





ORIGINAL ARTICLE

Association between eGFR and neurological outcomes among patients with out-of-hospital cardiac arrest: A nationwide prospective study in Japan

Kenji Kandori^{1,2}  | Asami Okada¹  | Satoshi Nakajima³ | Tasuku Matsuyama³  | Tetsuhisa Kitamura⁴  | Hiromichi Narumiya¹ | Ryoji Iizuka¹ | Masahito Hitosugi² | Yohei Okada^{5,6}

¹Department of Emergency and Critical Care Medicine, Japanese Red Cross Society, Kyoto Daini Hospital, Kyoto, Japan

²Department of Legal Medicine, Shiga University of Medical Science, Otsu, Shiga, Japan

³Department of Emergency Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan

⁴Division of Environmental Medicine and Population Sciences, Department of Social and Environmental Medicine, Graduate School of Medicine, Osaka University, Osaka, Japan

⁵Department of Preventive Services, Graduate School of Medicine, Kyoto University, Kyoto, Japan

⁶Health Services and Systems Research, Duke-NUS Medical School, National University of Singapore, Singapore

Correspondence

Kenji Kandori, Department of Emergency and Critical Care Medicine, Japanese Red Cross Society, Kyoto Daini Hospital, 355-5 Haruobi-cho Kamigyo-ku, Kyoto 602-8026, Japan. Email: knj.kandori@gmail.com

Funding information

Japan Society for the Promotion of Science, Grant/Award Number: JP22K21143; Zoll Foundation, Grant/Award Number: 2022

Abstract

Aim: We aimed to investigate the association between estimated glomerular filtration rate and prognosis in out-of-hospital cardiac arrest patients and explore the heterogeneity of the association.

Methods: Patients experiencing out-of-hospital cardiac arrest due to medical causes and registered in the JAAM-OHCA Registry between June 2014 and December 2019 were stratified into shockable rhythm, pulseless electrical activity, and asystole groups according to the cardiac rhythm at the scene. The primary outcome was a 1-month favorable neurological status. Adjusted odds ratios with 95% confidence intervals were calculated to investigate the association between estimated glomerular filtration rate and outcomes using a logistic model.

Results: Of the 19,443 patients included, 2769 had initial shockable rhythm at the scene, 5339 had pulseless electrical activity, and 11,335 had asystole. As the estimated glomerular filtration rate decreased, the adjusted odds ratio for a 1-month favorable neurological status decreased among those with initial shockable rhythm (estimated glomerular filtration rate, adjusted odds ratio [95% CI]: 45–59 mL/min/1.73 m², 0.61 [0.47–0.79]; 30–44 mL/min/1.73 m², 0.45 [0.32–0.62]; 15–29 mL/min/1.73 m², 0.35 [0.20–0.63]; and <15 mL/min/1.73 m², 0.14 [0.07–0.27]). Estimated glomerular filtration rate was associated with neurological outcomes in patients aged <65 years with initial shockable rhythm but not in those aged >65 years or patients with initial pulseless electrical activity or asystole.

Conclusion: The estimated glomerular filtration rate is associated with neurological prognosis in out-of-hospital cardiac arrest patients with initial shockable rhythm at the scene but not in those with initial non-shockable rhythm.

KEY WORDS

cardiac rhythm, comorbidity, estimated glomerular filtration rate, out-of-hospital cardiac arrest, renal dysfunction

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) is a serious public health concern owing to its low survival rate and potential for long-term neurological and functional disability. Many

patients with OHCA have comorbidities associated with a poor cardiac arrest (CA) prognosis.¹ However, quickly identifying them is difficult because OHCA patients often arrive at the hospital without sufficient medical records or their relatives provide insufficient information, making it challenging

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial](https://creativecommons.org/licenses/by-nc/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2024 The Authors. *Acute Medicine & Surgery* published by John Wiley & Sons Australia, Ltd on behalf of Japanese Association for Acute Medicine.

to decide whether to use advanced resuscitation techniques such as external cardiopulmonary resuscitation (ECPR).

