Incidence and risk of dialysis therapy within 30 days after contrast enhanced computed tomography in patients coded with chronic kidney disease: A nationwide population based study

Yun-Ju Shih [1], **Yu-Ting Kuo** [1, 2, 3], **Chung-Han Ho** [4, 5], **Chia-Chun Wu** [6, 7], **Ching-Chung Ko** [Corresp. 1]

[1] Department of Medical Imaging, Chi Mei Medical Center, Tainan, Taiwan
[2] Department of Medical Imaging, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan
[3] Department of Radiology, Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan
[4] Department of Medical Research, Chi Mei Medical Center, Tainan, Taiwan
[5] Department of Hospital and Health Care Administration, Chia Nan University of Pharmacy and Science, Tainan, Taiwan
[6] Division of Nephrology, Department of Internal Medicine, Chi Mei Medical Center, Tainan, Taiwan
[7] Department of Pharmacy, Chia Nan University of Pharmacy and Science, Tainan, Taiwan

Corresponding Author: Ching-Chung Ko
Email address: crazyboy0729@gmail.com

Background. Patients with chronic kidney disease (CKD) are considered at risk of contrast induced acute kidney injury and possible subsequent need for dialysis therapy. Moreover, computed tomography (CT) is the most common examination requiring intravenous iodinated contrast media (ICM) injection. The actual risk of dialysis in CKD patients receiving CT with ICM remains in controversy. Also, it is uncertain whether these patients at risk can be distinguished by administrative data or not. Therefore, we conducted this study to determine the incidence and risk of dialysis within 30 days after undergoing contrast enhanced CT in CKD coded patients.

Methods. This longitudinal, nationwide, populated-based study was carried out by analyzing the Taiwan National Health Insurance Research Database (NHIRD) retrospectively. We identified CKD coded patients who received CT within a dataset derived from NHIRD, which contained medical information of randomly selected one million subjects. During the period of January 2012 to December 2013, four hundred and eighty-seven eligible patients had undergone CT with ICM. Additionally, nine hundred and twenty-four CKD patients receiving CT without ICM were selected as controls. Patients who had advanced CKD or admitted to the intensive care unit (ICU) were identified for subgroup analysis. The primary outcome was measured by dialysis events within 30 days after CT scans. The cumulative incidence was assessed by the Kaplan-Meier method and log-rank test. The risk of 30-day dialysis relative to the controls was analyzed by using the Cox proportional hazards model after adjustments for age, sex and baseline comorbidities.

Results. The numbers and percentages of dialysis events within 30 days after CT scans were 20 (4.1%) in the CT with ICM group and 66 (7.1%) in the CT without ICM group (p=0.03). However, the adjusted hazard ratio (aHR) for 30-day dialysis was 0.84 (95% CI: 0.46-1.54, p=0.57), which was non-significant. In both advanced CKD and ICU subgroups, there were also no significant differences in 30-day dialysis risks with aHR of 1.12 (95% CI: 0.38-3.33, p=0.83) and 0.95 (95% CI: 0.44-2.05, p=0.90), respectively.

Conclusions. The incidence of 30-day dialysis in CKD coded patients receiving contrast enhanced CT was 4.1%, which appeared lower than those receiving non-contrast CT. However, there was no significant

difference in 30-day dialysis risk between CT with or without ICM groups after adjustment for other baseline conditions. The application of administrative data to identify CKD patients could not be viewed as a risk factor for dialysis within 30 days after contrast enhanced CT scans.

Incidence and risk of dialysis therapy within 30 days after contrast enhanced computed tomography in patients coded with chronic kidney disease: A nationwide population based study

Yun-Ju Shih[1], Yu-Ting Kuo[123], Chung-Han Ho[45], Chia-Chun Wu[67], Ching-Chung Ko[1]

Department of Medical Imaging, Chi Mei Medical Center, Tainan, Taiwan[1]
Department of Medical Imaging, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan[2]
Department of Radiology, Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan[3]
Department of Medical Research, Chi Mei Medical Center, Tainan, Taiwan[4]
Department of Hospital and Health Care Administration, Chia Nan University of Pharmacy and Science, Tainan, Taiwan[5]
Division of Nephrology, Department of Internal Medicine, Chi Mei Medical Center, Tainan, Taiwan[6]
Department of Pharmacy, Chia Nan University of Pharmacy and Science, Tainan, Taiwan[7]

Corresponding Author:
Ching-Chung Ko[1]
Postal address: No.901, Zhonghua Rd. Yongkang Dist., Tainan City 71004 Taiwan
Email address: crazyboy0729@gmail.com

Abstract

Background. Patients with chronic kidney disease (CKD) are considered at risk of contrast induced acute kidney injury and possible subsequent need for dialysis therapy. Moreover, computed tomography (CT) is the most common examination requiring intravenous iodinated contrast media (ICM) injection. The actual risk of dialysis in CKD patients receiving CT with ICM remains in controversy. Also, it is uncertain whether these patients at risk can be distinguished by administrative data or not. Therefore, we conducted this study to determine the incidence and risk of dialysis within 30 days after undergoing contrast enhanced CT in CKD coded patients.

