

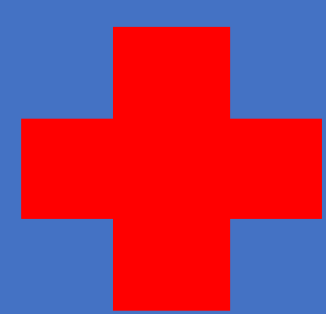


The Incidence and Risk factors of kidney injury in Patients Receiving Immune Checkpoint Inhibitors

A retrospective observational cohort study

Thanawat Suksomboon¹, Piyada Sitthideatphaiboon², Jeerath Phannajit^{3,4}, Pisut Katavetin³

¹ Department of Internal Medicine; ² Division of Medical Oncology; ³ Division of Nephrology; ⁴ Division of Clinical Epidemiology, Department of Internal Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand



King Chulalongkorn Memorial Hospital
The Thai Red Cross Society

INTRODUCTION

- Immune checkpoint inhibitors (ICPis) are approved for many hematological and solid organ malignancies treatments. However, they were associated with the occurrence of immune-related adverse events (irAEs).
- The kidney irAEs are less frequently reported than other irAEs, but they can affect the cancer treatment strategy.

METHODS

- A single-center retrospective observational study included cancer patients who received ICPis from January 2014 to December 2021 at King Chulalongkorn Memorial Hospital.
- Patients without a baseline serum creatinine or ESRD on dialysis or previous kidney transplants were excluded.
- Kidney injury was defined a ≥ 1.5 -fold increase in serum creatinine from baseline.
- The etiology of kidney injury was divided into 3 categories: Hemodynamic kidney injury, ICPis-related kidney injury, and Obstructive kidney injury.
- Cox regression was used to determine the risk factors of kidney injury. Multivariate models were developed by adjusting for covariates with $p < 0.1$ in univariate models and stepwise backward logistic regression to select the final model. Statistical significance was defined as $P < 0.05$.

OBJECTIVE

- This study evaluated the incidence and risk factors of kidney injury in patients receiving ICPis.

RESULTS

- Total 265 patients were included in this study. The overall cumulative incidence of kidney injury (over three years) was 9.4% (95%CI=6.4%-13.8%)
- Most of the patients were male (68.3%), median age 62 (56-70) years, baseline serum creatinine was 0.8 (0.7-1) mg/dl, and eGFR CKD-EPI was 94.2 (77.1-107.1) min/mL/1.73m².

Table 1: Baseline characteristics of patients receiving ICPis

Characteristic	Non-kidney injury (n=241)	Kidney injury (n=24)	P-Value
Age (years)	62 (55-70)	70.5 (63-75)	0.002
Male, n (%)	162 (67.2)	19 (79.2)	0.23
Serum Creatinine (mg/dL)	0.8 (0.7-1)	1 (0.8-1.3)	0.001
eGFR CKD-EPI (min/mL/1.73m ²)	93.8 (80.1-104.1)	69.9 (54.1-88.2)	<0.001
HT	78 (32.4)	15 (62.5)	0.03
Diabetes mellitus	41 (17)	11 (45.8)	0.001
Dyslipidemia	26 (10.8)	9 (37.5)	<0.001
CKD	17 (7.1)	5 (20.8)	0.02
Antibiotics	83 (34.4)	18 (75)	<0.001
NSIADs	20 (8.3)	1 (4.2)	0.70
PPI	96 (39.8)	14 (58.3)	0.08
ACEI/ARB	16 (6.6)	6 (25)	0.002
Diuretics	13 (5.4)	4 (16.7)	0.06
Melanoma	23 (9.5)	2 (8.3)	0.86
Lung cancer	109 (45.2)	8 (33.3)	0.26
Hepatocellular carcinoma	29 (12)	7 (29.2)	0.02
Nivolumab	44 (18.3)	6 (25)	0.42
Pembrolizumab	92 (38.2)	6 (25)	0.20
Atezolizumab	70 (29.1)	11 (45.8)	0.09
Combinations	9 (3.7)	1 (4.2)	0.92

Table 2: Clinical factors associated with kidney injury in patients receiving ICPis