Recently, renal dysfunction has been recognized as one of the most important comorbidities of many diseases, including hypertension and diabetes.² We expected estimated glomerular filtration rate (eGFR) as a good indicator of renal function and prognosis among OHCA patients because of its widespread use worldwide, availability relatively early in the emergency department, and ease of understanding. Previous studies targeting presumed cardiogenic OHCA patients revealed an association between eGFR and incidence of OHCA, and neurological outcomes.^{3,4} However, determining the cause of CA during resuscitation remains challenging, thus limiting the clinical applicability of such studies. Additionally, while cardiac rhythm is a dominant factor in characterizing the features of OHCA, it was not considered in the previous studies.⁵⁻⁷ Therefore, it would be necessary to analyze shockable and non-shockable rhythm separately, and we categorized patients based on initial rhythm to enhance clinical implications and interpretation. Moreover, since renal function declines with age, we hypothesized that the association between eGFR and outcomes would be heterogeneous among different age groups; however, few studies have investigated this heterogeneity. This study aimed to investigate the association between eGFR and prognosis in OHCA patients and explore the heterogeneity of the association.

METHODS

Study design and setting

This study was a secondary analysis of the Japanese Association for Acute Medicine OHCA Registry (JAAM-OHCA Registry), described previously.⁸ The JAAM-OHCA Registry is a nationwide, multicenter, prospective OHCA registry of pre- and in-hospital data from 93 medical institutions in Japan.

Study population

This study included adult patients aged ≥ 18 years who were in medical cause-related CA at the scene and were registered in the JAAM-OHCA Registry database between June 2014 and December 2019. We excluded patients who did not receive cardiopulmonary resuscitation (CPR) at the participating institutions, those who either refused to participate in the registry or their family members refused to register them, and those with missing data for eGFR calculation.

Data collection

Pre-hospital resuscitation data were collected from the All-Japan Utstein Registry of the Fire and Disaster Management

Agency, a prospective nationwide population-based registry of OHCA cases. "Initial cardiac rhythm at the scene" was defined as the first cardiac rhythm present when the monitor or defibrillator was attached to the patient. The JAAM-OHCA Registry collects additional patient information after hospital arrival. Blood samples were collected immediately after hospital arrival. Because there was no strict protocol for blood sampling, laboratory data were available only when the physicians requested blood tests. Therefore, the treating physicians were aware of all measured biomarker levels. "Cardiac rhythm at hospital arrival" was defined as the cardiac rhythm initially noted after hospital arrival. "Medical causes" were defined as causes of arrest other than external causes.

eGFR and classification

Internationally, the Cockcroft–Gault, Modification of Diet in Renal Disease Study, and Chronic Kidney Disease Epidemiology Collaboration Study equations are used to estimate eGFR²; however, since these equations tend to overestimate renal function in Japanese individuals, we used the Japanese Society of Nephrology eGFRcr formula to estimate GFR from serum creatinine level noted immediately after hospital arrival.⁹ Based on the modified National Kidney Foundation classification of chronic kidney disease (CKD), eGFR was categorized into five categories: ≥ 60 , 45–59, 30–44, 15–29, and < 15 mL/min/1.73 m².²

Outcome measures

The primary outcome was a favorable neurological status at 1 month after OHCA. A favorable neurological status was defined as a Glasgow-Pittsburgh cerebral performance category of 1 or 2.⁸ The secondary outcome was survival for at least 1 month after OHCA.

Selection of variables

Based on previous studies,⁵ the following five factors were considered as possible confounders: age, sex, presence of a witness, bystander CPR, and cardiac rhythm upon hospital arrival.

Statistical analysis

Data on patient characteristics are described as medians with interquartile ranges for continuous variables and as numbers with percentages for categorical variables. The associations of eGFR with a 1-month favorable neurological status and 1-month survival were investigated using multivariable logistic regression analyses, including all potential confounders. The adjusted odds ratios (AORs) and 95% confidence

intervals (CIs) were calculated. We also performed restricted cubic spline analysis with five knots (at the 5th, 25th, 50th, 75th, and 95th percentiles) to explore the nonlinear relationship between eGFR and a 1-month favorable neurological status, calculating odds ratios at each 1 mL/min/1.73 m² increment. An eGFR of 60 mL/min/1.73 m² was used as a reference. To enhance interpretability, we transformed these odds ratios into logarithmic values. In addition, subgroup analysis was conducted to determine whether differences in patient age affected the association between eGFR and a 1-month favorable neurological status. Patient age was divided into three groups ($\leq 64/65-74/\geq 75$ years). Missing data were not replaced or estimated. Data analyses were performed using R software (R Foundation for Statistical Computing, version 4.2.1; Saitama, Japan). All *p*-value analyses were two-sided and *p* < 0.05 was considered significant.