Methods. This longitudinal, nationwide, populated-based study was carried out by analyzing the Taiwan National Health Insurance Research Database (NHIRD) retrospectively. We identified CKD coded patients who received CT within a dataset derived from NHIRD, which contained medical information of randomly selected one million subjects. During the period of January 2012 to December 2013, four hundred and eighty-seven eligible patients had undergone CT with ICM. Additionally, nine hundred and twenty-four CKD patients receiving CT without ICM were selected as controls. Patients who had advanced CKD or admitted to the intensive care unit (ICU) were identified for subgroup analysis. The primary outcome was measured by dialysis events within 30 days after CT scans. The cumulative incidence was assessed by the Kaplan-Meier method and log-rank test. The risk of 30-day dialysis relative to the controls was analyzed by using the Cox proportional hazards model after adjustments for age, sex and baseline comorbidities.

Results. The numbers and percentages of dialysis events within 30 days after CT scans were 20 (4.1%) in the CT with ICM group and 66 (7.1%) in the CT without ICM group (p=0.03). However, the adjusted hazard ratio (aHR) for 30-day dialysis was 0.84 (95% CI: 0.46-1.54, p=0.57), which was non-significant. In both advanced CKD and ICU subgroups, there were also no significant differences in 30-day dialysis risks with aHR of 1.12 (95% CI: 0.38-3.33, p=0.83) and 0.95 (95% CI: 0.44-2.05, p=0.90), respectively.

Conclusions. The incidence of 30-day dialysis in CKD coded patients receiving contrast enhanced CT was 4.1%, which appeared lower than those receiving non-contrast CT. However, there was no significant difference in 30-day dialysis risk between CT with or without ICM groups after adjustment for other baseline conditions. The application of administrative data to identify CKD patients could not be viewed as a risk factor for dialysis within 30 days after contrast enhanced CT scans.

Introduction

Injection of intravenous iodinated contrast media (ICM) during computed tomography (CT) scans improve diagnostic performance in various situations; therefore they are widely used in clinical settings. More importantly, there is an increasing number of CT scan orders by clinicians in modern healthcare settings over the recent years, which inevitably leads to expanding ICM usage. [1] However, delivering intravenous ICM poses a major concern of developing contrast-

induced acute kidney injury (CI-AKI). After excluding other possibilities causing renal impairment, the diagnostic criteria for CI-AKI are serum creatinine elevation varying from 0.3 to 0.5 mg/dL in an absolute increase, or a 25 to 50% relative increase within the time period of 24 to 72 hours after contrast administration. [2-4]

It is known that patients with chronic kidney disease (CKD) are particularity at risk of developing CI-AKI due to diminished renal function reserve. [4-8] There is emerging evidence suggesting that risk of CI-AKI in CKD patients may have been overestimated in the past. [2 9-11] But meanwhile, pre-existing CKD is still the most important risk factor in current consensus of radiologic practice. [6 11] Moreover, the prevalence of CKD is high in many countries. [12] If the risk is truly overestimated, CT with ICM may be not performed in a large number of patients with legitimate clinical indications. There are chances for resultant diagnostic delays and unfavorable clinical outcomes.

CI-AKI is often but not always a reversible process. [5] One of the adverse events after CI-AKI causing the greatest concern is the possibility of dialysis therapy requirement due to sustained renal impairment. The exact figure for CKD patients receiving CT with ICM and who require dialysis therapy in the short-term is not well known, but yet an important issue that we are curious about. To identify CKD patients directly, it is essential to obtain laboratory information. Nonetheless, an alternative method is to select CKD patients in the diagnostic codes section of an administrative dataset. The usefulness for administrative data regarding CKD status were validated in various research articles, and they revealed inconsistent sensitivities but very high specificities. [13-16] In the literature, plentiful studies were conducted by the usage of diagnostic codes to identify CKD patients. [17-20] We therefore propose this longitudinal, nationwide, population-based study to evaluate the incidence and risk of dialysis therapy within 30 days after receiving contrast enhanced CT scans among CKD coded patients. We are also interested whether if the administrative data can successfully label CKD patients who are at risk.

Materials & Methods

Study design and setting. The National Health Insurance (NHI) program in Taiwan, launched in March 1995, is a compulsory single-payer social insurance plan aiming at healthcare delivery to all citizens. It covers nearly all of the twenty-three million people living in Taiwan. National Health Insurance Registry Database (NHIRD) is a database containing comprehensive information such as demographic data, diagnostic codes, drug prescription and procedure codes after encryption of patients' personal information. For research purposes, a subset of database namely Longitudinal Health Insurance Database 2010 (LHID2010) was provided by the National Health Research Institutes, and it had been implemented in many researches. [21-24] It consists of one million individuals chosen randomly from NHIRD at the year 2010 and contains medical information from January 1997 to December 2013 of each subject under the coverage. The Catastrophic Illness Registry Data file was supplemented for deaths identification during the study period. The Institutional Review Board in Chi Mei Medical Center approved this study (No: 10706-E03) and waived the requirement of informed consent.

Patient identification and selection. Within the LHID2010, CKD patients were identified by using relevant *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes with at least two outpatient claims or one inpatient claim documented in the diagnosis codes section. Patients receiving CT scans were selected by using the Taiwan NHI codes for procedures, including information on study date and the usage of ICM or not. The majority of ICM used in Taiwan is low-osmolar contrast media, i.e. non-ionic monomers. CKD patients receiving CT without ICM were classified as the control group. The specific date of CT scan was not available before year 2012 within LHID2010, therefore only CKD patients receiving CT during January 2012 to December 2013 were included for analysis. The following patients were excluded: ages below 20 or above 100 years old; patients who were already receiving regular dialysis before the date of the CT scan; patients receiving CT scans for 2 or more times within 30 days; and patients receiving any angiography or transarterial embolization within 30 days of CT scan. The flow diagram was shown in *Fig. 1*. All included patients were followed up for a 30-day period, to the occurrence of dialysis or death events, until the end of December 2013 or when leaving the NHI program. The follow-up period was not limited to 30 days when evaluating the time interval from CT to dialysis event as a secondary outcome described subsequently. Furthermore, since laboratory data was not available in LHID2010, the severity of CKD could not be directly assessed. An indirect approach was to select CKD patients receiving erythropoietin-stimulating agents (ESA) as the advanced CKD subgroup in this study. The NHI reimbursed ESA only in CKD patients with serum creatinine above 6 mg/dL, approximately equivalent to estimated glomerular filtration rate (eGFR) <15 mL/min/1.73m^2, and a hematocrit level below 28% concurrently. This approach to subdivide patients with advanced CKD had also been used in previous research papers. [20 25] Another subgroup was the status of admission to the intensive care unit (ICU) during the time the CT scan was performed.

Assessment of comorbidities and confounding factors. Age, sex and comorbidities data was collected and incorporated into the statistical analyses. The age was stratified into < 60 years old, 60-80 years old and > 80 years old groups. Baseline hypertension, diabetes mellitus, ischemic heart disease, peripheral arterial occlusive disease, congestive heart failure, liver cirrhosis, hyperlipidemia and anemia were recorded based on the ICD-9-CM codes before the date the CT scan was performed.

Outcomes measurement. The primary outcome was measured by the occurrence of dialysis events within 30 days of CT scans, which was recognized by Taiwan NHI codes for procedures. The secondary outcomes were dialyses within 30 days of CT scans in the two selected subgroups, dialysis in CKD excluding ICU patients, death within 30 days, and the time interval of dialysis therapies after CT scans in the advanced CKD subgroup.

ICD-9-CM codes and Taiwan NHI codes for procedures. CKD patients were identified using the ICD-9-CM codes and include the following groups: 585 (chronic kidney disease), 582 (chronic glomerulonephritis), 403 (hypertensive chronic kidney disease) and 404 (hypertensive heart and chronic kidney disease). Baseline comorbidities were also recognized with ICD-9-CM

codes as the following: hypertension (401-405), diabetes mellitus (250, 357.2, 362.01, 362.02, and 366.41), ischemic heart disease (411-414), peripheral arterial occlusive disease (440-444), congestive heart failure (428), liver cirrhosis (571.2, 571.5, and 571.6), hyperlipidemia (272-272.4) and anemia (280-285). CT with ICM studies were searched by Taiwan NHI codes for procedures, both 33071B (CT with contrast) and 33072B (CT without and with contrast); CT without ICM studies were identified by Taiwan NHI codes for procedures 33070B (CT without contrast). Dialysis events were identified by using Taiwan NHI codes for procedures 58001C/58029C/58027C (hemodialysis) and 58018C (continuous veno-venous hemofiltration dialysis).

Statistical analysis. Patient characteristics between the CT with ICM and CT without ICM groups, including age, sex and comorbidities, were compared by using the Pearson's chi-square test for categorical variables. Kaplan–Meier analysis was performed to assess the cumulative incidence of dialysis between these two groups, and the log-rank test was used to measure the difference of incidence curves. The Cox proportional hazard model adjusted for age, sex and comorbidities was used to demonstrate the risk ratio of dialysis and death between the two groups. Each of the baseline characteristic was viewed as a distinct dichotomous variable. Adjusted hazard ratios (aHR) and 95% confidence intervals (95% CI) were calculated. The result for the time interval leading up to dialysis in advanced CKD subgroup was not following the Gaussian distribution; therefore the median value, the first quartile, and the third quartile were reported. All statistical analyses were performed using Statistical Analysis System (SAS) statistical software (version 9.4; SAS Institute Inc., Cary, NC, USA). The Kaplan-Meier curves were plotted using STATA (version 12; Stata Corp., College Station, TX, USA). A two-tailed p-value of < 0.05 was considered statistically significant.