Variable	Univariate analysis		Multivariate analysis	
	HR (95%CI)	P-value	adjusted HR (95%CI)	P-value
eGFR CKD-EPI < 90 min/mL/1.73m ²	4.69 (1.75-12.56)	0.002	3.79 (1.39-10.36)	0.01
Diabetes mellitus	3.77 (1.69-8.43)	0.001	3.66 (1.59-8.45)	0.002
Cerebrovascular disease	14.81 (4.38-50.09)	<0.001	13.08 (3.57-47.88)	<0.001
Antibiotics	5.34 (2.12-13.47)	<0.001	3.58 (1.39-9.21)	0.01
Hepatocellular carcinoma	2.88 (1.19-6.95)	0.02	2.8 (1.12-6.98)	0.03

Figure 1: Cumulative incidence of kidney injury in patients receiving ICPis by eGFR CKD-EPI at baseline

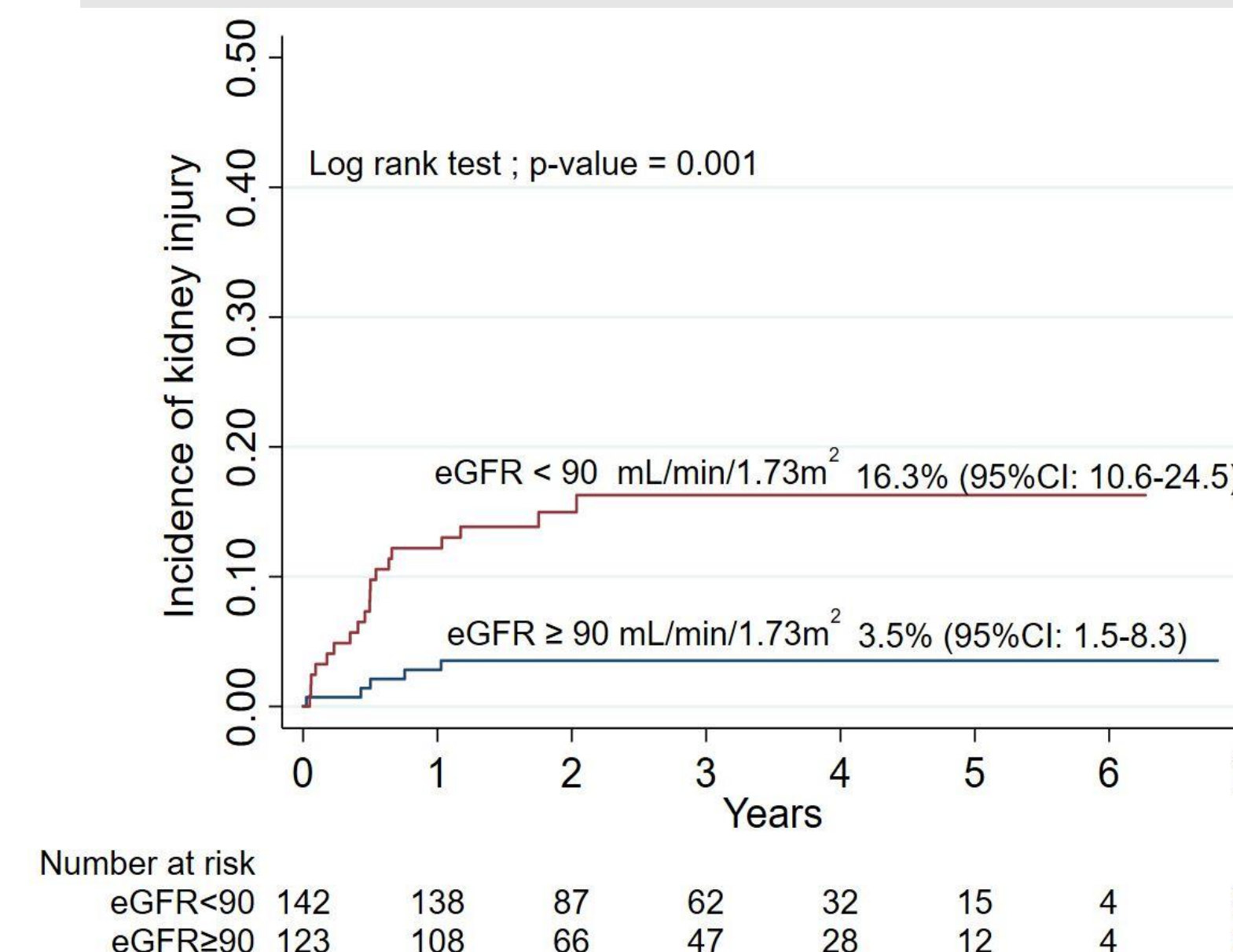
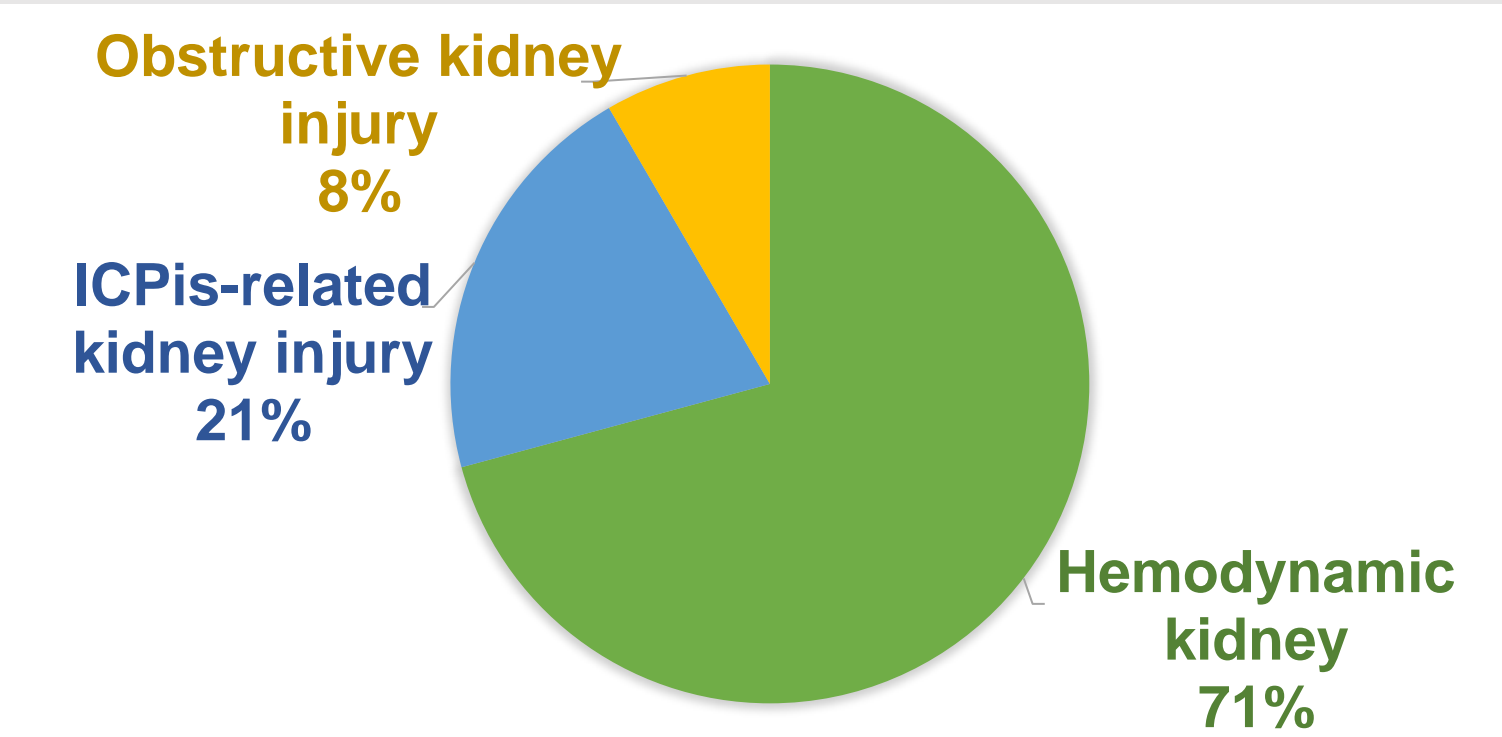


Figure 2: Etiology of kidney injury in patients receiving ICPis



CONCLUSION

- This study showed eGFR CKD-EPI < 90 min/mL/1.73m², diabetes mellitus, cerebrovascular disease, hepatocellular carcinoma, and concurrently used of antibiotics were significantly associated with a higher risk of kidney injury.
- Type of cancer and type of ICPis did not associate with kidney injury.
- Although kidney injuries were relatively rare irAEs; however, primary physicians, nephrologists, and oncologists should aware of this problem in patients receiving ICPis
- Kidney function needs to be monitored in high-risk patients receiving ICPis.

ACKNOWLEDGEMENT

- Excellence Chulalongkorn Comprehensive Cancer Center of the King Chulalongkorn Memorial Hospital, the Thai Red Cross Society
- Department of Internal Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand