for TRI on long-term renal outcomes.

Methods and materials: We extracted data from the National Health Insurance Research Database (NHIRD) of Taiwan from 1999 to 2013 and identified patients with TRI. Adverse kidney outcomes (AKOs), including lifelong dialysis and chronic kidney disease (CKD), were chosen as endpoints of the study.

Results: A total of 16,320 eligible patients were identified in the NHIRD. The incidence of lifelong dialysis was 0.6% (99/15,789) for patients without nephrectomy, while the incidence was 1.1% (6/531) for nephrectomized patients. Overall, the incidence of AKOs was 2.1% (11/531) in the group that underwent nephrectomy and 1.1% (166/15,789) in the group without nephrectomy. Before matching, differences in overall AKO incidence between the groups were significant, while propensity score matching eliminated this significance.

Conclusions: The results of our study did not indicate that AKOs would occur in patients with TRI who underwent nephrectomy.

1. Introduction

With an incidence of less than 5% [1], traumatic renal injury (TRI) rarely occurs in trauma patients, although it is the most common traumatic genitourinary injury [2]. The management of TRI has evolved over recent decades [3]. Nonoperative management (NOM), including clinical observation and adjunct transarterial embolization (TAE), is the current standard of treatment for both blunt and penetrating injury [1,4,5], even for American Association for the Surgery of Trauma (AAST) high-grade TRI [6]. The advantages of NOM for TRI include decreases in local complications [7], hospital stays [8], and impairments in renal function during the perioperative period [8]. Therefore, surgical treatment for TRI is currently reserved for patients with unstable hemodynamic status.

Although surgical treatment, particularly nephrectomy, for TRI is increasingly utilized less frequently, this treatment option has not been completely abandoned. Unlike patients with malignancy, patients with TRI undergoing surgical management are still expected to survive for many years. Therefore, in addition to immediate surgical complications, long-term sequelae should also be of concern. The most concerning long-term sequela related to nephrectomy is impaired renal function. Many relevant studies of long-term renal function focused on donor nephrectomy and nephrectomy due to urinary malignancy have been published; however, relevant studies evaluating TRI are relatively scarce.

Because surgical treatment, particularly nephrectomy, is inevitable in devastating circumstances, clinicians should focus on long-term renal outcomes. In this study, we analyzed data from the National Health Insurance Research Database (NHIRD) of Taiwan to investigate the impact of nephrectomy for TRI on long-term renal outcomes.

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2. Methods and materials

2.1. Data source

The NHIRD is derived from the government-operated single-payer National Health Insurance (NHI) program, a universal public program in Taiwan that was launched in 1995 and covers nearly all (99.5%) of the approximately 23 million residents of Taiwan [9]. Information, including the costs of all procedures, surgeries, and medications, can be extracted from the database with a specific code. All personal information in the NHIRD is anonymized; thus, this study was exempt from a full review by the Ethics Institutional Review Board. The work has been reported in line with the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) criteria [10].

Patients suffering from trauma are in a specific group that has been well audited under the NHI program. A catastrophic illness certificate (CIC) is issued to each patient with an injury severity score (ISS) [11,12] exceeding 16. Those patients are exempt from paying insurance premiums and copayments for a period of 1 year. Every CIC application is carefully reviewed by the NHI program, and CIC data are accurate and reliable [13]. In addition, the Ministry of Health and Welfare of Taiwan established a standard of accreditation for the capability of emergency medical care (management of trauma is a major audit item), and the result of accreditation affects the level of an institute under the NHI system. In other words, the level of an institution that is incapable of providing trauma care would be downgraded, and the amount of reimbursement for all medical services would decrease. Therefore, the data on trauma patients extracted from the NHIRD are reliable due to their importance in determining the level of payment from the NHI program.

