Repeated intravenous administration of iodinated contrast media and its association with prolonged renal dysfunction in early gastric cancer patients

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ABSTRACT

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Purpose

This retrospective investigation explored the potential influence of recurrent administration of intravenous iodinated contrast media (ICM) on the prolonged kidney dysfunction of patients undergoing surgical procedures intended to achieve curative outcomes in the management of early gastric cancer (EGC) utilizing data sourced from the nationwide dataset.

Materials and Methods

Patients who received a diagnosis of gastric cancer during the period from 2010 to 2013 received routine computed tomography (CT) imaging for surveillance of extragastric recurrence. Individuals with pre-existing chronic kidney disease (CKD) prior to diagnosis of cancer or those who had received chemotherapy or undergone multiple surgeries were not included in the study cohort. A nested case-control study was selected to assess the impact of recurrent exposure to ICM on the CKD. This analysis involved the comparison of individuals who manifested CKD 2 years subsequent to their cancer diagnosis against those who did not experience CKD during this timeframe.

Results

From a cohort of 59,971 patients identified based on predefined inclusion and exclusion criteria in the HIRA database, 1,021 individuals received a diagnosis of CKD two years following their cancer diagnosis. Following adjustments for age, gender, and the day when the cancer was diagnosed, a 1:5 matching strategy was employed, resulting in 5,097 control patients being matched to the 1,021 case patients. A marginal elevation in the likelihood of CKD with each increment in the number of CT scans utilizing ICM (odds ratio: 1.080; 95% confidence interval: 1.059 to 1.100; $P < 0.0001$) was revealed using conditional logistic regression analysis.

Conclusion

The utilization of ICM may be associated with the onset of chronic renal function deterioration.

Key words: intravenous iodinated contrast media; computed tomography; chronic kidney disease; early gastric cancer

1. INTRODUCTION

Computed tomography (CT) is extensively employed for cancer diagnosis, with intravenous iodinated contrast media (ICM) serving a crucial role in identifying remaining or recurring gastric malignancies and distant metastatic lesions.[1] While there is agreement regarding the essential role of contrast media in diagnostic procedures, ongoing discourse continues regarding its potential impact on renal function. Certain investigations propose that apprehensions regarding the potential negative influence of contrast media on kidney function, even with repeated administration, might be exaggerated.[2-4] Nonetheless, in alternative investigations, contrast-associated acute kidney injury was correlated with adverse short-term and prolonged consequences, including extended hospital stays, increased risk of cardiac and neurological events, and elevated mortality rates.[5-7] While uncertainties persist regarding the precise risk posed by iodinated contrast media (CM),[8] emerging evidence from both animal and human studies suggests a potential association between the occurrence of acute kidney injury and CM administration.[7,9-11] The precise mechanism underlying nephrotoxicity induced by iodinated CM remains incompletely understood. Proposed factors contributing to this phenomenon include direct injury to renal tubular epithelium, elevated viscosity and osmolarity leading to heightened oxidative burden, diminished urine flow, vasoconstriction, and accumulation of CM within the renal system. These factors may ultimately culminate in medullary hypoxia and a decline in kidney function.[12]

In the year 2020, gastric carcinoma stood as the fifth most prevalent malignancy and the fourth leading contributor to cancer-associated mortality. The incidence of stomach cancer varies by region, and is higher in eastern Asia countries such as Japan, and South Korea.[13,14] In 2002, a nationwide gastric cancer screening program was initiated for people 40 years old and older in South Korea, and with its implementation, the age-standardized rates for gastric cancer deaths have continuously decreased by an average of 6.7% per year since 2003.[15,16] Furthermore, the overall 5-year survival rates in early 2010s were 75.4% which were notably higher compared to worldwide 5-year survival rates (approximately 20%).[13,15] This relatively high survival rate may be due to the early detection of stomach cancer through screening with early gastric cancer (EGC) defined as stomach cancer staged T1 regardless of lymph node metastasis is more frequently found.[16,17] Standard treatment of early gastric cancer is gastrectomy with lymph node dissection and ESD (endoscopic submucosal dissection) could be used in certain criteria.[18] Recent studies has reported the 5-year survival rate of EGC to exceed 97% compared to survival rates of 20.2~80.7% for stage II and stage III gastric cancer.[19-22]

A standardized protocol of postoperative CT follow-up for stomach cancer has not been definitively established. Japanese guidelines recommend CT surveillance every six months during the initial postoperative year, followed by annual evaluations for up to five years for individuals diagnosed with stage I gastric cancer. For patients classified under stages II-III, the recommendation is for semiannual CT scans during the initial three years post-surgery, followed by annual monitoring thereafter.[18] Unlike colorectal cancer, where intensive postoperative monitoring unequivocally enhances overall survival,[23,24] the efficacy of such rigorous surveillance remains uncertain for patients undergoing curative resection for gastric cancer.[25,26] Consequently, the approach to post-gastrectomy surveillance varies among clinicians and institutions, guided by respective country-specific protocols.[18,27]

CT surveillance is commonly performed once a year for 5 years after surgery and is used more frequently within 2 years after surgical resection in some institution.[27-29] Concerns have emerged regarding radiation exposure associated with CT surveillance imaging in individuals treated with curative surgical intervention for EGC, given the minimal extragastric recurrence rate of only 1.4%, which constitutes the primary focus of CT surveillance.[30,31]

The utilization of contrast media is prevalent in the majority of CT scans, necessitating careful consideration of its nephrotoxic effects. Consequently, the potential risks associated with radiation exposure and repeated contrast media administration must be carefully assessed. While numerous studies have investigated contrast-associated acute kidney injury following a solitary CT scan with ICM,[32-35] limited attention has been given to the adverse impact of repetitive ICM exposure on prolonged renal dysfunction.[3,4,36]

Therefore, the objective of the analysis was to explore whether repeated administration of ICM during CT scans influences the prolonged kidney function of individuals who have undergone curative surgery for EGC, utilizing patient data sourced from a comprehensive national dataset.

2. MATERIALS AND METHODS

The analysis adhered to the ethical principles of the Declaration of Helsinki. This retrospective investigation received approval from the Institutional Review Board of our institution, with the necessity for obtaining informed consent was waived due to its retrospective design.

2.1. Origin of Data

In the Korean Health Insurance and Review Assessment (HIRA) dataset, identified under the reference number M20200206280, all data were obtained. This database contains comprehensive data regarding medication prescriptions and medical procedures conducted under a payment system based on fee-for-service. It encompasses medical records of all individuals enrolled in healthcare coverage in South Korea.[37] The data are encoded utilizing the Korean Classification of Diseases, 7th Revision (KCD-7), which incorporates diagnosis, procedural, fee codes, and derived from the International Classification of Diseases, 10th Revision (ICD-10), includes an additional subdivision tailored to prevalent diseases observed in Republic of Korea.

2.2. Patients

Given that both the malignancy per se and chemotherapy drugs may precipitate kidney injury,[38-41] this study encompassed patients with early gastric cancer (EGC) who received curative treatment and did not experience recurrence during the follow-up period. Since these individuals presented with negligible tumor load, which was subsequently eradicated through treatment, and the absence of preoperative or postoperative chemotherapy,[42] it was anticipated that any potential impact on renal function from both the chemotherapy drugs and malignancy would be mitigated.

Initially, we conducted a search within the HIRA database between 2010 and 2013 to identify patients aged over 20 years who received a diagnosis of gastric cancer. Among these patients, those who received curative gastrectomy or endoscopic submucosal dissection (ESD) and were subsequently followed up for a period of 5 years were included in the analysis. To assess prolonged renal dysfunction, individuals who were diagnosed with chronic kidney disease (CKD) throughout the surveillance period were evaluated. Subsequently, the exclusion criteria were employed: [1] patients who had been detected with additional cancer over 2 years prior to the diagnosis of gastric cancer (considered as a washout period), [2] patients who received any form of chemotherapeutic agents at any time, [3] patients with a pre-existing diagnosis of underlying renal disease prior to the diagnosis of gastric cancer, [4] patients identified with CKD within two years following their diagnosis of cancer, aiming to reduce the likelihood of CKD development owing to factors unrelated to contrast media, such as subclinical kidney disease, [5] Individuals who underwent multiple instances of gastric surgery or ESD as a result of recurrent tumors.

2.3. Protocol of CT follow-up in gastric cancer

Post-surgical CT surveillance for early gastric cancer was performed once a year for 5 years after surgery and was used more frequently within 2 years after surgical resection in our institution. Typically, CT surveillance was conducted biannually in two years post-surgery, followed by annual CT follow-up was performed for 5 years. Therefore, 6 to 8 time of CT were taken during 5 years of follow-up. Physicians tended to follow-up less frequently for patients who received ESD for early gastric cancer. Similar strategy was used for advanced gastric cancer but CT was taken more frequently by physician's discretion.

2.4. Data analysis

To address potential confounding variables, the existence or non-existence of factors recognized to impact kidney function, such as hyperlipidemia, diabetes, hypertension, stroke, coronary artery occlusive disease, heart failure, and chronic hepatitis virus infection were examined. Additionally, data pertaining to prescribed medications known to impact kidney function, including non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme inhibitors (ACEi), loop diuretics, angiotensin II receptor blockers (ARBs), acetaminophen, and statins were also assessed. Medications administered within a one-month timeframe following the diagnosis of cancer and utilized for a duration exceeding two weeks were included into the analysis. Moreover, the frequency of CT scans using ICM during the follow-up duration was assessed. We conducted a comparison of the number of CT scans administered with ICM between patients who were diagnosed CKD two years following their diagnosis of cancer and those who were not suffered CKD. This analysis aimed to assess the impact of recurrent administration of ICM on long-term renal function.

2.5. Statistical analysis

A nested case-control design was adopted in order to examine the potential impact of repeated exposure to ICM on the chronic kidney dysfunction of EGC patients. We picked individuals who served as case patients and were diagnosed with CKD two years or more following their gastric cancer diagnosis. Subsequently, for each case patient, we selected four control patients from among those who were not CKD identified at the moment of diagnosis in the corresponding case patients. Based on gender and age at the time of cancer diagnosis (within a one-year difference), as well as being detected within the identical month and year as the corresponding case participant, these control patients were matched.

Subsequent to the matching process, the baseline characteristics of both the case and control groups were evaluated using suitable statistical techniques, taking into consideration the dependency of the data. To analyze the baseline demographics of both the control and case groups and to examine potential correlations between the frequency of CT scans and the incidence of CKD following the diagnosis of gastric cancer, a conditional logistic regression was conducted as univariate analysis. Furthermore, following adjustments for prescribed medications and underlying medical conditions, a multivariate analysis was conducted. SAS Enterprise Guide version 9.4 (SAS Institute Inc., Cary, NC, USA) was used to perform statistical analyses. Statistical significance was determined by p-values below 0.05.

3. RESULTS

3.1. Patients

Out of 254,422 gastric cancer patients between 2010 and 2013, 128,760 were excluded due to the diagnosis of other malignancies throughout or prior to the washout period. Additional exclusion criteria comprised chemotherapy (n=38,876), underlying renal disorder (n=23,651), repeated surgery or ESD (n=2,605), and being diagnosed with CKD over a two-year period following the initial diagnosis of gastric cancer (n=559). After exclusion, 59,971 patients diagnosed with gastric cancer were included. Among this cohort, 1,021 individuals were identified as having developed CKD two years subsequent to their diagnosis of cancer, forming the case group. Through a 1:5 matching process, each case patient was paired with at least one individual from the control group, resulting in a total of 5,097 patients being matched to those in the case group to form the control group. Figure 1 illustrates a thorough flow chart delineating the patient selection process. Subsequently, Table 1 illustrated the baseline characteristics of the case and control groups after the matching procedure. Also, detailed distribution of the number of CT taken between case and control was described in figure 2. Figure 3 displays the time intervals between the diagnosis of CKD and EGC. Figure 4 depicts the cumulative number of CKD diagnoses following gastric cancer diagnosis.