RESULTS

Patient characteristics

Of the 57,754 individuals enrolled in the JAAM-OHCA Registry, 19,443 were included, with 2769 (14.2%), 5339 (27.5%), and 11,335 (58.3%) patients categorized into the shockable rhythm, PEA, and asystole groups, respectively

(Figure 1). The patient characteristics are shown in Table 1 and Tables S1–S4.

Primary and secondary outcomes

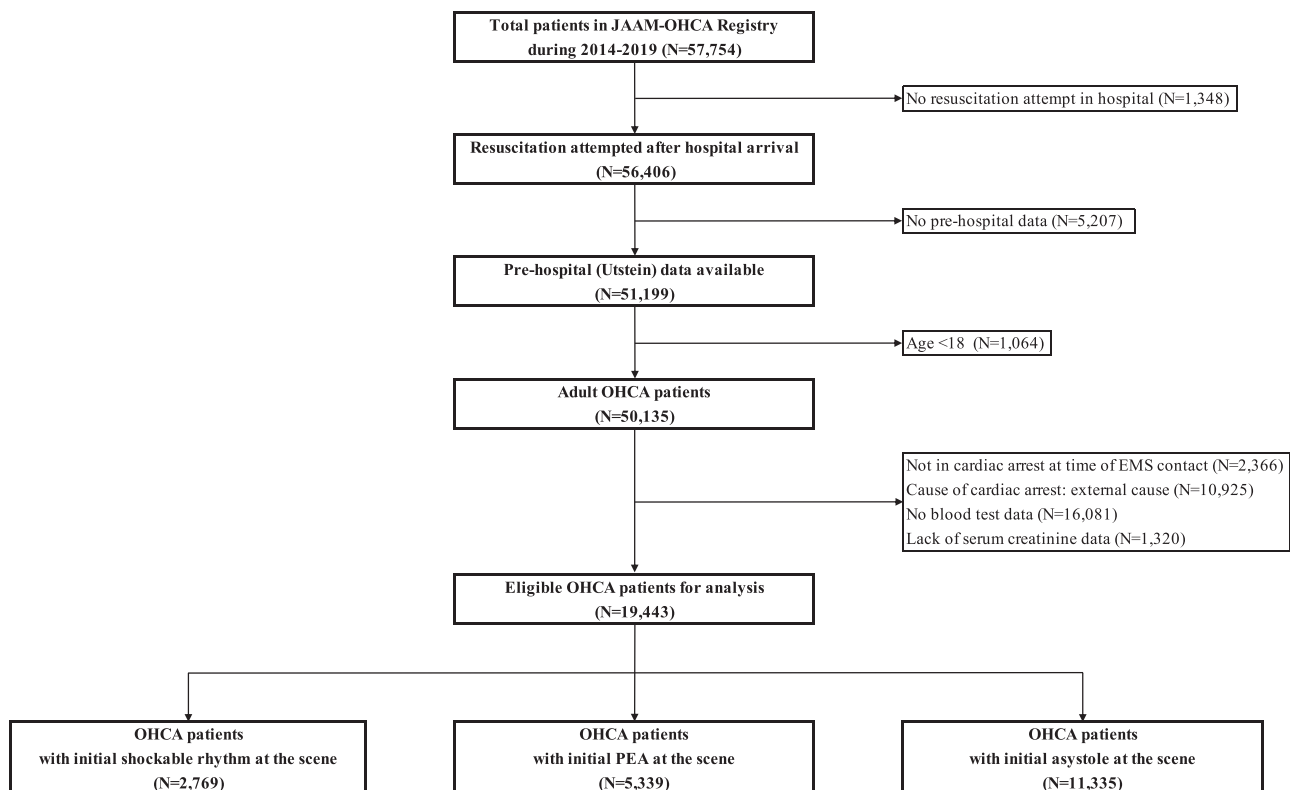
The proportions of patients who had a 1-month favorable neurological status and 1-month survival for each eGFR category are shown in Table 2.

Primary analysis

As eGFR decreased, the AOR of a 1-month favorable neurological status decreased among OHCA patients with initial shockable rhythm (Table 3). Similarly, the AORs for a 1-month favorable neurological status of patients with PEA and asystole are shown in Table 3.

In the restricted cubic spline analysis, patients with initial shockable rhythm showed a monotonically decreasing pattern, suggesting a poor neurological prognosis with lower eGFR levels when eGFR was below 60 (Figure 2A). For patients with PEA, a U-shaped association was observed in the eGFR below 60 range (Figure 2B). However, no significant association was found for patients with asystole (Figure 2C).

The AORs for 1-month survival are shown in Table S5.



EMS, emergency medical services; estimated glomerular filtration; JAAM, the Japanese Association for Acute Medicine; OHCA, out-of-hospital cardiac arrest; PEA, pulseless electrical activity.

FIGURE 1 Study flowchart.

TABLE 1 Demographics and characteristics, stratified by the first documented cardiac arrest rhythm at the scene.

Variables, number, (% or IQR)	First documented cardiac arrest rhythm at the scene							
	All patients		Shockable rhythm		PEA		Asystole	
	(N = 19,443)		(N = 2769)		(N = 5339)		(N = 11,335)	
Age, years	76	[65–85]	66	[53–75]	77	[66–85]	78	[68–86]
Age group, <i>n</i>								
18–64 years	4635	(23.8%)	1291	(46.6%)	1165	(21.8%)	2179	(19.2%)
65–74 years	4263	(21.9%)	782	(28.2%)	1190	(22.3%)	2291	(20.2%)
≥75 years	10,545	(54.2%)	696	(25.1%)	2984	(55.9%)	6865	(60.6%)
Sex, Male, <i>n</i>	12,010	(61.8%)	2236	(80.8%)	3219	(60.3%)	6555	(57.8%)
Cause of cardiac arrest, <i>n</i>								
Cardiac disease	12,982	(66.8%)	2601	(93.9%)	3084	(57.8%)	7297	(64.4%)
Cerebrovascular disease	960	(4.9%)	19	(0.7%)	366	(6.9%)	575	(5.1%)
Respiratory disease	1431	(7.4%)	25	(0.9%)	472	(8.8%)	934	(8.2%)
Malignant tumor	489	(2.5%)	13	(0.5%)	139	(2.6%)	337	(3.0%)
Others or unknown	3581	(18.4%)	111	(4.0%)	1278	(23.9%)	2192	(19.3%)
Pre-hospital information								
Witnessed arrest, <i>n</i>	9133	(47.0%)	2099	(75.8%)	3823	(71.6%)	3211	(28.3%)
Bystander CPR, <i>n</i>	9637	(49.6%)	1547	(55.9%)	2113	(39.6%)	5977	(52.7%)
Response time, min	7	[6–9]	7	[5–8]	7	[5–8]	7	[6–9]
Pre-hospital epinephrine administration, <i>n</i>	6341	(32.6%)	896	(32.4%)	2067	(38.7%)	3378	(29.8%)
Pre-hospital advanced airway management, <i>n</i>	10,792	(55.5%)	1328	(48.0%)	2945	(55.2%)	6519	(57.5%)
Call-to-hospital interval, min	33	[27–40]	31	[25–38]	33	[27–40]	33	[27–40]
In-hospital information								
First documented cardiac rhythm at hospital arrival, <i>n</i>								
Shockable rhythm	1251	(6.4%)	939	(33.9%)	147	(2.8%)	165	(1.5%)
PEA	4495	(23.1%)	560	(20.2%)	2540	(47.6%)	1395	(12.3%)
Asystole	11,725	(60.3%)	543	(19.6%)	1954	(36.6%)	9228	(81.4%)
ROSC	1972	(10.1%)	727	(26.3%)	698	(13.1%)	547	(4.8%)
eGFR at hospital arrival, mL/min/1.73 m ²	43.2	[28.1–56.9]	50.9	[40.5–61.4]	43.7	[29.6–57.6]	40.2	[25.3–54.5]
eGFR group, <i>n</i>								
0–14	2072	(10.7%)	150	(5.4%)	543	(10.2%)	1379	(12.2%)
15–29	3330	(17.1%)	179	(6.5%)	832	(15.6%)	2319	(20.5%)
30–44	5083	(26.1%)	625	(22.6%)	1452	(27.2%)	3006	(26.5%)
45–59	4944	(25.4%)	1052	(38.0%)	1367	(25.6%)	2525	(22.3%)
≥60	4014	(20.6%)	763	(27.6%)	1145	(21.4%)	2106	(18.6%)
Intervention, <i>n</i>								
VA-ECMO	1344	(6.9%)	908	(32.8%)	285	(5.3%)	151	(1.3%)
IABP	1134	(5.8%)	810	(29.3%)	195	(3.7%)	129	(1.1%)
CAG	2169	(11.2%)	1536	(55.5%)	388	(7.3%)	245	(2.2%)
PCI	1075	(5.5%)	807	(29.1%)	165	(3.1%)	103	(0.9%)
TTM	1687	(8.7%)	1079	(39.0%)	366	(6.9%)	242	(2.1%)
ROSC achieved at or after hospital arrival, <i>n</i>	7730	(39.8%)	1938	(70.0%)	2715	(50.9%)	3077	(27.1%)
Hospitalization, <i>n</i>	6108	(31.4%)	1982	(71.6%)	2080	(39.0%)	2046	(18.1%)
1-month survival, <i>n</i>	1755	(9.0%)	1113	(40.2%)	450	(8.4%)	192	(1.7%)
1-month favorable neurological status, <i>n</i>	989	(5.1%)	774	(28.0%)	176	(3.3%)	39	(0.3%)

Note: Values are presented as medians (IQR) or numbers (percentages).

Abbreviations: CAG, coronary angiography; CPR, cardiopulmonary resuscitation; eGFR, estimated glomerular filtration rate; IABP, intra-aortic balloon pumping; IQR, interquartile range; PCI, percutaneous coronary intervention; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; TTM, targeted temperature management; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

TABLE 2 Probabilities of 1-month favorable neurologic status and 1-month survival by the first documented cardiac arrest rhythm at the scene, stratified by the eGFR group.

Outcomes, n/N, (%)	eGFR at hospital arrival (mL/min/1.73 m ²)					
	All patients	0-14	15-29	30-44	45-59	≥60
First cardiac arrest rhythm at the scene						
1-month favorable neurological status						
Shockable rhythm	774/2769 (28.0)	14/150 (9.3)	23/179 (12.9)	108/625 (17.3)	293/1052 (27.9)	336/763 (44.0)
PEA	176/5339 (3.3)	23/543 (4.2)	15/832 (1.8)	40/1452 (2.8)	49/1367 (3.6)	49/1145 (4.3)
Asystole	39/11,335 (0.3)	4/1379 (0.3)	7/2319 (0.3)	10/3006 (0.3)	7/2525 (0.3)	11/2106 (0.5)
1-month survival						
Shockable rhythm	1113/2769 (40.2)	21/150 (14.0)	46/179 (25.7)	179/625 (28.6)	440/1052 (41.8)	427/763 (56.0)
PEA	450/5339 (8.4)	43/543 (7.9)	49/832 (5.9)	116/1452 (8.0)	126/1367 (9.2)	116/1145 (10.1)
Asystole	192/11,335 (1.7)	16/1379 (1.2)	25/2319 (1.1)	40/3006 (1.3)	48/2525 (1.9)	63/2106 (3.0)

Abbreviations: eGFR, estimated glomerular filtration rate; PEA, pulseless electrical activity.

TABLE 3 One-month favorable neurological status by eGFR group, stratified by the first documented CA rhythm at the scene.

eGFR at hospital arrival (mL/min/1.73 m ²)	First documented cardiac arrest rhythm at the scene					
	Shockable rhythm			PEA		
	n/N	(%)	AOR ^a	n/N	(%)	AOR ^a
0-14	14/150	(9.3)	0.14	23/543	(4.2)	1.35
15-29	23/179	(12.9)	0.35	15/832	(1.8)	0.70
30-44	108/625	(17.3)	0.45	40/1452	(2.8)	1.00
45-59	293/1052	(27.9)	0.61	49/1367	(3.6)	1.04
≥60	336/763	(44.0)	Reference	49/1145	(4.3)	Reference

Abbreviations: AOR, adjusted odds ratio; CA, cardiac arrest; CI, confidence interval; eGFR, estimated glomerular filtration rate; PEA, pulseless electrical activity.

^a Adjusted for confounding variables, including eGFR at hospital arrival, patient age, sex, presence of a witness, bystander cardiopulmonary resuscitation, and first documented cardiac rhythm at hospital arrival.

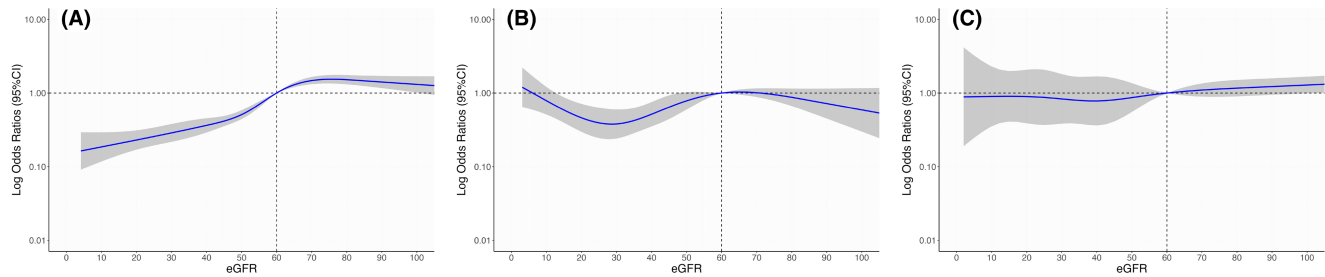


FIGURE 2 Adjusted restricted cubic spline analysis, per the first documented cardiac arrest rhythm at the scene.

Subgroup analysis

For OHCA patients younger than 65 years with shockable rhythm, the odds ratio of a 1-month favorable neurological status decreased as eGFR decreased (Table 4). For OHCA patients aged >65 years with initial shockable rhythm, the odds ratio significantly differed only between eGFR <15 mL/min/1.73 m² and eGFR ≥60 mL/min/1.73 m². Subgroup analysis by age showed that patients with initial PEA or asystole had poor neurological prognoses, regardless of eGFR (Tables S6 and S7).

DISCUSSION

Key observation

eGFR was associated with neurological outcomes among OHCA patients with initial shockable rhythm but not among those with non-shockable rhythm. Additionally, eGFR was associated with neurological outcomes among young OHCA patients with initial shockable rhythm but not among older patients.

Interpretation of the results

The prognoses of OHCA patients varied according to their eGFR when the initial CA rhythm at the scene was shockable, possibly because patients with initial shockable rhythm are highly likely to have reversible underlying causes and a cardiac origin for their arrest.⁶ Renal dysfunction is reportedly associated with a high incidence of cardiogenic CA and mortality.^{3,4} The relationship between renal dysfunction and neurological outcomes after CA might be explained by the mechanism of the brain's original vulnerability to ischemia, impaired cerebral autoregulation, and cardiovascular dysfunction in the presence of renal dysfunction. Renal dysfunction is associated with cerebral white matter lesions, which are ischemic lesions also linked to dementia and other disorders.¹⁰ This suggests that the brain with renal dysfunction might be more susceptible to ischemia. Additionally, the kidney and brain have similar microvascular bed characteristics, and both possess autoregulation to maintain blood flow

through myogenic responses. Considering this similarity, microvascular damage that causes renal dysfunction may also result in similar damage to the brain.¹⁰ In essence, the presence of renal dysfunction may reduce not only the myogenic autoregulation of the renal vasculature but also that of the cerebral vasculature, potentially leading to a direct relationship between cerebral blood flow (CBF) and cerebral perfusion pressure, which is dependent on the mean arterial pressure.¹¹ Moreover, since renal dysfunction is associated with cardiovascular dysfunction,¹² it could hinder the stabilization of hemodynamics after CA resuscitation. Consequently, coupled with impaired cerebral autoregulation, cerebral blood flow is reduced, leading to poor oxygenation of brain tissue and potentially irreversible damage to the brain, which is originally vulnerable to ischemia. Therefore, the lower the eGFR, the poorer the neurological prognosis when the initial rhythm at the scene is shockable, as observed in this study.

