# Does Exposure to Computed Tomography Contrast Media Increase Risk of End-Stage Renal Disease?

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ADEF 1 **Eunsoo Lim**
BC 2 **Jong-Hwan Jang**
BC 2,3 **Dukyong Yoon**
AEF 1 **Young-Gi Min**
ACD 1 **Hyuk-Hoon Kim**

1 Department of Emergency Medicine, Ajou University School of Medicine, Suwon, South Korea
2 Department of Biomedical Informatics, Ajou University School of Medicine, Suwon, South Korea
3 Department of Biomedical Sciences, Ajou University School of Medicine, Suwon, South Korea

Corresponding Author: Hyuk-Hoon Kim, e-mail: hyukhoon82@gmail.com
Source of support: Departmental sources

Background: There are many studies on acute kidney injury (AKI) after exposure to contrast media in patients with chronic kidney disease (CKD). However, whether the risk of end-stage renal disease (ESRD) increases after exposure to contrast media in the long term, regardless of development of AKI after such exposure, has not been studied.

Material/Methods: The electronic health records of patients diagnosed with CKD and followed up from 2014 to 2018 at a tertiary university hospital were retrospectively collected. Patients were divided into patients who progressed to ESRD (ESRD group) and those who did not (non-ESRD group). Patients in the non-ESRD group were matched 1: 1 to those in the ESRD group by using disease risk score generation and matching. Multivariate logistic regression analysis was performed to assess the effect of contrast media exposure on progression to ESRD.

Results: In total, 179 patients were enrolled per group; 178 (99.4%) were in CKD stage 3 or above in both groups. Average serum creatinine was 4.31±3.02 mg/dl and 3.64±2.55 mg/dl in the ESRD and non-ESRD groups, respectively (p=0.242). Other baseline characteristics were not statistically significant, except for the number of times contrast-enhanced computed tomography (CECT) was performed (0.00 [Interquartile range (IQR) 0.00–2.00] in the ESRD group and 0.00 [IQR 0.00–1.00] in the non-ESRD group [p=0.006]); in multivariate logistic regression, this number (OR=1.24, 95% CI=1.08–1.47, p=0.006) was significantly related to progression to ESRD.

Conclusions: The use of CECT increased the risk of ESRD 1.2-fold in advanced and stable CKD outpatients after 5-year follow-up.

MeSH Keywords: **Contrast Media • Kidney Failure, Chronic • Renal Replacement Therapy**

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/921303

📄 2490    ▦ 2    📊 2    📖 21

## Background

Contrast-enhanced computed tomography (CECT) is becoming one of the most important diagnostic modalities, and there is no doubt regarding its usefulness. CECT occasionally causes contrast-induced acute kidney injury (CI-AKI), which is defined as an acute decrease in kidney function after injection of contrast media, without other explainable etiologies [1–3]. The incidences of CI-AKI range from 2% to 15% in the general population [2,4–6]. Old age, known chronic kidney disease (CKD), diabetes, hypertension, heart failure, proteinuria, anemia, nonsteroidal anti-inflammatory drug use, use of more than 100 ml of contrast media, and intraarterial injection are known risk factors for CI-AKI [2,4,7–11]. The incidence of CI-AKI in patients with CKD of varying degrees was slightly higher, ranging from 5% to 22% [1,5,12]. There are many studies on the effects of contrast media; however, most studies focused on acute kidney injury (AKI) caused by contrast media and regard AKI after contrast media exposure as a transient and reversible event.

As the prevalence of CKD is quite substantial, ranging from 11% to 13% worldwide [13], many CKD patients and physicians encounter clinical situations that force them to choose between diagnostic accuracy using CECT or preserving kidney function at the expense of accurate diagnosis. CI-AKI is by definition a type of AKI; however, irrespective of CI-AKI development, whether the risk of end-stage renal disease (ESRD) after contrast media exposure increases in CKD patients after a long period has not yet been fully studied. Thus, we aimed to investigate the long-term effect of contrast media exposure on advanced CKD patients in this study.