2.2. Study population and grouping

This study employed an open, observational, longitudinal cohort design to compare adverse kidney outcomes (AKOs; definition will be provided in the next paragraph) between patients who did and did not receive surgical treatment for TRI. Based on the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), we selected patients who suffered from torso trauma and were hospitalized. The ICD-9 codes for torso trauma included 860.xx to 862.xx for cardiac and thoracic trauma, 863.xx for gastrointestinal injury, 864.xx for injury of the liver, 865.xx for injury of the spleen, 866.xx for injury of the kidney, and 867.xx for injury of the pelvic organs. Trauma episodes occurring from January 1996 to December 1998 were excluded from the analysis to ensure that medical information for all patients was available for at least 3 years before the index year. We then excluded patients with incomplete records or with external code E87, indicating iatrogenic injury, before further analysis. The study period was indexed from 1999 to 2013. Subjects eligible for inclusion in our study were patients experiencing torso trauma during the aforementioned period with an ICD-9 code of 866.xx (injury of the kidney). The exclusion criteria included regular dialysis, known CKD, nephrectomy not due to the index trauma episode, nephrectomy other than unilateral total nephrectomy for TRI, AKOs diagnosed less than 1 year after index episode of trauma, or hospital mortality. We excluded patients with nephrectomy other than unilateral total nephrectomy because kidney volume is correlated with renal function [14] and the extent of partial nephrectomy is heterogeneous. In addition, we excluded patients with AKOs occurring within 1 year after nephrectomy. According to a published study, renal function steadily improves one year after nephrectomy after a sudden and initial decrease in the estimated glomerular filtration rate (eGFR) [15]. Therefore, we postulated that AKOs occurring more than 1 year after the trauma episode would not be related to the acute episode and that the actual long-term outcome would be revealed.

The grouping factor in our study, the presence or absence of nephrectomy, was based on NHI procedure codes. The NHI program reimburses medical costs according to the procedure code. The accuracy is good, and validation has been carried out for certain specific medical conditions [16]. If the analysis reveals a significant difference in renal outcomes between nonnephrectomized patients and nephrectomized patients, we will investigate the risk factors for AKOs within the group of nephrectomized patients.

2.3. Comorbidities, associated injuries, and outcomes

The baseline characteristics and surgical details of the patients were identified using ICD-9-CM and NHI procedure codes for the index hospitalization and prior hospitalizations. The comorbidities that were considered in our analysis included coronary artery disease (CAD), hypertension, diabetes mellitus, and liver cirrhosis. Associated injuries, ISS, amount of transfusion, and mechanism of injury (blunt or penetrating) were also considered in the subsequent matched analysis. Associated injuries were categorized into craniofacial, cardiac, pulmonary, gastrointestinal, splenic, hepatic, pelvic, and spinal injuries.

The outcomes of interest in this study were end-stage renal disease (ESRD) with lifelong dialysis and CKD. AKOs were defined as either of the aforementioned conditions. Patients with ESRD must receive lifelong dialysis and qualify for a lifelong CIC issued by the NHI program of Taiwan. Therefore, we easily identified patients with ESRD on the basis of the issuance of a CIC. CKD was identified based on ICD-9-CM coding in the NHIRD.

2.4. Statistical analysis

We used R (version 3.3.2) open source statistical software with the appropriate statistical packages for analysis. Curves of the cumulative incidence of AKOs were generated using the Kaplan-Meier method, and the log-rank test was used for comparisons. A p value < 0.05 was considered indicative of statistical significance. Due to the rarity of nephrectomy for TRI in Taiwan based on the NHIRD (3.4%), propensity score matching was applied to the statistical analysis. In this study, we used the most common fashion of propensity score matching: one-to-one matching to construct pairs of treated and untreated subjects with the greedy neighbor approach and a caliper setting of 0.1 [17]. After matching, we also performed a test to confirm that the matching result was balanced. The use of balance diagnostics is important and should be reported in matched samples [18]. In our study, we used standardized differences, which should be less than 0.1 when the matching result is considered balanced. Only adequately balanced matched samples provide unbiased analysis. The R software packages for propensity score matching and later analysis and graphing included *MatchIt, tableone, ggplot2,* and *survminer.*

3. Results

Within the study period from 1999 to 2013, 165,910 patients fulfilled the criteria for the selected ICD-9-CM codes for torso trauma. A total of 17,143 patients in the cohort were diagnosed with kidney injury. After excluding patients fulfilling the aforementioned exclusion criteria, 16,320 patients were enrolled and subsequently analyzed (Fig. 1). Five hundred thirty-one (3.3%) of these patients underwent a unilateral total nephrectomy, and the remaining 15,789 patients served as the nonnephrectomy group. Demographic data, clinical information, and renal outcomes are all summarized in Table 1. The median follow-up time was 97.6 months.