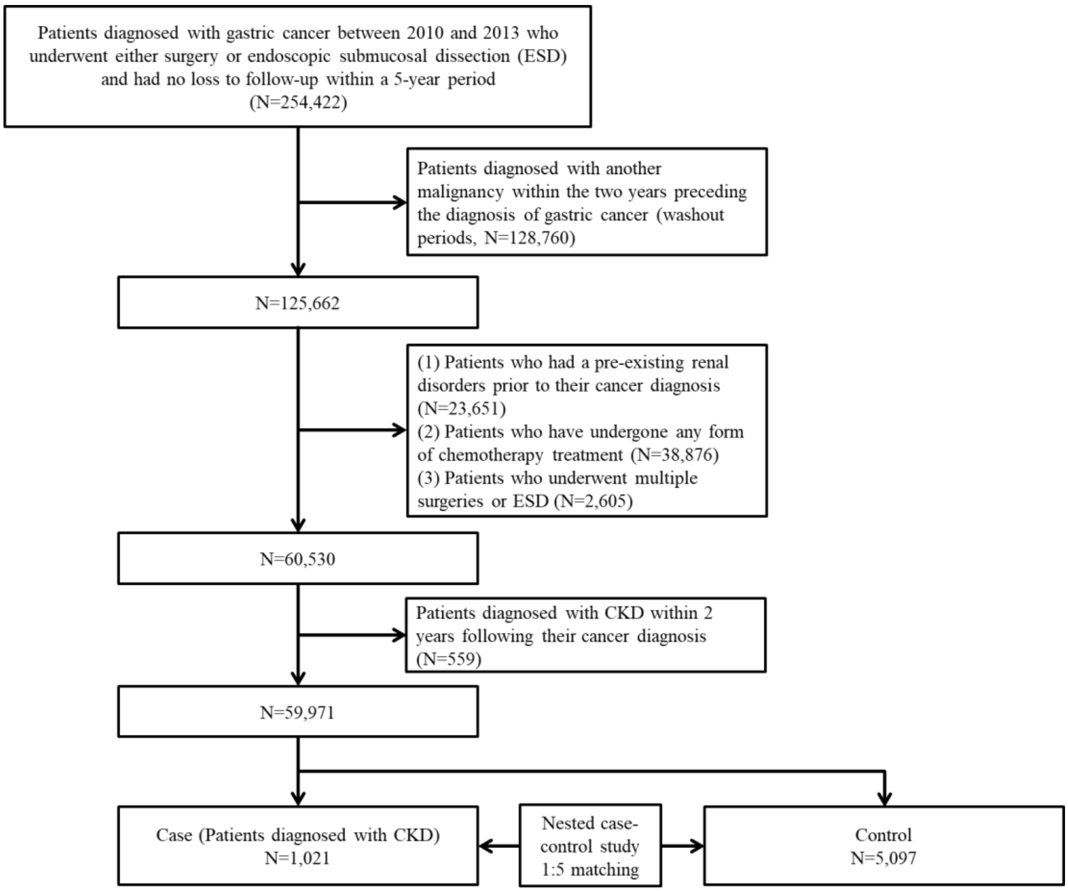

Figure 1. Flow diagram illustrating patient cohort identification from the HIRA dataset

Table 1. Characteristics of baseline demographics and clinical presentation in patients with CKD more than 2 years following initial diagnosis of cancer, compared to matched control cohorts

Parameters	Case (n = 1,021)	Control (n = 5,097)	P-value
Age (years)	68.41±9.30	68.40±9.21	0.972[a)]
Gender			0.9645[a)]
Male	795 (77.86 %)	3972 (77.93 %)	
Female	226 (22.14 %)	1125 (22.07 %)	
Drugs			
NSAIDs	211 (20.67 %)	716 (14.05 %)	<0.0001[b)]
ACEi	27 (2.64 %)	94 (1.84 %)	0.0056[b)]
Loop diuretics	25 (2.45 %)	35 (0.69 %)	<0.0001[b)]
ARBs	131 (12.83 %)	339 (6.65 %)	<0.0001[b)]
Acetaminophen	35 (3.43 %)	197 (3.87 %)	0.2489[b)]
Statins	137 (13.42 %)	377 (7.40 %)	<0.0001[b)]
Hypertension	357 (34.97 %)	1226 (24.05 %)	<0.0001[b)]
DM	426 (41.72 %)	1209 (23.72 %)	<0.0001[b)]
Hyperlipidemia	211 (20.67 %)	633 (12.42 %)	<0.0001[b)]
CAOD	161 (15.77 %)	546 (10.71 %)	<0.0001[b)]
Stroke	8 (0.78 %)	13 (0.26 %)	0.0002[b)]
Heart failure	49 (4.80 %)	119 (2.33 %)	<0.0001[b)]
Chronic hepatitis	30 (2.94 %)	115 (2.26 %)	0.029[b)]
The number of CT taken	6.02±3.88	4.99±3.73	<0.0001[a)]

DM: Diabetes mellitus, CAOD: Coronary artery occlusive disease.

Mean ± standard deviation

a) Two-sample *t*-test was utilized; b) Pearson's chi-square test was utilized.