## Material and Methods

### Data source

We used a clinical research database containing basic information on patient demographics, diagnoses, drug prescriptions, and laboratory test results originating from the electronic health records (EHR) of a tertiary university-affiliated hospital in Korea (Ajou University Hospital) between January 1995 and March 2018. The EHR system includes information based on unique, de-identified patient numbers, combined with age and sex, diagnostic codes based on the International Classification of Diseases-10 (ICD-10), laboratory test results, and prescribed procedures/treatments from approximately 2.9 million patients (including 543 617 inpatients). This study was approved by the local institutional review board (MED-MDB-16-443). Patient information was anonymized and de-identified prior to analysis. Requirement for informed consent was waived due to the study's retrospective nature.

### Study design and patient selection

This was a retrospective, single-hospital, nested, case-control study. To investigate the effect of CECT on progression to ESRD in CKD patients, we selected 3544 patients as follows: (a) Outpatients whose diagnosis included CKD or ESRD from January 2014 to December 2018; (b) patients who had at least 1 set of baseline laboratory results, including serum creatinine level within the 6-month window prior to the study period; and (c) patients who had sufficient information about the procedures and diagnoses during the study period. The following patients were excluded from the study: (a) patients who were on maintenance dialysis before the study period; (b) patients who were newly diagnosed with CKD after beginning the study period; and (c) patients who lacked critical clinical and laboratory data. The enrolled patients were divided into ESRD and non-ESRD groups. ICD-10 codes N18.1, N18.2, N18.3, N18.4, N18.5, and N18.9 were used to identify CKD patients from EHR. Likewise, ICD-10 codes N18.5C, N18.5CA, and N18.5CB were used to distinguish ESRD patients from EHR. Diagnosis of CKD patients who progressed to ESRD and started renal replacement therapy during the study period were classified into the ESRD group and patients who did not were classified into the non-ESRD group.

### Variables

Demographic data, including age at the beginning of the study period and sex, were extracted from the EHR. Predisposing medical conditions reportedly associated with development of kidney injury after contrast media administration, including diabetes, hypertension, and heart failure, were also identified using the corresponding ICD-10 code. Enrolled patients with CKD were graded by their estimated glomerular filtration rate (eGFR), which is calculated by the Modification of Diet in Renal Disease Study equation. By definition, CKD stage 1 was defined as eGFR $\geq$90 mL/min/1.73 m$^2$, stage 2 as 60 mL/min/1.73 m$^2$ $\leq$eGFR <90 mL/min/1.73 m$^2$, stage 3 as 30 mL/min/1.73 m$^2$ $\leq$eGFR <60 mL/min/1.73 m$^2$, stage 4 as 15 mL/min/1.73 m$^2$ $\leq$eGFR <30 mL/min/1.73 m$^2$, and stage 5 as eGFR <15 mL/min/1.73 m$^2$. Laboratory results, including serum creatinine, blood urea nitrogen (BUN), hemoglobin, hematocrit, alanine aminotransferase (ALT), aspartate aminotransferase (AST), potassium, sodium, and total protein levels in the 6-month window prior to the study period, were also evaluated. The number of times CECT was performed during the study period before the diagnosis of ESRD in enrolled patients was counted.

### Contrast media used

Two types of low-osmolality nonionic contrast agents, iohexol and iopamidol, were used while performing CECT throughout the
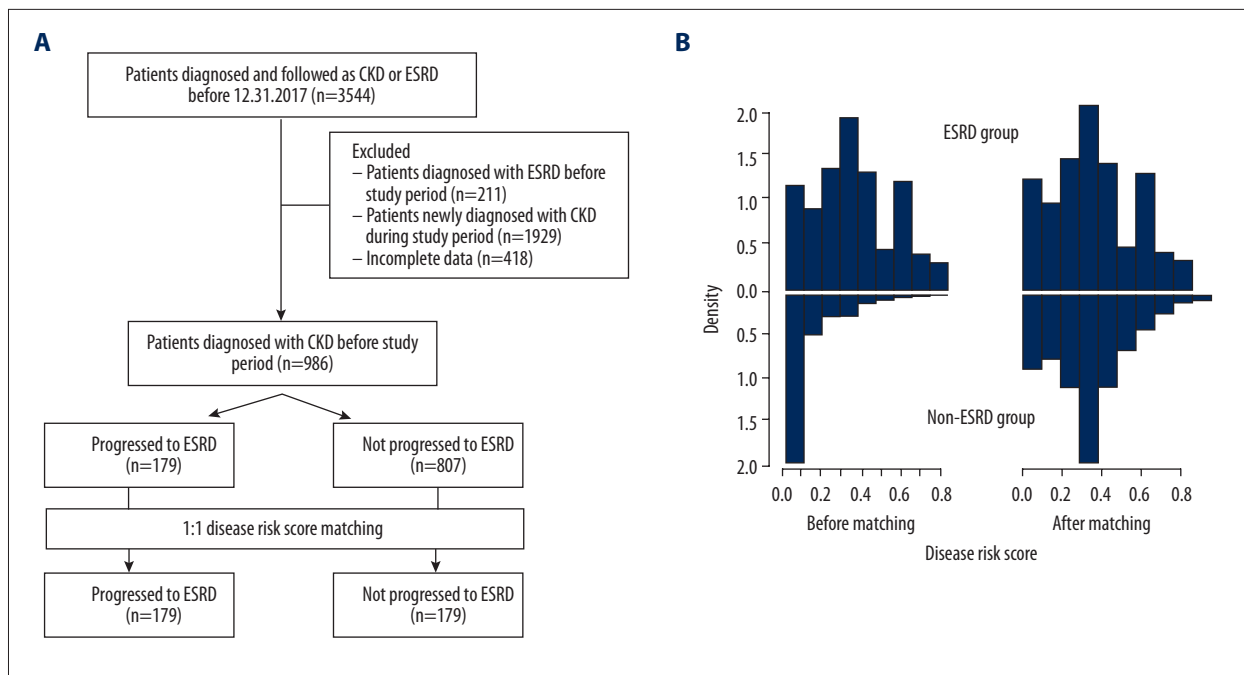
**Figure 1.** (**A**) Study flow chart. (**B**) Histogram showing the density of propensity score distribution in the end-stage renal disease group and non-end-stage renal disease group before and after matching.

study: Iohexol were used for routine abdomen CT (Omnihexol®, Korean United Pharm Inc, Seoul, South Korea), CT for gastrointestinal tract bleeding (Scanlux®, Tecmed Pharma, Midrand, Republic of South Africa), routine chest CT (Scanlux®), pulmonary CT angiography (Omnipaque®, GE Healthcare, Princeton, NJ), brain CT angiography and perfusion CT (Omnihexol®), neck CT (Omnipaque®), facial CT (Omnipaque®), CT for aortic dissection (Omnihexol®), and lower-extremity CT angiography (Omnihexol®). Iopamidol was used for liver and pancreas CT (Iopamiro®, Ilsung pharmaceuticals, Seoul, South Korea) and brain CT angiography (Pamiray®, DK Life Science, Seoul, South Korea). In total, 140 mL of contrast agent was used in CT protocols involving intra-abdominal organs (e.g., routine abdomen, liver, pancreas, and kidney), CT for aortic dissection, and lower-extremity CT angiography. In all other protocols, 90 mL of contrast agent was used. In all cases, contrast media were administered intravenously.

The prophylaxis protocol for CI-AKI at our institution is not unified, and patients received prophylactic treatment on a case-by-case basis. Even though the protocols consistently included isotonic saline hydration and N-acetylcysteine pretreatment, the indications for this prophylaxis protocol varied among clinicians.

## Disease risk score analysis

Disease risk score generation and matching were performed using the R package MatchIt (R Foundation for Statistical Computing, Vienna, Austria). Briefly, disease risk score estimates, which represent the probability of progression to ESRD for enrolled patients, were generated using a logistic regression model derived from clinical variables. Following disease risk score generation, patients were matched by using a 1: 1 optimal matching method. Matching was performed without replacement, and non-matched results were discarded. Accordingly, the patients diagnosed with ICD-code N18.1 were included at first. However, after disease scoring matching, no patients diagnosed with ICD-code N18.1 in the non-ESRD group were matched with patients diagnosed with ICD-code N18.1 in the ESRD group.

## Statistical analysis

All variables were subjected to normality testing. Continuous variables with normal distribution were reported as mean and standard deviation (SD) using the two-tailed $t$ test. Continuous variables with skewed distribution were reported as either median with interquartile range (IQR) using the Mann-Whitney U test. Categorical variables were presented as frequencies and percentages, using the chi-square test. Univariate analysis was performed to identify factors associated with progression to ESRD in CKD patients. Logistic regression analysis was performed to identify whether the CECT count was positively correlated with progression to ESRD. Two-sided P values <0.05 were considered statistically significant. Statistical analysis was performed using the R program software for Mac, version 3.2.2 (The R Foundation for Statistical Computing, c/o Institute

**Table 1.** Baseline characteristics of enrolled patients.

| | | ESRD group (%) | | Non-ESRD group (%) | | P-value |
|---|---|---|---|---|---|---|
| Sex | Male | 113 | (63.1) | 105 | (58.7) | 0.448 |
| | Female | 66 | (36.9) | 74 | (41.3) | |
| Age (years) | | 56.34±13.99 | | 56.98±13.72 | | 0.664 |
| CKD stage* | 2 | 1 | (0.6) | 1 | (0.6) | 0.614 |
| | 3 | 28 | (15.6) | 27 | (15.1) | |
| | 4 | 84 | (46.9) | 96 | (53.6) | |
| | 5 | 66 | (36.9) | 55 | (30.7) | |
| Underlying disease | Diabetes | 83 | (46.4) | 68 | (38.0) | 0.134 |
| | Hypertension | 66 | (36.9) | 51 | (28.5) | 0.115 |
| | Heart failure | 8 | (4.5) | 9 | (5.0) | 1 |
| Blood urea nitrogen (mg/dL) | | 44.86±22.17 | | 40.55±21.18 | | 0.06 |
| Serum creatinine (mg/dL) | | 4.31±3.02 | | 3.64±2.55 | | 0.242 |
| Hemoglobin (g/dL) | | 10.80±1.76 | | 10.70±1.93 | | 0.601 |
| Hematocrit (%) | | 32.50±5.43 | | 32.26±5.82 | | 0.685 |
| Alanine aminotransferase (U/L) | | 15.00 | [11.00–23.50] | 15.00 | [10.00–21.00] | 0.242 |
| Aspartate aminotransferase (U/L) | | 18.00 | [15.00–24.00] | 19.00 | [16.00–25.00] | 0.06 |
| Serum potassium (mMol/L) | | 4.93±0.78 | | 4.82±0.81 | | 0.203 |
| Serum sodium (mMol/L) | | 139.13±3.23 | | 139.51±3.51 | | 0.295 |
| Total protein (g/dL) | | 6.73±0.67 | | 6.86±0.83 | | 0.09 |
| Number of times contrast-enhanced CT was performed (n) | | 0.00 | [0.00–2.00] | 0.00 | [0.00–1.00] | 0.006 |
| Average amount of administered contrast media (mL) | | 139.55 | [0.00–205.00] | 96.26 | [0.00–115.00] | 0.04 |

ESRD – end-stage renal disease; CKD – chronic kidney disease; CT – computed tomography. * CKD stage 2=60 mL/min/1.73 m$^2$ ≤estimated glomerular filtration rate (eGFR) <90 mL/min/1.73 m$^2$, stage 3=30 mL/min/1.73 m$^2$ ≤eGFR <60 mL/min/1.73 m$^2$, stage 4=15 mL/min/1.73 m$^2$ ≤eGFR <30 mL/min/1.73 m$^2$, stage 5=eGFR <15 mL/min/1.73 m$^2$.

for Statistics and Mathematics, Wirtschaftsuniversität Wien, Vienna, Austria).