We also performed subgroup analysis based on the trauma mechanism, and in our cohort, blunt injury accounted for 98.4% (16060/16320). We extracted patients suffering from blunt injury for further analysis. Demographic data are summarized in Table 2; in our cohort, 261 (1.6%) patients suffered from penetrating injury. However, the percentage of patients undergoing nephrectomy for penetrating injury

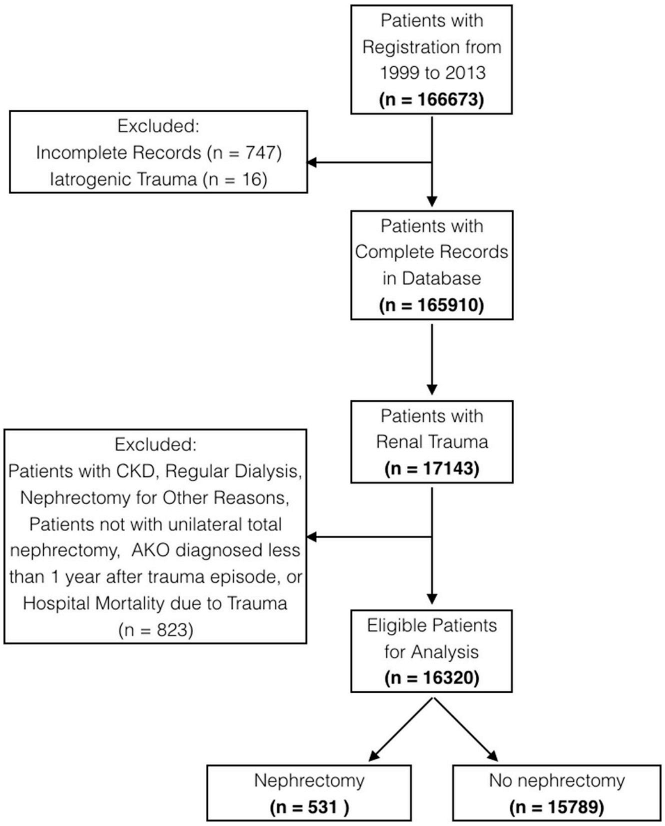

Fig. 1. Enrollment of the population-based cohort of 189,341 patients who suffered from torso trauma between 1996 and 2013, extracted from the Taiwan NHIRD. CKD: chronic kidney disease; AKOs: adverse kidney outcomes.

was much higher than that of patients with blunt injury (16.5% vs. 3%).

3.1. Adverse kidney outcomes

The incidence of lifelong dialysis was 0.6% for patients without nephrectomy, while the incidence was 1.1% for nephrectomized patients. Overall, the incidence of AKOs was 2.1% in the group that underwent nephrectomy and 1.1% in the group without nephrectomy (Table 1). Cumulative incidence curves of lifelong dialysis and AKOs before and after propensity score matching are both illustrated (Fig. 2). Interestingly, no significant differences in the lifelong dialysis was found between those 2 groups ($p = 0.16$), while statistically significant differences ($p = 0.026$) were identified in AKO incidence before matching. After propensity score matching, neither lifelong dialysis nor AKOs were noted to have a significant difference between the groups. A similar result was also revealed in the analysis for blunt injury only (Fig. 3). For patients with penetrating injury, all the analyses were nonsignificant. On the basis of the aforementioned results, we did not investigate the risk factors for AKOs within the group of nephrectomized patients.

4. Discussion

Nephrectomy for TRI is a last resort for management and is usually reserved for patients with unstable hemodynamic status. Based on the NHIRD, less than 4% of patients with TRI underwent a nephrectomy during the study period. This result is consistent with most published studies and supports the preferred use of NOM for the treatment of TRI [6,19–21]. Some complications of NOM have been identified, such as urinary leakage, arteriovenous fistula, and delayed bleeding [8]. Spontaneous improvement with or without interventional radiology has been noted for urinary leakage [22,23], while other vascular complications have been properly treated with angioembolization, resulting in a high rate of organ preservation [24]. Delayed nephrectomy is rarely adopted as a treatment modality for complications associated with

Table 1
Basic demographic data and adverse kidney outcome for patients with and without nephrectomy. Both pre-matching and post-matching data are revealed. SD, standardized difference; sd, standard deviaton; CAD, coronary artery disease; DM diabetes mellitus; ISS. Injury severity score.

	Pre-matching			Post-matching		
	No Nephrectomy (n = 15789)	Nephrectomy (n = 531)	SD	No Nephrectomy (n = 511)	Nephrectomy (n = 511)	SD
Male gender (%)	11054 (70.0)	391 (73.6)	0.081	370 (72.4)	374 (73.2)	0.018
Age (sd)	36.95 (18.17)	34.16 (17.94)	0.155	33.53 (15.78)	34.12 (17.92)	0.035
Dialysis during admission (%)	38 (0.2)	15 (2.8)	0.212	12 (2.3)	12 (2.3)	< 0.001
Sepsis (%)	803 (5.1)	20 (3.8)	0.064	14 (2.7)	20 (3.9)	0.066
Acute kidney injury (%)	54 (0.3)	10 (1.9)	0.147	5 (1.0)	7 (1.4)	0.036
Associated injury						
Craniofacial (%)	2498 (15.8)	64 (12.1)	0.109	69 (13.5)	63 (12.3)	0.035
Cardiac (%)	50 (0.3)	0 (0.0)	0.08	0 (0.0)	0 (0.0)	< 0.001
Pulmonary (%)	1477 (9.4)	81 (15.3)	0.18	94 (18.4)	81 (15.9)	0.068
Gastrointestinal (%)	457 (2.9)	90 (16.9)	0.484	72 (14.1)	79 (15.5)	0.039
Splenic (%)	1540 (9.8)	173 (32.6)	0.582	154 (30.1)	163 (31.9)	0.038
Hepatic (%)	1826 (11.6)	119 (22.4)	0.292	128 (25.0)	117 (22.9)	0.050
Pelvic (%)	717 (4.5)	33 (6.2)	0.074	35 (6.8)	32 (6.3)	0.024
Spine (%)	1100 (7.0)	14 (2.6)	0.204	14 (2.7)	14 (2.7)	< 0.001
Underlying medical conditions						
CAD (%)	418 (2.6)	9 (1.7)	0.065	10 (2.0)	9 (1.8)	0.014
Hypertension (%)	1274 (8.1)	26 (4.9)	0.129	25 (4.9)	26 (5.1)	0.009
DM (%)	929 (5.9)	22 (4.1)	0.08	16 (3.1)	22 (4.3)	0.062
Cirrhosis (%)	197 (1.2)	9 (1.7)	0.037	7 (1.4)	9 (1.8)	0.032
ISS16 > 16 (%)	975 (6.2)	164 (30.9)	0.671	149 (29.2)	145 (28.4)	0.017
Penetrating injury of kidney	217 (1.4)	43 (8.1)	0.318	30 (5.9)	36 (7.0)	0.048
Massive transfusion (%)	1571 (9.9)	430 (81.0)	2.035	413 (80.8)	410 (80.2)	0.015
Adverse kidney outcome (%)	166 (1.1)	11 (2.1)	0.082	4 (0.8)	10 (2.0)	0.101
Dialysis (%)	99 (0.6)	6 (1.1)	0.054	3 (0.6)	6 (1.2)	0.063

Table 2
Basic demographic data and adverse kidney outcome for patients of blunt TRI with and without nephrectomy. Both pre-matching and post-matching data are revealed. TRI, traumatic renal injury; SD, standardized difference; sd, standard deviation; CAD, coronary artery disease; DM diabetes mellitus; ISS. Injury severity score.

	Pre-matching			Post-matching		
	No Nephrectomy (n = 15572)	Nephrectomy (n = 488)	SD	No Nephrectomy (n = 471)	Nephrectomy (n = 471)	SD
Male gender (%)	10879 (69.9)	357 (73.2)	0.073	344 (73.0)	343 (72.8)	0.005
Age (sd)	36.97 (18.20)	34.16 (18.13)	0.155	34.30 (16.42)	34.38 (18.19)	0.005
Dialysis during admission (%)	36 (0.2)	13 (2.7)	0.205	11 (2.3)	10 (2.1)	0.014
Sepsis (%)	802 (5.2)	19 (3.9)	0.061	14 (3.0)	19 (4.0)	0.058
Acute kidney injury (%)	53 (0.3)	9 (1.8)	0.145	4 (0.8)	7 (1.5)	0.059
Associated injury						
Craniofacial (%)	2481 (15.9)	64 (13.1)	0.080	57 (12.1)	63 (13.4)	0.038
Cardiac (%)	50 (0.3)	0 (0.0)	0.080	0 (0.0)	0 (0)	< 0.001
Pulmonary (%)	1444 (9.3)	74 (15.2)	0.181	79 (16.8)	74 (15.7)	0.029
Gastrointestinal (%)	418 (2.7)	69 (14.1)	0.422	61 (13.0)	61 (13.0)	< 0.001
Splenic (%)	1510 (9.7)	164 (33.6)	0.607	149 (31.6)	154 (32.7)	0.023
Hepatic (%)	1791 (11.5)	109 (22.3)	0.292	102 (21.7)	105 (22.3)	0.015
Pelvic (%)	715 (4.6)	32 (6.6)	0.086	37 (7.9)	32 (6.8)	0.041
Spine (%)	1090 (7.0)	13 (2.7)	0.203	16 (3.4)	13 (2.8)	0.037
Underlying medical conditions						
CAD (%)	414 (2.7)	9 (1.8)	0.055	7 (1.5)	9 (1.9)	0.033
Hypertension (%)	1264 (8.1)	25 (5.1)	0.121	19 (4.0)	25 (5.3)	0.060
DM (%)	923 (5.9)	22 (4.5)	0.064	21 (4.5)	22 (4.7)	0.010
Cirrhosis (%)	194 (1.2)	8 (1.6)	0.033	5 (1.1)	8 (1.7)	0.055
ISS16 > 16 (%)	953 (6.1)	149 (30.5)	0.665	118 (25.1)	134 (28.5)	0.077
Massive transfusion (%)	1526 (9.8)	394 (80.7)	2.031	378 (80.3)	377 (80.0)	0.005
Adverse kidney outcome (%)	163 (1.0)	10 (2.0)	< 0.001	6 (1.3)	10 (2.1)	0.066
Dialysis (%)	99 (0.6)	6 (1.2)	0.062	3 (0.6)	6 (1.3)	0.066

NOM. Furthermore, the local kidney complication rate in patients with mild to moderate TRI (AAST grades 1 to 3) undergoing surgery has been proposed to be twice as high as the rate in patients with a similarly severity of disease who do not undergo surgery [7]. Therefore, NOM should be the first therapeutic choice for TRI based on the current published literature, contemporary clinical practice and the results of our population-wide study of the NHIRD in Taiwan.

Nephrectomy is more frequently adopted in cases of genitourinary neoplasm and kidney transplantation compared with cases of TRI. Therefore, the investigation of long-term renal outcomes has mainly focused on nephrectomy for neoplasms and donor nephrectomy. Studies of renal function in patients with renal cell carcinoma after nephrectomy revealed that approximately half (49%) of the patients regained their prenephrectomy renal function within 2 years [25]. Compared with partial nephrectomy, radical nephrectomy exposes patients to a higher risk of CKD [26,27]. Regarding living donor nephrectomy for transplantation, the risk of ESRD in living donors is considered lower than or no different from the risk in the general population, likely because living donors are thoroughly screened and may be healthier than controls, who are not screened [28]. However, relevant studies comparing nephrectomy and NOM for TRI are rare [29]. In our study, we investigated the renal outcomes of patients with TRI who underwent a nephrectomy, an analysis that can be performed only with the aid of a nationwide database due to the very low incidence of both nephrectomy for TRI and AKOs. Based on our results, no significant inferior outcomes were found for patients with TRI undergoing nephrectomy.

Unlike renal malignancy or organ transplantation, renal trauma can be grouped into two major categories based on the mechanism of trauma: blunt and penetrating injuries. Different mechanisms of trauma may have different kinds of anatomic and physiologic impacts on patients, who consequently have different responses to a single treatment strategy [30]. In the NHIRD of Taiwan, most TRI patients (98.4%) suffered from blunt injury rather than penetrating injury. Therefore, an investigation of the impact of nephrectomy for TRI on long-term renal outcomes may be performed properly with data from patients with blunt injury in the NHIRD. For penetrating injury, the patient number was small, and no lifelong dialysis events were observed in the nephrectomy group in our selected cohort.