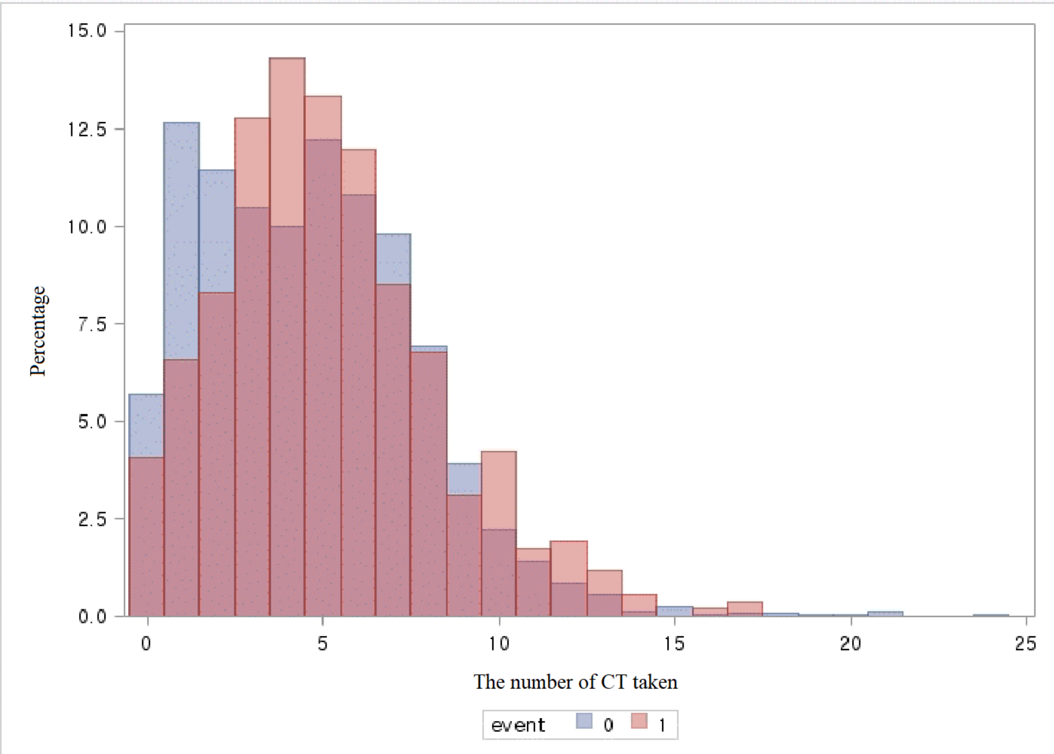

Figure 2. Distribution of the number of CT taken between case and control in HIRA database. (0: control, 1: case)

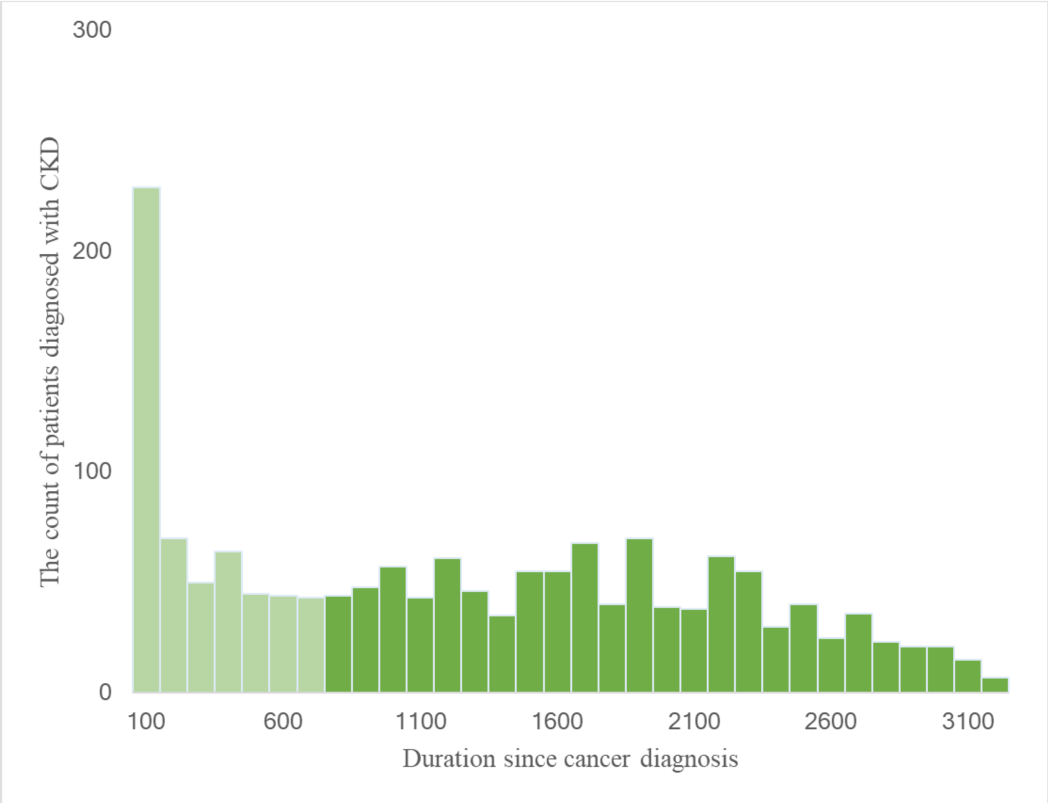

Figure 3. Temporal gap between CKD diagnosis and gastric cancer diagnosis within the HIRA database. (Patients identified with CKD within two years subsequent to cancer diagnosis are represented by the color light green)

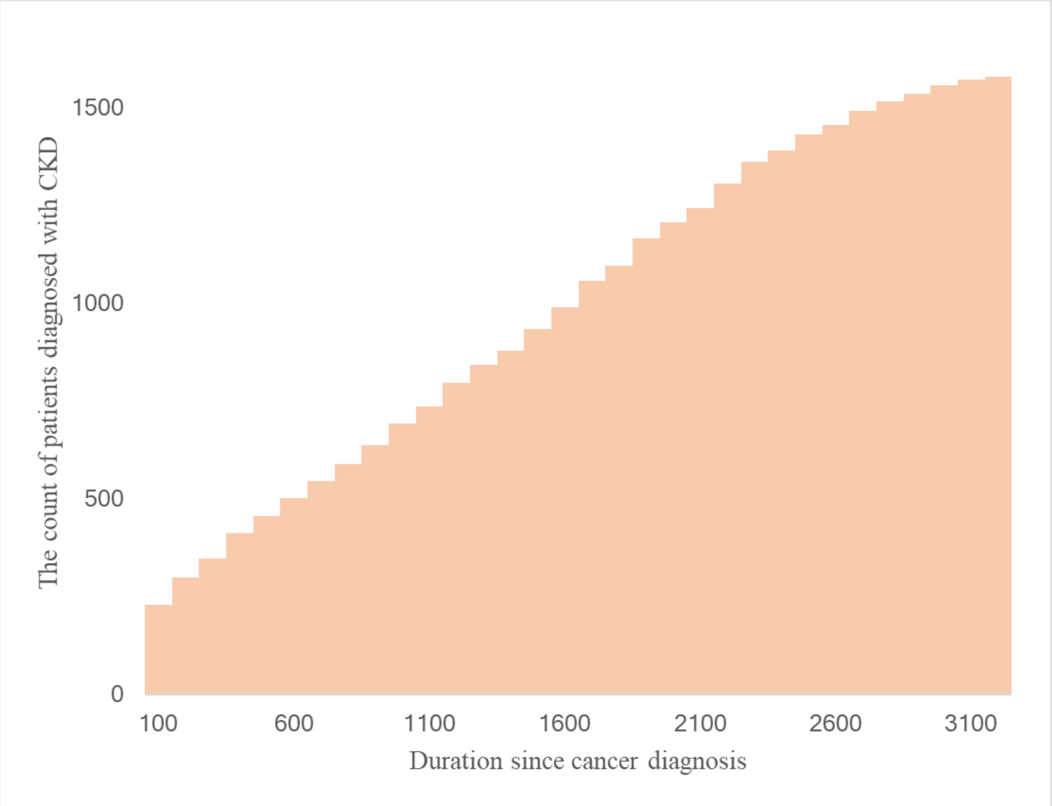

Figure 4. Cumulative number of CKD diagnoses following gastric cancer diagnosis

3.2. Protocol for CT surveillance in gastric cancer

The average quantity of CT scans conducted was notably higher within the case group compared to the control group (6.02±3.88 vs. 4.99±3.73, respectively, $p<0.001$). Figure 5 illustrates the distribution of CT scans according to the duration since diagnosis of stomach cancer among all patients (n = 59,971), while Figure 6 represents this distribution post-matching. As anticipated, the frequency of CT scans peaked consistently at 6 months, and annually until 5 years following diagnosis. The average number of CT scans per patient was 6.12, with a standard deviation of 3.62. The median was 6, with an interquartile range of 3 to 8.

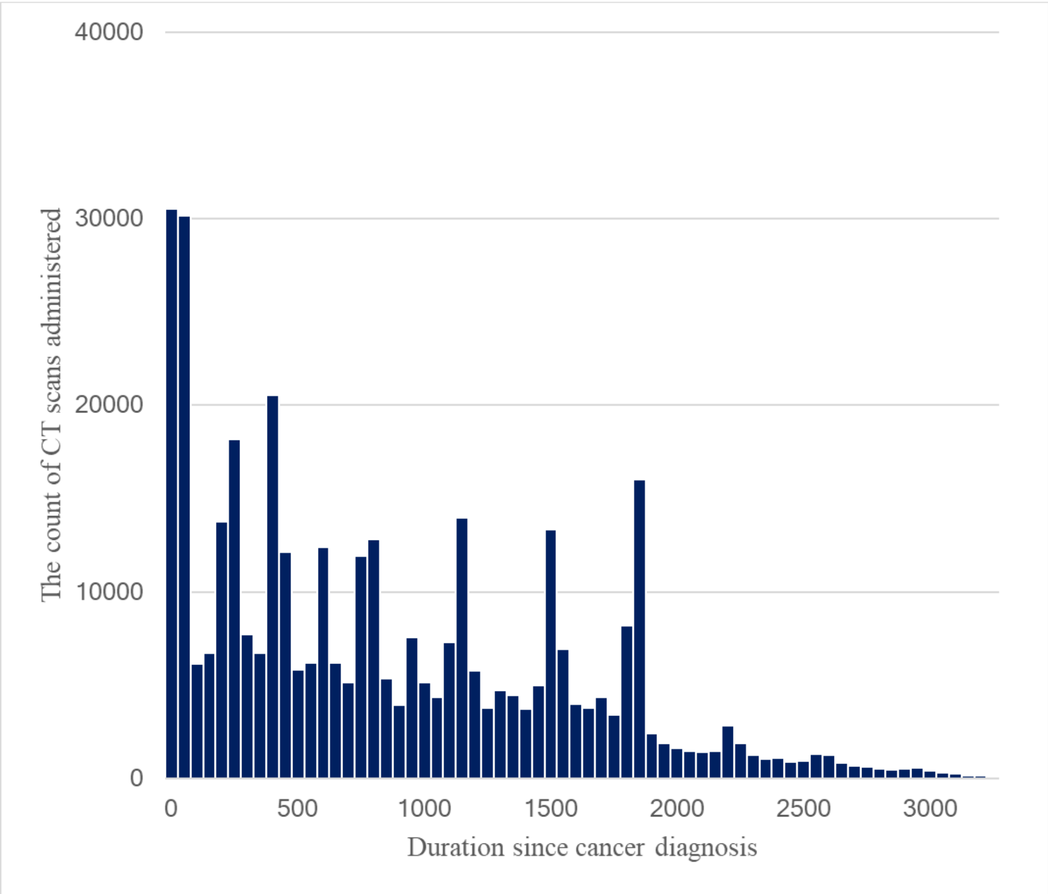

Figure 5. The count of CT imaging following cancer diagnosis, stratified by days elapsed since cancer diagnosis, among all patients prior to the matching.