Results

Baseline characteristics of the study participants. There were 1411 eligible CKD patients who underwent CT studies, including 487 patients receiving CT with ICM and 924 patients receiving CT without ICM. Patient characteristics are listed in *Table 1*. In the CT with ICM group, there were younger, more male patients, and a greater number of subjects with liver cirrhosis. On the other hand, there were more patients with hypertension, diabetes mellitus, hyperlipidemia and anemia in the CT without ICM group. We identified 99 patients with advanced CKD who received treatment of ESA: 15 of them received CT with ICM and 84 patients received CT without ICM. There were also 227 patients (16.1%) staying in the ICU, and a greater number of these subjects underwent CT without ICM.

Necessity for dialysis and death within 30 days of CT. There were 20 patients (4.11%) in the CT with ICM group and 66 patients (7.14%) in the CT without ICM group requiring dialysis within 30 days of CT scan. The cumulative incidences of dialysis events were drawn in *Fig. 2*. A greater number of patients underwent dialysis therapy in the CT without ICM group (p=0.0295). However, no statistically significance difference was found after the adjustment of age, sex and listed comorbidities (aHR 0.84, 95% CI 0.46-1.54, p=0.5700). Sixteen patients (3.29%) died in

the CT with ICM group, which was also not significantly different from the 61 patients (6.60%) who died in the group of CT without ICM group (aHR 0.62, 95% CI 0.35-1.10, p=0.1012). In the advanced CKD and ICU admission subgroups, neither dialysis within 30 days after CT nor death rates differ significantly between the CT with or without ICM groups. After excluding the critically-ill patients in the ICU, the percentages of patients requiring dialysis in 30 days was 1.61% in the CT with ICM and 2.81% in the CT without ICM groups, respectively (aHR 1.11, 95% CI 0.40-3.06, p=0.8371). The events, percentages and adjusted hazard ratios of dialysis and death are shown in *Table 2*.

Time to dialysis in advanced CKD subgroup. The time interval leading up to dialysis in the advanced CKD subgroup is demonstrated in *Table 3*. A total of 75 patients (75.8%) required dialysis after CT. The median time interval leading to dialysis was 12 days (Q1-Q3: 4-139) in the CT with ICM group and 38 days (Q1-Q3: 4-184.5) in the CT without ICM group.

Discussion

In our study, the risks of dialysis and death within 30 days after CT scans in CKD patients and advanced CKD patients were not increased, regardless of whether the patient received ICM or not. A similar result was reported in three retrospective studies from the same institution. [26-28] The incidences of dialysis and death rates were also not affected by ICM, regardless of CKD stage 3, 4 or 5 in some research papers. [9 27 28] Therefore, CT with ICM was probably not an independent risk factor for necessity of dialysis and death in CKD patients in the short-term. The crude dialysis rate was elevated in CKD stage 3 patients receiving CT without ICM in one of the studies, however it became non-significant after adjusting for predisposing factors [28]. This finding resemble our result. In the aforementioned study, more patients who received CT without ICM were in the ICU and experienced AKI within 7 days before the examination. It is possible that these predisposing conditions lead to concerns of developing CI-AKI, and clinicians may have ordered non-contrast CTs instead. The underlying causes may have resulted in renal failure and subsequent elevation in the crude dialysis rate.

Reported post-CT dialyses within 30 days were few in the reviewed studies, with an overall percentage of 0.2 to 0.3% in CKD patients and only 5.1% in CKD 4-5 patients. [26 28] However, our study revealed higher rates of post-CT dialyses within 30 days at 4.1 to 7.1%. When excluding the critically-ill ICU patients, the percentages were still high at 1.6 to 2.8%. This finding could be related to the fact that Taiwan has the highest incidence of end-stage renal disease (ESRD) in the world. [29] Abundant dialysis-related resources are available, and the NHI provides full coverage of incurred expenses. Due to this relatively common practice, doctors, patients and their family members would probably prefer dialysis therapy in the occurrence of renal failure in most situations. Another possible cause is that some CKD patients were unlabeled from ICD-9-CM, especially those with less severe disease. [30] Therefore, the reported incidences of dialyses could be overestimated in our study.

The importance of critical illness was mentioned in a previous study, stating that ICU patients with eGFR < 45 mL/min/1.73m^2 demonstrated an increased risk of emergent dialysis

within 7 days after contrast enhanced CT scans. [31] An earlier article also demonstrated that the development of CI-AKI may result in increased need for dialysis in the ICU [32]. However, in our results, the necessity for post-CT dialysis within 30 days and death rates did not differ in the ICU subgroup. A more detailed stratification of patient condition, especially any acute illness, might be required to reveal any undesirable effect of ICM injected during CT particularly in the critically ill setting.

The advanced CKD subgroup appeared interesting since they were presumed to be most susceptible to CI-AKI and the possibility of dialysis. It is noteworthy that one previous study mentioned that CKD patients who underwent exposure to ICM during CT scans more than once per year may develop ESRD earlier in the time scale of years [25]. However, CKD patients with concurrent usage of ESA were excluded from their study due to proposed short-interval deterioration of residual renal function. We therefore targeted these pre-dialysis patients and aimed on whether the time-interval to dialysis requirement after intravenous contrast exposure shortens. The result however included only small numbers of patients as the median time decreased from 38 to 12 days. It was inconclusive while containing wide interquartile ranges. Further investigation is warranted to clarify whether contrast exposure truly shortened the time to dialysis requirement in advanced CKD patients.

The advantage of this study is the conduction of a nationwide population-based design to include more patients while minimizing potential single institution related biases. The short-term risk and incidence of dialysis in CKD patients after contrast enhanced CT are also not yet reported in Asian races. In addition, it is unknown if CKD patients identified from administrative data can be viewed as a risk factor in terms of 30-day dialysis requirement before our present study. Nevertheless, this study has some limitations. First, the recognition of diagnoses including CKD and comorbidities were based on ICD-9-CM diagnoses codes, and cases of mis-registration cannot be excluded. The indications for CT scans were unknown, and presence of any acute medical illness was also not analyzed due to database restrictions. Furthermore, details on the volume and specific contrast medium agent injected were not retrievable in our dataset. Additionally, this is a retrospective cohort, which inevitably contains biases inherently related to the study design.

Conclusions

The dialysis rate within 30 days after contrast enhanced CT was 4.1% in our studied CKD coded population, which was lower than those receiving non-contrast CT. However, the risk to require dialysis in 30 days after CT scan was not significantly different whether if ICM was given after adjustment for other baseline conditions. The application of administrative data did not reveal CKD coded patients to be at-risk.

References

1. Hu SY, Hsieh MS, Lin MY, et al. Trends of CT utilisation in an emergency department in Taiwan: a 5-year retrospective study. BMJ open 2016;**6**(6):e010973 doi:

10.1136/bmjopen-2015-010973[published Online First: Epub Date]|.
2. McDonald JS, McDonald RJ, Comin J, et al. Frequency of acute kidney injury following intravenous contrast medium administration: a systematic review and meta-analysis. Radiology 2013;**267**(1):119-28 doi: 10.1148/radiol.12121460[published Online First: Epub Date]|.
3. Meinel FG, De Cecco CN, Schoepf UJ, et al. Contrast-induced acute kidney injury: definition, epidemiology, and outcome. BioMed research international 2014;**2014**:859328 doi: 10.1155/2014/859328[published Online First: Epub Date]|.
4. Mehran R, Nikolsky E. Contrast-induced nephropathy: definition, epidemiology, and patients at risk. Kidney international Supplement 2006(100):S11-5 doi: 10.1038/sj.ki.5000368[published Online First: Epub Date]|.
5. Scharnweber T, Alhilali L, Fakhran S. Contrast-Induced Acute Kidney Injury: Pathophysiology, Manifestations, Prevention, and Management. Magnetic resonance imaging clinics of North America 2017;**25**(4):743-53 doi: 10.1016/j.mric.2017.06.012[published Online First: Epub Date]|.
6. ACR manual on contrast media. Version 10.3. ACR committee on drugs and contrast media. American College of Radiology. 2017.
7. Kim SM, Cha RH, Lee JP, et al. Incidence and outcomes of contrast-induced nephropathy after computed tomography in patients with CKD: a quality improvement report. American journal of kidney diseases : the official journal of the National Kidney Foundation 2010;**55**(6):1018-25 doi: 10.1053/j.ajkd.2009.10.057[published Online First: Epub Date]|.
8. Davenport MS, Khalatbari S, Cohan RH, et al. Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material: risk stratification by using estimated glomerular filtration rate. Radiology 2013;**268**(3):719-28 doi: 10.1148/radiol.13122276[published Online First: Epub Date]|.
9. Garfinkle MA, Stewart S, Basi R. Incidence of CT Contrast Agent-Induced Nephropathy: Toward a More Accurate Estimation. AJR American journal of roentgenology 2015;**204**(6):1146-51 doi: 10.2214/ajr.14.13761[published Online First: Epub Date]|.
10. Hinson JS, Ehmann MR, Fine DM, et al. Risk of Acute Kidney Injury After Intravenous Contrast Media Administration. Annals of emergency medicine 2017;**69**(5):577-86.e4 doi: 10.1016/j.annemergmed.2016.11.021[published Online First: Epub Date]|.
11. van der Molen AJ, Reimer P, Dekkers IA, et al. Post-contrast acute kidney injury - Part 1: Definition, clinical features, incidence, role of contrast medium and risk factors : Recommendations for updated ESUR Contrast Medium Safety Committee guidelines. European radiology 2018;**28**(7):2845-55 doi: 10.1007/s00330-017-5246-5[published Online First: Epub Date]|.
12. Hill NR, Fatoba ST, Oke JL, et al. Global Prevalence of Chronic Kidney Disease - A Systematic Review and Meta-Analysis. PloS one 2016;**11**(7):e0158765 doi: 10.1371/journal.pone.0158765[published Online First: Epub Date]|.
13. Ronksley PE, For the Alberta Kidney Disease N, Tonelli M, et al. Validating a case definition for chronic kidney disease using administrative data. Nephrology Dialysis Transplantation 2012;**27**(5):1826-31 doi: 10.1093/ndt/gfr598[published Online First: Epub Date]|.