## Results

There were 3544 outpatients whose diagnosis included CKD or ESRD before December 31, 2017. Patients who were diagnosed with ESRD before the study period (n=211), patients who were newly diagnosed with CKD during the study period (n=1929), and patients with incomplete data (n=418) were excluded. Among the 986 patients who were diagnosed with CKD before the study period, 179 patients progressed to ESRD during the study period. Through 1: 1 disease score matching, the other 179 matched patients were chosen from the non-ESRD group who did not progress to ESRD during the study period (Figure 1A). Figure 1B shows a histogram of the density of disease score distribution in the ESRD group and non-ESRD group before and after matching.

Baseline characteristics of the ESRD group and non-ESRD group are shown in Table 1. CKD stages categorized by eGFR were not different between the 2 groups. A total of 178 patients (99.4%) were in CKD stage 3 or above in both groups, and their average serum creatinine was 4.31±3.02 mg/dl and 3.64±2.55 mg/dl in the ESRD group and non-ESRD group, respectively (p=0.242). Other demographic characteristics, underlying diseases that can contribute to CKD progression, and laboratory results were

**Table 2.** Logistic regression for ESRD progression.

| | Univariate OR (95% CI) | | P-value | Multivariate OR (95% CI) | | P-value |
|---|---|---|---|---|---|---|
| Sex (Male) | 1.21 | (0.79–1.85) | 0.39 | – | | – |
| Age | 1.00 | (0.98–1.01) | 0.66 | – | | – |
| CKD stage* | | | | – | | – |
| 3 | 1.04 | (0.04–27.12) | 0.98 | – | | – |
| 4 | 0.88 | (0.04–22.36) | 0.93 | – | | – |
| 5 | 1.20 | (0.05–30.82) | 0.90 | – | | – |
| Diabetes | 1.41 | (0.93–2.15) | 0.11 | – | | – |
| Hypertension | 1.47 | (0.94–2.29) | 0.09 | – | | – |
| Heart failure | 0.88 | (0.32–2.36) | 0.80 | – | | – |
| Serum creatinine | 1.09 | (1.01–1.18) | 0.03* | – | | – |
| Blood urea nitrogen | 1.01 | (1.00–1.02) | 0.06 | – | | – |
| Hemoglobin | 1.03 | (0.92–1.15) | 0.60 | – | | – |
| Alanine aminotransferase | 1.00 | (0.99–1.00) | 0.32 | 1.03 | (1.00–1.05) | 0.022 |
| Aspartate aminotransferase | 1.00 | (0.99–1.00) | 0.18 | 0.97 | (0.94–0.99) | 0.023 |
| Serum potassium | 1.19 | (0.91–1.55) | 0.20 | – | | – |
| Serum sodium | 0.97 | (0.91–1.03) | 0.30 | – | | – |
| Total protein | 0.78 | (0.59–1.04) | 0.09 | – | | – |
| Number of times contrast-enhanced CT was performed | 1.21 | (1.06–1.40) | 0.008* | 1.24 | (1.08–1.47) | 0.006 |

OR – odds ratio; CI – confidence interval; CT – computed tomography; CKD – chronic kidney disease. * CKD stage 3=30 mL/min/1.73 m$^2$ ≤eGFR <60 mL/min/1.73 m$^2$, stage 4=15 mL/min/1.73 m$^2$ ≤eGFR <30 mL/min/1.73 m$^2$, stage 5=eGFR <15 mL/min/1.73 m$^2$. Adjustment for multiple confounders included sex, age, chronic kidney disease stage, past history of diabetes, hypertension, heart failure, serum creatinine, blood urea nitrogen, hemoglobin, alanine aminotransferase, aspartate aminotransferase, serum potassium level, serum sodium level, serum total protein level, and number of times contrast-enhanced CT was performed. Hosmer-Lemeshow X-squared=5.84, df=8, p-value=0.67, indicating a good model fit. Hosmer-Lemeshow test (binary model).

not significantly different between the 2 groups. CECT was performed 0.00 [IQR 0.00–2.00] times in the ESRD group and 0.00 [IQR 0.00–1.00] times in the non-ESRD group (p=0.006). And average amount of applied contrast media was 139.55 [IQR 0.00–205.00] mL in the ESRD group and 96.26 [IQR 0.00–115.00] mL in the non-ESRD group, and the difference was statistically significant (p=0.04).

Univariate and multivariate logistic regression regarding factors contributing to progression to ESRD are shown in Table 2. In univariate logistic regression, serum creatinine level (odds ratio [OR]=1.09, 95% confidence interval [CI]=1.01–1.18, p=0.03), and number of times CECT was performed (OR=1.21, 95% CI=1.06–1.40, p=0.008) were statistically significant factors for predicting progression to ESRD. After adjusting

multiple confounders, the number of times CECT was performed (OR=1.24, 95% CI=1.08–1.47, p=0.006), serum ALT (OR=1.03, 95% CI=1.00–1.05, p=0.022), and AST (OR=0.97, 95% CI=0.94–0.99, p=0.023) were significantly related to progression to ESRD in multivariate logistic regression.

To compare the 2 models including and excluding the number of times CECT was performed, DeLong's test was performed for 2 correlated receiver operating characteristic (ROC) curves. The results are shown in Figure 2. The 2 models were significantly different (p=0.04). The area under the ROC curve (AUROC) of the model including the number of times CECT was performed was 0.6595, and it was higher than the AUROC of the model excluding the number of times CECT was performed, which was 0.0689.
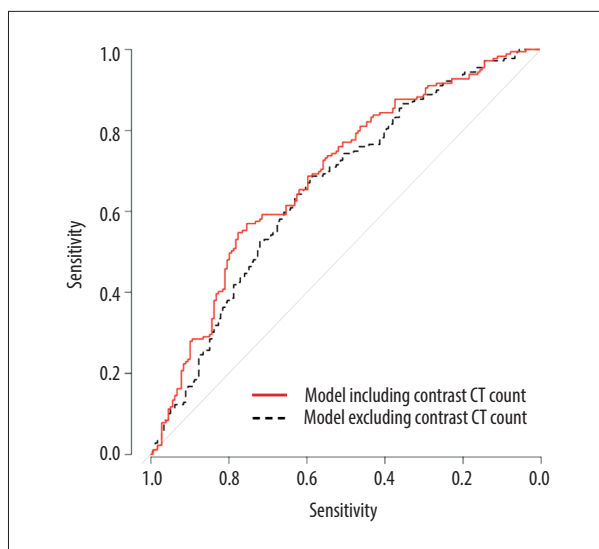
**Figure 2.** Receiver operating characteristic curve for end-stage renal disease progression including/excluding the number of times contrast-enhanced computed tomography was performed, in the multivariate logistic model.

## Discussion

In this study, the use of CECT increased the risk of ESRD by 1.2-fold in advanced, yet stable CKD outpatients after 5 years of follow-up. Two uniform groups, except for the number of times CECT was performed, were generated via disease risk score matching.

In the past, AKI after contrast media exposure was generally considered a transient and reversible event. In most cases, serum creatinine rises within 24 to 48 h after contrast media exposure and returns to baseline within 7 to 10 days [3,7,8]. However, several previous studies have suggested that contrast media exposure might be one of the contributing factors for CKD progression [10,14].