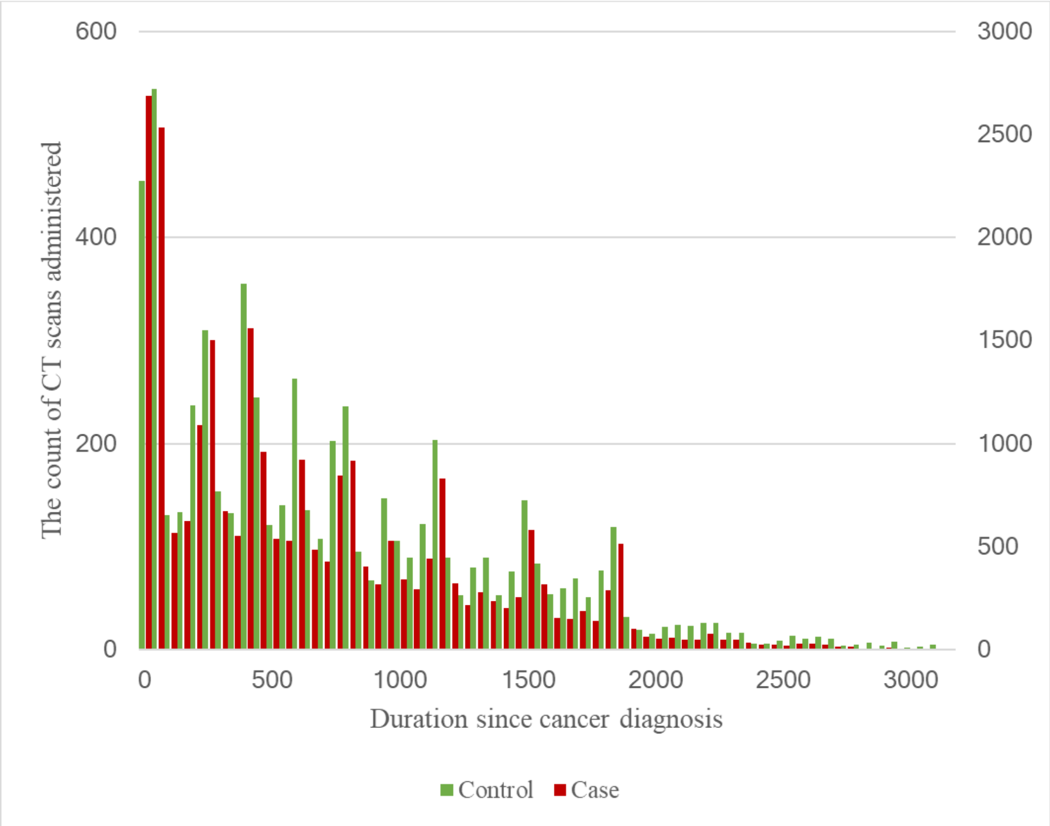

Figure 6. The count of CT scans taken following cancer diagnosis, stratified by days elapsed since cancer diagnosis, among patients after matching. (The control group is represented in the right Y-axis, whereas, the case group is depicted in the left Y-axis.)

3.3. Association between CKD incidence and CT utilization

Uunivariate analysis as Model 1 in Table 2 revealed that an increased CT numbers performed using ICM was associated with higher odds of CKD (Odds Ratio (OR) = 1.084; 95% confidence interval (CI): 1.064, 1.104; P <0.001). Subsequent to adjusting for additional confounding variables as delineated in Table 2, the multivariate analysis was performed (Model 2 in Table 2). The association persisted, demonstrating an increased frequency of CT scans utilizing ICM marginally elevated the odds of CKD (OR= 1.080; 95% CI: 1.059, 1.100; P <0.001). Notably, established CKD risk factors, including hyperlipidemia (OR= 1.349 95% CI: 1.109, 1.641; P =0.003), diabetes mellitus (OR= 1.996; 95% CI: 1.714, 2.324; P <0.001), and hypertension (OR= 1.584; 95% CI: 1.312, 1.911;

P <0.001), contributed to an elevated likelihood of CKD development.

Table 2. The correlation between CT scan frequency and CKD

Model	Parameters	OR (95% C.I.)	P-value
Model 1	The count of CT scans administered	1.084 (1.064, 1.104)	<0.001
Model 2	The count of CT scans administered	1.080 (1.059, 1.100)	<0.001
	NSAIDs	1.135 (0.936, 1.377)	0.199
	Acetaminophen	0.736 (0.503, 1.078)	0.116
	ARBs	1.340 (1.057, 1.700)	0.016
	Statins	1.164 (0.915, 1.480)	0.216
	Loop diuretics	2.697 (1.511, 4.815)	0.001
	ACEi	0.913 (0.571, 1.459)	0.704
	Hypertension	1.584 (1.312, 1.911)	<0.001
	DM	1.996 (1.714, 2.324)	<0.001
	Hyperlipidemia	1.349 (1.109, 1.641)	0.003
	CAOD	1.012 (0.817, 1.254)	0.914
	Stroke	2.608 (1.051, 6.472)	0.039
	Heart failure	1.460 (0.995, 2.143)	0.053
	Chronic hepatitis	1.141 (0.743, 1.752)	0.547

OR: odds ratio; C.I.: confidence intervals

4. DISCUSSION

Our results suggest that the utilization of ICM in CT imaging might represent a potential risk factor for the onset of CKD, despite a modest odds ratio of 1.080 for one CT imaging. Nevertheless, individuals undergoing diagnosis and treatment for various malignancies, such as early gastric cancer (EGC), typically undergo multiple CT imaing using ICM over a period of at least five years. Hence, the importance of the relatively subtle odds ratio linked with the onset of CKD should not be underestimated.

Previous studies have identified iodinated contrast media as a plausible factor correlated with contrast-induced acute kidney injury and was found to be linked with unfavorable short-term and prolonged consequences, such as extended hospital stays, increased incidences of neurogenic and cardiac events, and heightened mortality rates.[5,6,9] However, current research has questioned the concept that CM has a substantial impact on kidney function, even with repeated use. These studies have mainly concentrated on contrast-induced acute kidney injury or prolonged impact of ICM during 3-6 months which were relatively shorter periods.[2-4] Our findings, on the other hand, delved into the extended repercussions of ICM over a period of 5 years. Consequently, our findings reveal that administration to ICM escalates the modest but significant odds of the CKD onset.

Iodine contrast media such as CT contrast agent have a nephrotoxic potential.[43,44] There were two possible mechanisms to induce renal damage from intravenous contrast.[45,46] Direct mechanisms of renal damage from contrast media are thought to be because of injury to the tubular epithelium, causing loss of function, apoptosis, and finally, necrosis. Indirect mechanisms of contrast media are causing ischemic damage owing to mediation of vasoactive materials including nitric oxide, endothelin, and prostaglandins.[47] The outer portion of renal medulla particularly susceptible to ischemic damage from disturbances in regional or global renal blood flow.[12] Acute kidney injury triggered by post-contrast administration of iodinated contrast media can prompt a sudden decline in renal function, occurring from 2 days to a week following the administration of the contrast media.[48,49]

Conventionally, while acute kidney injury is recognized to elevate both morbidity and mortality, it has typically been regarded as an isolated event, and individuals who experience acute kidney injury resolution are expected to demonstrate positive long-term prognoses.[50,51] Nonetheless, contemporary observational investigations have indicated a correlation between acute kidney injury and CKD, highlighting acute kidney injury as one of the contributing risk factors for CKD. Moreover, the length, intensity, and recurrence of acute kidney injury serve as significant indicators of adverse prognoses.[50,51] Some pathologic mechanisms which were assessed in animal models persist subsequent to acute kidney injury are comparable to those that have been thought to induce the development of CKD.[51] The reversibility of the renal damage, the degree of the decrease in glomerular filtration rate and the equilibrium of adaptive and maladaptive repair processes affected the progression to chronic kidney disease after an event of acute kidney injury.[50,52] Cell-cycle modulators such as hypoxia-inducible factors, transforming growth factor β1, vascular endothelial growth factor, and heme oxygenase 1 have been established as defensive elements in acute kidney injury, however, some of them could affect the progression of chronic kidney disease.[53-56] Also, repetitive injury could induce aggravated long-term outcomes.[53,57,58] Hence, if acute kidney injury episodes disrupt the equilibrium of repair processes, it has the potential to advance into chronic kidney disease.[50,52,59] Thus, overlooked and undetected contrast induced acute kidney injury might affect to progression of CKD and it is possible explanation for results of our study. In our investigation, the odds ratio of the developing CKD due to one CT imaging was slightly modest (1.080). However, this odds ratio holds significance and cannot be dismissed as trivial for patients requiring repetitive CT imaging for disease monitoring or treatment evaluation.

It is well known that numerous chemotherapy drugs are nephrotoxic.[60] Recommended standard adjuvant chemotherapy regimen is S-1 or capecitabine plus oxaliplatin for patients of pathological stage II or II of gastric cacner.[42] Among them, oxaliplatin and capecitabine were known to be nephrotoxic.[61,62] In rare occasions, cancer-associated glomerulopathies could occur by tumor antigen.[63,64] The overall survival of EGC was reported very high as more than 97%.[20,21,65,66] Hence, we chose to analyze patients who had early gastric cancer for evaluating effects of repetitive administration of iodine contrast to renal function impairment to exclude the effect from nephrotoxic chemotherapeutic agents and to minimize the effect from tumor burden.

The individuals within our case group demonstrated a significantly elevated incidence of concurrent health conditions, such as diabetes and hypertension, when compared to our control cohort, as delineated in Table 6. Both diabetes and hypertension are universally acknowledged as predisposing factors for CKD.[67] Therefore, these factors potentially exert an influence on our results. Thus, to attenuate the effect of these confounding variables, we used conditional logistic regression as a multivariate analysis. This test unveiled that both diabetes and hypertension were correlated with an elevated odds ratio, alongside the discernible yet subtle effect of ICM administration. Further investigations concerning the use of CT scans with ICM in patients already predisposed to risk factors for CKD are warranted.

Loop diuretics usage was appeared to increase odds of chronic kidney disease in our multivariate analysis. (OR, 2.697; 95% CI: 1.511, 4.815; P =0.0008) Loop diuretics were commonly used to treat acute kidney injury.[68] However, there were some reports that loop diuretics might be nephrotoxic.[69,70]

The frequency of loop diuretics usage was found to be rare in our case and control groups. (2.5%, 0.7%, respectively) Although, it appeared to statically significant, it was not reliable due to a few number of usage.

Typically, endoscopic examinations are routinely conducted for the detection of mucosal recurrence or development of secondary gastric cancer during follow-up.[71] In gastric cancer follow-up, CT plays a crucial role in extragastric recurrence detection. But, Seo et al. performed a research to stratify the risk of extragastric recurrence among patients with EGC. They identified five risk factors, namely male gender, positive lymphovascular invasion, elevated macroscopic type, lymph node metastasis, and indications for endoscopic resection. Their findings revealed that the 10-year survival rate free from extragastric recurrence of low risk group for extragastric recurrence was remarkably high, reaching 99.7%. Hence, their conclusion suggests that CT surveillance is not warranted for individuals deemed to be at low risk.[30] In patients with an extremely low risk of cancer recurrence, it becomes imperative to carefully balance the diagnostic benefits of CT scans against the potential harm posed by contrast media administration to the chronic kidney dysfunction. Our investigation revealed a notable discrepancy in CKD onset between the case and control cohorts, notwithstanding that the average disparity in the count of CT scans taken was just about one. Consequently, it is essential to reevaluate and adapt the surveillance duration and frequency of CT scans based on the future research findings.