In addition to nephrectomy, the most concerning confounding factors in patients with TRI are hemorrhagic shock and sepsis, both of which are sometimes encountered in patients with major torso trauma. Hemorrhagic shock definitely induces prerenal insult and subsequent acute kidney injury. The detailed physiological parameters, such as vital signs, blood pressure, and Glasgow Coma Scale score, are impossible to include in a nationwide database. Therefore, we used massive transfusion (over 20 Taiwanese units of packed red blood cells (RBCs) or whole blood) as a surrogate and included that information into the matching procedure. The blood product and transfusion procedure must be clearly documented, and the cost is positively correlated with transfusion units; therefore, a massive transfusion is a reliable surrogate for hemorrhagic shock. For sepsis, however, we could base the results only on the ICD-9 coding.

Our study has some limitations. First, the ICD-9-CM does not reflect the actual disease severity. The categories of the ICD system are very different from those of the AAST system, which indicates anatomical significance [31]. The diagnostic code for renal injury may include diseases with variable severity, which is related to the clinical management strategy. We identified patients with CIC for major trauma to calibrate disease severity and create balanced groups for analysis in an attempt to address this problem, because only patients with ISS over 16 are issued a CIC for major trauma. In addition, we also matched for associated injuries. We combined these two strategies to balance the disease severity between the two groups in our study. Second, we were not able to obtain information on the patients' previous medical histories prior to the launch of the NHI project or the medical history of citizens with previous residence in a foreign country. Although we did not enroll patients with episodes of trauma within the 3-year period of 1996–1998 in order to increase the accuracy of information on comorbidities and related renal surgical history, some bias likely exists. If we increased the length of the period to greater than 3 years, more eligible subjects who underwent nephrectomy would be lost, which is an inevitable dilemma. Third, because we were unable to obtain the specific data regarding patients' renal function, such as creatinine levels

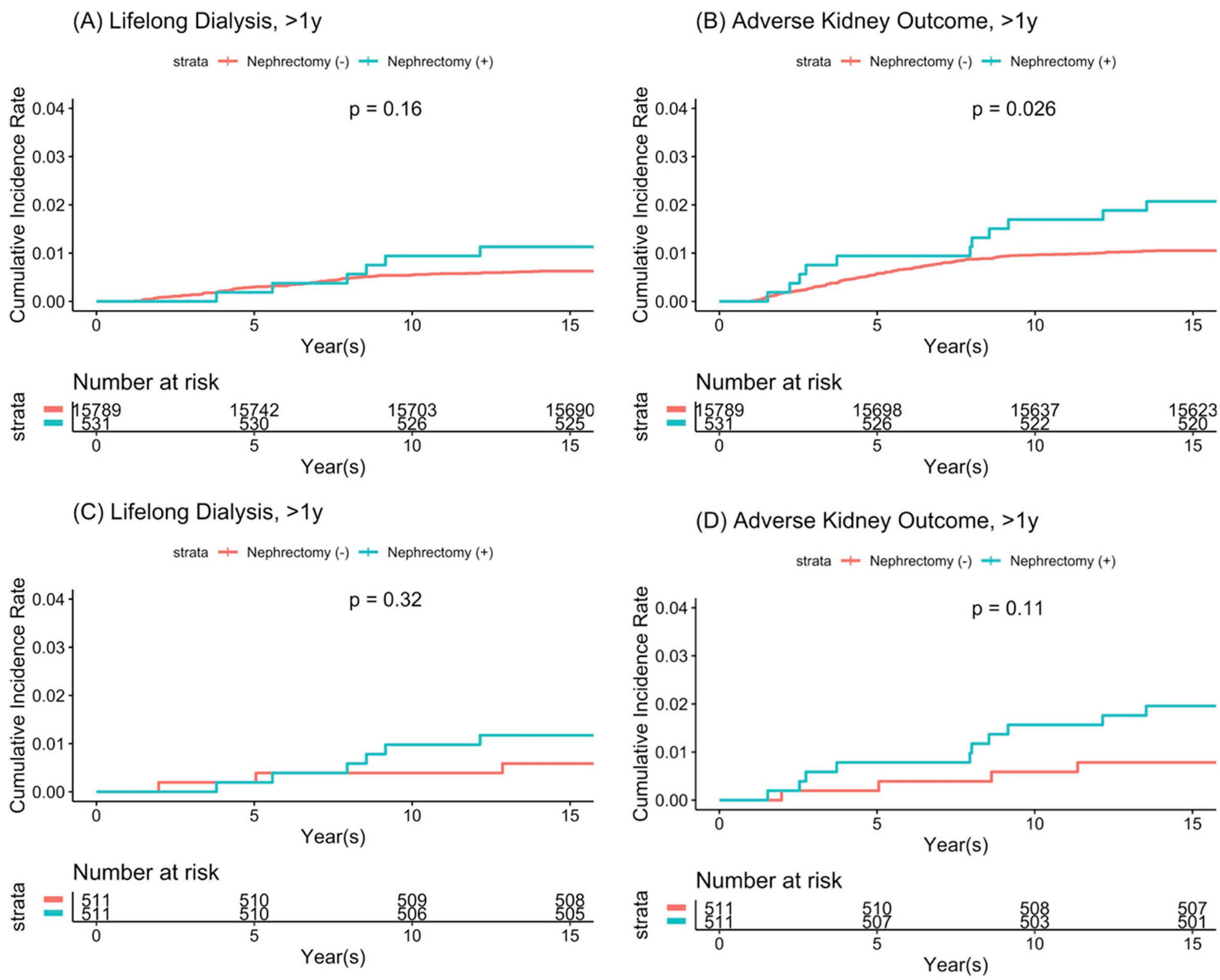

Fig. 2. Cumulative incidences of AKOs and lifelong dialysis in patients who underwent nephrectomy and those without nephrectomy. (A) and (B) reveal the results of the prematching dataset, while (C) and (D) illustrate the postmatching results. AKOs: adverse kidney outcomes.

and eGFR, we attempted to evaluate renal outcomes using two other factors, namely, ESRD with long-term dialysis and CKD. As mentioned above, diagnosis of ESRD is based on the identification of CIC for ESRD and is therefore reliable. The diagnosis of CKD, however, is simply based on the ICD-9-CM code, and coding errors cannot be avoided, although validation of the coding in the NHIRD was performed for other diseases with accuracy of up to 90% [16,32]. Finally, we were not able to investigate the impact of TAE using the NHIRD dataset. Although TAE has been recognized as an important aspect of NOM for trauma, the coding is the same as TAE performed for other regions. Therefore, we cannot evaluate its impact on renal trauma in our study.

In conclusion, nephrectomy for TRI does not impose a risk of AKOs based on our 13-year nationwide database analysis. Therefore, the decision to administer NOM or nephrectomy for TRI is based simply on the clinical conditions of the patient and the available medical resources. Unfavorable long-term renal outcomes are not an indicator for clinicians to make every effort to perform NOM.

Ethical approval

This study was exempt from a full review by the Ethics Institutional Review Board of Chang Gung Memorial Hospital (ref. 201601409B1).

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Conflicts of interest

All authors has no conflicts of interest related to this submitted manuscript.

Research registration number

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Guarantor

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Chih Hsiang Chang (nephrologistchange@gmail.com).

Provenance and peer review

Not commissioned, externally peer-reviewed.

Data statement

The dataset from NHIRD can only be distributed under permission from National Health Insurance Administration and confidentiality agreement is necessary for dataset access. Therefore we are not entitled to distribute the dataset freely.

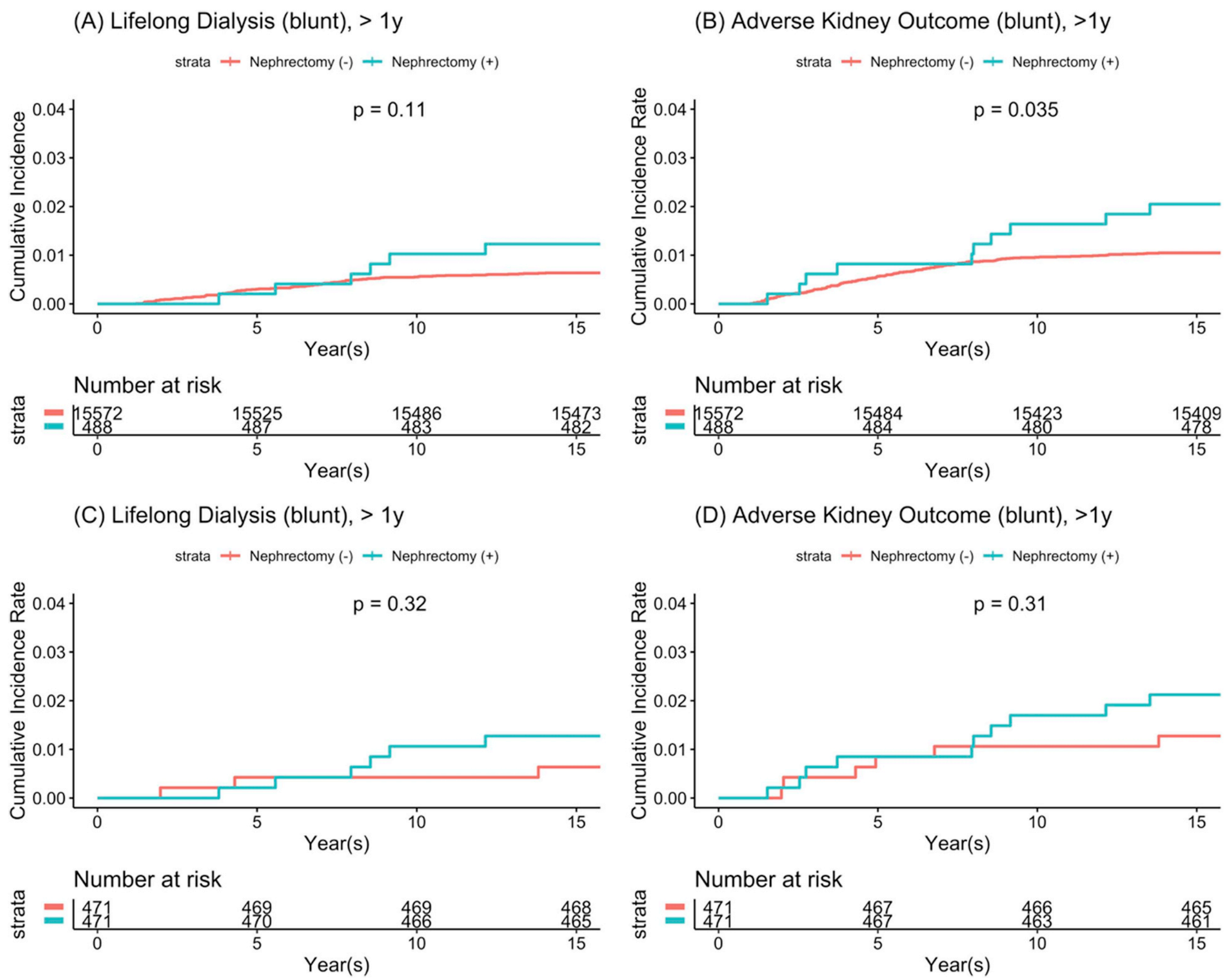

Fig. 3. Cumulative incidences of AKOs and lifelong dialysis for patients suffering from blunt renal injury. (A) and (B) reveal the results of the prematching dataset, while (C) and (D) illustrate the postmatching results. AKOs: adverse kidney outcomes.

CRediT authorship contribution statement

Shang-Yu Wang: Project administration, Formal analysis, Writing - original draft. **Kuo-Jen Lin:** Methodology, Validation, Supervision. **Shao-Wei Chen:** Conceptualization, Methodology. **Chi-Tung Cheng:** Data curation, Methodology, Formal analysis. **Chih-Hsiang Chang:** Conceptualization, Project administration, Writing - review & editing. **Yu-Tung Wu:** Visualization. **Chien-An Liao:** Data curation. **Chien-Hung Liao:** Methodology, Validation. **Chih-Yuan Fu:** Conceptualization, Writing - review & editing. **Jr-Rung Lin:** Methodology, Formal analysis, Software. **Chi-Hsun Hsieh:** Conceptualization, Writing - review & editing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2019.04.001.

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