There are several mechanisms that explain AKI after contrast media exposure, at which time vasoconstriction of intrarenal vessel occurs. Intrarenal vasoconstriction leads to decreased renal blood flow, thereby making ischemic injury to renal parenchyma similar to ischemic acute tubular necrosis [1,7,8,15,16] Although most patients recover from ischemic acute tubular necrosis, chronic kidney damage remains in some [17]. Besides ischemic injuries, contrast media also acts as a direct cytotoxin for renal tubular and vascular cells [1,2,7,8,15]. Some of the damaged tubule and vascular cells recover, but others do not. Therefore, theoretically, the contrast media might cause a permanent sequela in the renal parenchyma, as well as in other kinds of AKI.

There are several studies supporting this hypothesis that also are consistent with this study. Hsieh et al. investigated the risk of ESRD after CECT in non-advanced CKD patients, and concluded that more than 1 contrast media exposure per year is statistically related to the development of ESRD [8]. Although CKD stages were not included in propensity score matching, repeated exposure to contrast media did influence progression to ESRD in this nationwide study. There are other studies, from Canada, that analyzed the risk of ESRD in patients who underwent coronary angiography [10,12]. They showed sustained kidney injury in patients who had CI-AKI after the procedure and reported that the risk of ESRD is also increased in patients who have had CI-AKI. In these studies, baseline eGFR distribution of CI-AKI and non-CI-AKI groups was different. On the contrary, McDonald et al. suggested that risk of CI-AKI and emergent dialysis is not increased by CECT in advanced CKD patients [18]. They matched 32 clinical variables in this well-designed study, but patients were followed up only for 1 month.

AST and ALT were associated with progression to ESRD in multivariate logistic regression. It is known that both liver enzymes tend to be lower in CKD patients than in the general population, and researchers suggest that a lower upper margin of liver enzyme level should be applied to CKD patients [19,20]. However, the prognostic implication of liver enzymes in progression to ESRD is unknown to date. Although the result turned out to be statistically significant, the clinical importance seemed unclear because of the opposing tendencies of the 2 liver enzymes.

The present study has some distinct strengths. First, major risk factors for progression to ESRD were included in the disease risk score matching. Consequently, the possibility of selection bias was decreased. Second, we only included outpatients and excluded patients who were admitted to the hospital during the study period. In other words, only clinically stable patients were enrolled, and the enrolled patients did not experience any serious illness that might accelerate the decline of their kidney function.

Conversely, there are several limitations to this study. First, this study was conducted in a single tertiary medical center and included only Koreans. Therefore, the number of enrolled patients was relatively small, and the results of this study might not be generalizable across all racial groups. Second, although disease risk score matching was used, there is a possibility of undetected confounding factors. Furthermore, several variables known as risk factors for progression to ESRD, such as glomerulonephritis or nephrotoxic drug usage, were not included in the disease risk score matching. Third, we did not analyze whether preventive measures such as intravenous hydration were performed. Fourth, we did not separate the patients who underwent CT without contrast media from those who did not undergo CT at all. Fifth, as we did not analyze post-CECT

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)

e921303-6

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System]
[ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica]
[Chemical Abstracts/CAS]

creatinine levels or post-CECT eGFR, the exact incidence of AKI after CECT is unknown. However, based on the study conducted by Winther et al., we assumed that there will be no statistically significant relationship between AKI after contrast media exposure and the need for permanent renal replacement therapy in advanced CKD patients [21].

## Conclusions

The risk of ESRD was increased 1.2-fold by using contrast media in advanced, yet stable, CKD outpatients after 5-year follow-up. The number of times CECT was performed, rather than baseline kidney function, affects the progression to

ESRD. However, with its limitations, the results presented in this study are not conclusive and should be further validated in an independent cohort before they can be applied to real clinical practice. Finally, studies with a larger number of patients and more matched variables are required in the future.

### Acknowledgements

### Conflict of interest

None.

## References:

1. Fukushima Y, Miyazawa H, Nakamura J et al: Contrast-induced nephropathy (CIN) of patients with renal dysfunction in CT examination. Jpn J Radiol, 2017; 35(8): 427–31

2. Tao SM, Wichmann JL, Schoepf UJ et al: Contrast-induced nephropathy in CT: Incidence, risk factors and strategies for prevention. Eur Radiol, 2016; 26(9): 3310–18

3. Thomsen H, Morcos S, Erley C et al: The ACTIVE Trial: Comparison of the effects on renal function of iomeprol-400 and iodixanol-320 in patients with chronic kidney disease undergoing abdominal computed tomography. Invest Radiol, 2008; 43(3): 170–78

4. Mitchell AM, Jones AE, Tumlin JA, Kline JA: Incidence of contrast-induced nephropathy after contrast-enhanced computed tomography in the outpatient setting. Clin J Am Soc Nephrol, 2010; 5(1): 4–9

5. Harjai KJ, Raizada A, Shenoy C et al: A comparison of contemporary definitions of contrast nephropathy in patients undergoing percutaneous coronary intervention and a proposal for a novel nephropathy grading system. Am J Cardiol, 2008; 101(6): 812–19

6. McDonald J, McDonald R, 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

7. Barrett B, Parfrey P: Preventing nephropathy induced by contrast medium. N Engl J Med, 2006; 354: 379–86

8. 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 (Baltimore), 2016; 95(16): e3388

9. Weisbord SD, Palevsky PM: Prevention of contrast-induced nephropathy with volume expansion. Clin J Am Soc Nephrol, 2008; 3(1): 273–80

10. James MT, Ghali WA, Tonelli M et al: Acute kidney injury following coronary angiography is associated with a long-term decline in kidney function. Kidney Int, 2010; 78(8): 803–9

11. Taniguchi Y, Sakakura K, Wada H et al: Contrast induced exacerbation of renal dysfunction in the advanced chronic kidney disease. Cardiovasc Interv Ther, 2013; 28(2): 157–61

12. James MT, Ghali WA, Knudtson ML et al: Associations between acute kidney injury and cardiovascular and renal outcomes after coronary angiography. Circulation, 2011; 123(4): 409–16

13. 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

14. Maioli M, Toso A, Leoncini M, Gallopin M et al: Persistent renal damage after contrast-induced acute kidney injury: Incidence, evolution, risk factors, and prognosis. Circulation, 2012; 125(25): 3099–107

15. Hossain M, Costanzo E, Cosentino J et al: Contrast-induced nephropathy: Pathophysiology, risk factors, and prevention. Saudi J Kidney Dis Transpl, 2018; 29(1): 1–9

16. Fernandes SM, Martins DM, da Fonseca CD et al: Impact of iodinated contrast on renal function and hemodynamics in rats with chronic hyperglycemia and chronic kidney disease. Biomed Res Int, 2016; 2016: 3019410

17. Foley RN, Sexton DJ, Reule S et al: End-stage renal disease attributed to acute tubular necrosis in the United States, 2001–2010. Am J Nephrol, 2015; 41(1): 1–6

18. 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 Clin Proc, 2015; 90(8): 1046–53

19. Ray L, Nanda SK, Chatterjee A et al: A comparative study of serum aminotransferases in chronic kidney disease with and without end-stage renal disease: Need for new reference ranges. Int J Appl Basic Med Res, 2015; 5(1): 31–35

20. Ravel V, Streja E, Molnar MZ et al: Association of aspartate aminotransferase with mortality in hemodialysis patients. Nephrol Dial Transplant, 2016; 31(5): 814–22

21. Winther S, Svensson M, Jorgensen HS et al: Repeated contrast administration is associated with low risk of postcontrast acute kidney injury and long-term complications in patients with severe chronic kidney disease. Am J Transplant, 2016; 16(3): 897–907