From a prior research, almost half of old individuals aged 65 years or older are afflicted with CKD, yet less than 10% have received an official diagnosis within the United States.[72] These findings align with our outcomes, as out of 1,021 patients, 229 (14.5%, as illustrated in Figure 3) were diagnosed with CKD concurrent with gastric cancer diagnosis. This indicates that these individuals might have harbored CKD prior to their cancer diagnosis, albeit the condition went undetected until perioperative renal function assessment was conducted. Therefore, CKD often went unnoticed and unacknowledged in numerous cases. The concept of a washout period is commonly employed in national databases to distinguish new incident cases from prevalent ones.[73] Similarly, we opted to exclude patients diagnosed with chronic kidney disease (CKD) within two years of their diagnosis of cancer to diminish the likelihood of CKD arising from factors unrelated to contrast media. Patients without a confirmed diagnosis of CKD but exhibiting declining renal function from causes unrelated to contrast media could pose as potential confounding factors if CKD is later diagnosed after contrast media administration. Recognizing that CKD typically develops gradually over an extended period, we implemented a substantial two-year washout period to minimize the enrollment of such cases in our analysis.

International guidelines commonly advise undergoing a CT surveillance every six months for the initial two years post-surgery, followed by annual CT follow-ups for the subsequent five years.[18,27,74] The universal protocol aligns with our investigation, evident in the peak of CT scans occurring at 6 months, then annually until 5 years post-diagnosis, as depicted in Figures 5 and 6. Both the mean and median number of CT scans hovered around 6, attributable to this pattern. Notably, the highest frequency of CT scans was observed immediately following diagnosis, likely attributed to the need for postoperative complication assessment during the perioperative phase.

This study has several limitations. Firstly, the HIRA dataset lacks detailed information regarding the ICM, including osmolality and administered volume, both recognized as risk factors for kidney damage.[12,75] However, most institutions have adapted an adjusted contrast media injection protocol in which the amount of contrast media to be administered is adjusted to the body weight of patients (600 mg I/kg),[76,77] so the difference in contrast media administered per body weight may not be a significant factor affecting our results. Additionally, definition of CKD relied upon the diagnostic codes stipulated in the KCD-7 and data regarding eGFR was unavailable. Moreover, the HIRA database lacked specific information on pathologic stages. Second, the heterogeneity resulting from distinct institutional protocols and CT scanning procedures must be taken into consideration when examining the HIRA dataset. Third, there may be a presence of selection bias since physicians often restrict the usage of ICM in patients deemed to be at a heightened risk of kidney dysfunction. Fourth, serious postoperative complications might necessitate increased utilization of CT scans, potentially impacting renal function. Nonetheless, due to the constraints of the HIRA dataset, data regarding complications are not available, precluding an analysis of their potential influence on renal function in this study. Fifth, our results are applicable to only intravenous contrast media usage, although intraarterial contrast administration has been reported to be related with a higher frequency of dialysis, acute kidney injury and mortality compared to intravenous admiration of contrast media.[78] Finally, follow-up data beyond 10 years post-ICM administration were unavailable for collection. Hence, there is a need for studies incorporating data from extended follow-up periods to provide a more comprehensive understanding of the long-term effects of ICM administration.

5. CONCLUSION

The use of ICM could potentially pose a risk factor for kidney dysfunction over the long term. Therefore, the potential advantages and disadvantages of contrast-enhanced CT scans should be carefully reconsidered in patients who exhibit a low probability of recurrence, including patients diagnosed with EGC.

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ABSTRACT IN KOREAN

조기 위암 환자에서 반복적인 정맥내 요오드 조영제 사용이 장기적인 신장기능에 미치는 악영향

목적

완치적 수술을 받은 조기 위암 환자에서 반복적인 정맥내 요오드 조영제의 사용이 신장기능에 미치는 영향을 알아보기 위해 건강보험심사평가원 자료를 이용한 후향적 연구이다.

재료 및 방법

건강보험심사평가원 자료를 이용하여 반복적인 요오드 조영제의 사용이 만성콩팥병에 미치는 영향을 조사하였다. 2010년 1월부터 2013년 12월까지 위암으로 진단된 환자중 재발유무를 알기 위해 정기적으로 컴퓨터 단층촬영(CT)를 시행한 환자들을 조사하였다. 위암 진단전에 이미 콩팥병을 기저질환으로 가지고 있었거나 반복적인 위절제술 및 점막절제술, 항암치료를 받은 환자는 제외하였다. 코호트내 환자대조군연구법을 이용하여 위암 진단날짜로부터 2년이후에 만성 콩팥병을 진단 받은 환자와 그렇지 않은 환자를 비교하여 반복적인 정맥내 요오드 조영제의 노출이 장기적인 신장 기능에 미치는 영향을 알아보았다.

결과

59,971명이 조사되었고 이중에서 위암 진단 후 2년 이후에 만성콩팥병이 발병한 환자는 1021명이었다. 나이, 성별, 위암 진단날짜를 기준으로 1:5 매칭을 시행하여 5097명의 대조군이 매칭되었다. 다변수분석을 통해 정맥내 요오드 조영제를 사용한 CT 시행건수가 만성콩팥병의 오즈를 조금 증가시키는 것으로 나타났다. (오즈비 1.080; 95% 신뢰구간: 1.059-1.100, $p<0.0001$)

결론

정맥내 요오드 조영제의 사용은 만성적인 신장기능 장애에 영향을 미칠 수 있다.

핵심되는 말 : 콩팥부전, 사구체여과율, 다검출기 컴퓨터 단층촬영, 정맥내 요오드 조영제, 조기위암