14. Navaneethan SD, Jolly SE, Schold JD, et al. Development and validation of an electronic health record-based chronic kidney disease registry. Clinical journal of the American Society of Nephrology : CJASN 2011;**6**(1):40-9 doi: 10.2215/cjn.04230510[published Online First: Epub Date]|.
15. Tonelli M, Wiebe N, Fortin M, et al. Methods for identifying 30 chronic conditions: application to administrative data. BMC medical informatics and decision making 2015;**15**:31 doi: 10.1186/s12911-015-0155-5[published Online First: Epub Date]|.
16. Grams ME, Plantinga LC, Hedgeman E, et al. Validation of CKD and related conditions in existing data sets: A systematic review. American journal of kidney diseases : the official journal of the National Kidney Foundation 2011;**57**(1):44-54 doi: 10.1053/j.ajkd.2010.05.013[published Online First: Epub Date]|.
17. Chen JS, Lu CL, Huang LC, et al. Chronic Kidney Disease is Associated With Upper Tract Urothelial Carcinoma: A Nationwide Population-Based Cohort Study in Taiwan. Medicine 2016;**95**(14):e3255 doi: 10.1097/md.0000000000003255[published Online First: Epub Date]|.
18. Sebastian Yu H-PT, Chu-Ling Yu, Chih-Hung Lee, Chien-Hui Hong. Is psoriasis an independent risk factor of renal disease? A nationwide retrospective cohort study from 1996 to 2010. Dermatologica Sinica 2017;**35**(2):78-84 doi: 10.1016/j.dsi.2017.02.004[published Online First: Epub Date]|.
19. Chang CH, Lee YC, Tsai CT, et al. Continuation of statin therapy and a decreased risk of atrial fibrillation/flutter in patients with and without chronic kidney disease. Atherosclerosis 2014;**232**(1):224-30 doi: 10.1016/j.atherosclerosis.2013.11.036[published Online First: Epub Date]|.
20. Chung CM, Lin MS, Hsu JT, et al. Effects of statin therapy on cerebrovascular and renal outcomes in patients with predialysis advanced chronic kidney disease and dyslipidemia. Journal of clinical lipidology 2017;**11**(2):422-31.e2 doi: 10.1016/j.jacl.2017.01.001[published Online First: Epub Date]|.
21. Ho SW, Tsai MC, Teng YH, et al. Population-based cohort study on the risk of pneumonia in patients with non-traumatic intracranial haemorrhage who use proton pump inhibitors. BMJ open 2014;**4**(11):e006710 doi: 10.1136/bmjopen-2014-006710[published Online First: Epub Date]|.
22. Wu MH, Wu MJ, Chou LF, et al. Patterns of nonemergent visits to different healthcare facilities on the same day: a nationwide analysis in Taiwan. TheScientificWorldJournal 2014;**2014**:627580 doi: 10.1155/2014/627580[published Online First: Epub Date]|.
23. Chang CM, Chu HT, Wei YH, et al. The Core Pattern Analysis on Chinese Herbal Medicine for Sjogren's syndrome: A Nationwide Population-Based Study. Scientific reports 2015;**5**:9541 doi: 10.1038/srep09541[published Online First: Epub Date]|.
24. Chou YY, Lai KL, Chen DY, et al. Rheumatoid Arthritis Risk Associated with Periodontitis Exposure: A Nationwide, Population-Based Cohort Study. PloS one 2015;**10**(10):e0139693 doi: 10.1371/journal.pone.0139693[published Online First: Epub Date]|.
25. Hsieh MS, Chiu CS, How CK, et al. Contrast Medium Exposure During Computed Tomography and Risk of Development of End-Stage Renal Disease in Patients With Chronic Kidney Disease: A Nationwide Population-Based, Propensity Score-Matched,

Longitudinal Follow-Up Study. Medicine 2016;**95**(16):e3388 doi: 10.1097/md.0000000000003388[published Online First: Epub Date]|.
26. McDonald RJ, McDonald JS, Carter RE, et al. Intravenous contrast material exposure is not an independent risk factor for dialysis or mortality. Radiology 2014;**273**(3):714-25 doi: 10.1148/radiol.14132418[published Online First: Epub Date]|.
27. McDonald JS, McDonald RJ, Lieske JC, et al. Risk of Acute Kidney Injury, Dialysis, and Mortality in Patients With Chronic Kidney Disease After Intravenous Contrast Material Exposure. Mayo Clinic proceedings 2015;**90**(8):1046-53 doi: 10.1016/j.mayocp.2015.05.016[published Online First: Epub Date]|.
28. McDonald JS, McDonald RJ, Williamson EE, et al. Is Intravenous Administration of Iodixanol Associated with Increased Risk of Acute Kidney Injury, Dialysis, or Mortality? A Propensity Score-adjusted Study. Radiology 2017;**285**(2):414-24 doi: 10.1148/radiol.2017161573[published Online First: Epub Date]|.
29. United States Renal Data System. 2017 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2017.
30. Ferris M, Shoham DA, Pierre-Louis M, et al. High prevalence of unlabeled chronic kidney disease among inpatients at a tertiary-care hospital. The American journal of the medical sciences 2009;**337**(2):93-7 doi: 10.1097/MAJ.0b013e318181288e[published Online First: Epub Date]|.
31. McDonald JS, McDonald RJ, Williamson EE, et al. Post-contrast acute kidney injury in intensive care unit patients: a propensity score-adjusted study. Intensive care medicine 2017;**43**(6):774-84 doi: 10.1007/s00134-017-4699-y[published Online First: Epub Date]|.
32. Valette X, Parienti JJ, Plaud B, et al. Incidence, morbidity, and mortality of contrast-induced acute kidney injury in a surgical intensive care unit: a prospective cohort study. Journal of critical care 2012;**27**(3):322.e1-5 doi: 10.1016/j.jcrc.2011.08.005[published Online First: Epub Date]|.

Table 1(on next page)

Baseline characteristics of the studied CKD patients

* $p<0.05$ and are considered statistically significant by Pearson's chi-square test

ICM, iodinated contrast media; HTN, hypertension; DM, diabetes mellitus; PAOD, peripheral arterial occlusive disease; CHF, congestive heart failure; ESA, erythropoietin-stimulating agents; ICU, intensive care unit

Table 1:
Baseline characteristics of the studied CKD patients

	CT with ICM N=487 (%)	CT without ICM N=924 (%)	p-value
Age group, years			
<60	146 (29.98)	171 (18.51)	<0.0001*
60-80	238 (48.87)	466 (50.43)	
≧80	103 (21.15)	287 (31.06)	
Sex			
Female	197 (40.45)	432 (46.75)	0.0236*
Male	290 (59.55)	492 (53.25)	
Comorbidities			
HTN	401 (82.34)	824 (89.18)	0.0003*
DM	267 (54.83)	582 (62.99)	0.0029*
IHD	263 (54.00)	528 (57.14)	0.2587
PAOD	108 (22.18)	221 (23.92)	0.4621
CHF	113 (23.20)	238 (25.76)	0.2913
Cirrhosis	53 (10.88)	47 (5.09)	<0.0001*
Hyperlipidemia	273 (56.06)	568 (61.47)	0.0488*
ESA usage (advanced CKD)			
Yes	15 (3.08)	84 (9.09)	<0.0001*
ICU admission			
Yes	51 (10.47)	176 (19.05)	<0.0001*

* $p<0.05$ and are considered statistically significant by Pearson's chi-square test
ICM, iodinated contrast media; HTN, hypertension; DM, diabetes mellitus; PAOD, peripheral arterial occlusive disease; CHF, congestive heart failure; ESA, erythropoietin-stimulating agents; ICU, intensive care unit

Table 2(on next page)

Adjusted hazard ratios (HR) for dialysis and death within 30 days after contrast enhanced CT scans in CKD patients, advanced CKD subgroup, ICU admission subgroup and CKD patients excluding ICU admissions

n/N, event numbers/total numbers

* The HRs were adjusted by the age, sex and comorbidities listed in Table 1.

Table 2:
Adjusted hazard ratios (HR) for dialysis and death within 30 days after contrast enhanced CT scans in CKD patients, advanced CKD subgroup, ICU admission subgroup and CKD patients excluding ICU admissions

	Outcome	CT with ICM N=487 n/N (%)	CT without ICM N=924 n/N (%)	Adjusted HR* (95% CI)	p-value
CKD patients	30-day dialysis	20 (4.11)	66 (7.14)	0.84 (0.46-1.54)	0.5700
	30-day mortality	16 (3.29)	61 (6.60)	0.62 (0.35-1.10)	0.1012
Advanced CKD subgroup	30-day dialysis	7 (46.67)	30 (35.71)	1.12 (0.38-3.33)	0.8333
	30-day mortality	2 (13.33)	4 (4.76)	3.87 (0.16-92.07)	0.4032
ICU admission subgroup	30-day dialysis	13 (25.49)	45 (25.57)	0.95 (0.44-2.05)	0.8973
	30-day mortality	6 (11.76)	42 (23.86)	0.84 (0.22-1.33)	0.1788
CKD patients excluding ICU admission	30-day dialysis	7 (1.61)	21 (2.81)	1.11 (0.40-3.06)	0.8371
	30-day mortality	10 (2.29)	19 (2.54)	1.24 (0.54-2.85)	0.6158

n/N, event numbers/total numbers
* The HRs were adjusted by the age, sex and comorbidities listed in Table 1.

Table 3(on next page)

Median time to dialysis in the advanced CKD subgroup after CT scans

n/N, event numbers/total numbers; Q1-Q3, interquartile range

Table 3:
Median time to dialysis in the advanced CKD subgroup after CT scans

	CT with ICM N=15	CT without ICM N=84
Dialysis events n/N (%)	11 (73.33%)	64 (76.19%)
Median time, days (Q1-Q3)	12 (4-139)	38 (4-184.5)

n/N, event numbers/total numbers; Q1-Q3, interquartile range

Figure 1

Flow diagram for patient selection

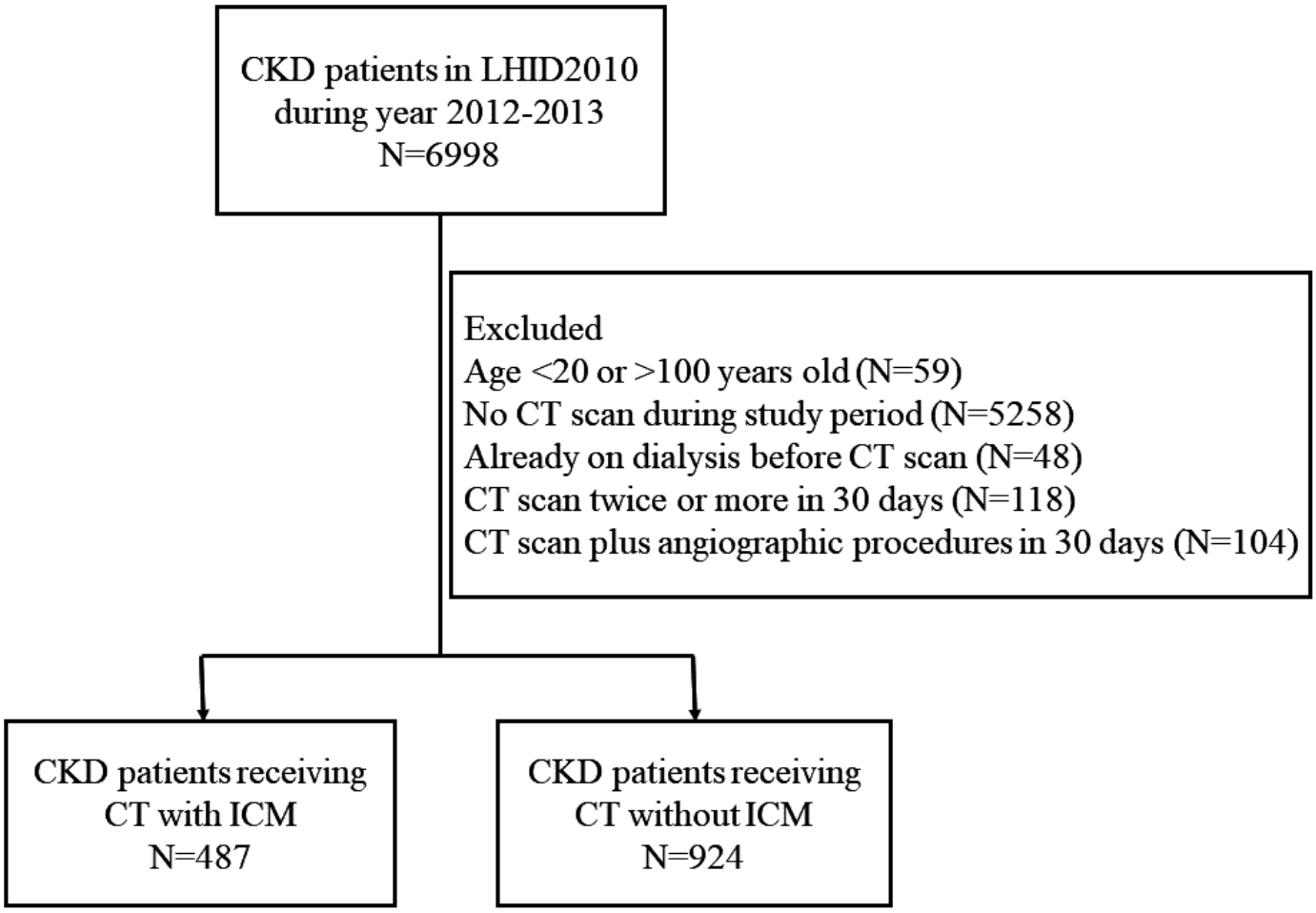

Figure 2

Cumulative incidence of dialysis events within 30 days of CT scans in CKD patients