Subgroup analysis showed an association between eGFR and prognosis in patients younger than 65 years but not in those older than 65 years. This may be because although renal function, as assessed by eGFR, is preserved in older individuals, aging decreases renal function and changes the kidney structure.¹³ Renal tubules, which comprise more than 90% of the renal mass, are greatly affected by kidney aging because renal tubular cells exhibit more pronounced cellular senescence than other renal cells.¹³ In aging kidneys, the ability of renal tubular cells to regenerate after acute injury is significantly reduced, promoting fibrosis and maladaptive renal repair.¹³ In other words, although aging itself does not cause kidney disease, age-related structural and functional changes in the kidneys may predispose patients to kidney disease, and undoubtedly, kidney aging increases the susceptibility to AKI and CKD.¹³ Furthermore, older patients, even those with preserved renal function as assessed by eGFR, may have poor prognoses owing to the severe damage caused by CA itself, poor response to resuscitation, irreversible damage to organs including the brain, and low perseverance in post-resuscitation intensive care management.

Here, the prognosis differed based on eGFR when the initial CA rhythm at the scene was shockable; however, there was no association between eGFR and prognosis when the initial rhythm was PEA or asystole. The

TABLE 4 Subgroup analysis for a 1-month favorable neurological status in OHCA patients with initial shockable rhythm by eGFR group, stratified by age group.

eGFR at hospital arrival (mL/min/1.73 m ²)	Age group (years)											
	18–64			65–74			≥75					
	n/N	(%)	AOR ^a [95% CI]	n/N	(%)	AOR ^a [95% CI]	n/N	(%)	AOR ^a [95% CI]	n/N	(%)	AOR ^a [95% CI]
0–14	7/51	(13.7)	0.10 [0.04–0.28]	5/61	(8.2)	0.19 [0.06–0.56]	2/38	(5.3)	0.24 [0.05–1.23]			
15–29	2/29	(6.9)	0.09 [0.01–0.53]	10/53	(18.9)	0.59 [0.23–1.51]	11/97	(11.3)	0.51 [0.21–1.27]			
30–44	40/228	(17.5)	0.23 [0.14–0.39]	43/181	(23.8)	0.85 [0.47–1.54]	25/216	(11.6)	0.66 [0.32–1.34]			
45–59	154/499	(30.9)	0.50 [0.35–0.71]	91/329	(27.7)	0.75 [0.45–1.25]	48/224	(21.4)	0.97 [0.51–1.83]			
≥60	249/484	(51.4)	Reference	52/158	(32.9)	Reference	35/121	(28.9)	Reference			

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate.

^aAdjusted for confounding variables, including eGFR at hospital arrival, patient sex, presence of a witness, bystander cardiopulmonary resuscitation, and first documented cardiac rhythm at hospital arrival.

mechanism behind the U-shaped association observed in PEA through spline analysis remains unclear. It might be possible that patients with low eGFR levels, such as those below 30, routinely undergo medical interventions like dialysis or pharmacological therapy, which might contribute to better outcomes than those at the boundary region. Additionally, such patients might not be included in this registry due to either in-hospital CA or OHCA with a do-not-attempt-resuscitation directive. Subgroup analysis also revealed no association between eGFR and prognosis, regardless of age. In countries other than Japan, resuscitation may be discontinued when the initial rhythm is non-shockable or when an OHCA patient does not respond to resuscitation.⁶ Such patients would not be enrolled in the registry and would not be eligible for inclusion in the research. However, in Japan, most OHCA patients are resuscitated and transported to hospitals by the emergency medical services, and this registry enrolls almost all patients transported to participating hospitals. Therefore, we believe that the analysis of OHCA patients with initial non-shockable rhythm in this registry is more robust than that in previous studies. In patients who present with PEA or asystole at the scene, cardiac causes are uncommon, even after excluding obvious non-cardiac causes, such as trauma and primary respiratory failure, and likely to be irreversible.⁷ Therefore, we believe that PEA and asystole, with or without renal dysfunction, result in a poor neurological prognosis across all ages.

Clinical and research implications

eGFR, calculated from the creatinine level, maybe a practical predictor of prognosis in OHCA patients with initial shockable rhythm as it considers individual differences and can be used worldwide without specialized equipment. This is because, unlike lactate and pH levels, creatinine levels are not significantly affected by CA in the early post-CA period,¹⁴ making them a static surrogate biomarker for the pre-CA condition. Additionally, eGFR can be a valuable objective indicator for decision-making, especially when the patient's identity and medical history are unknown. In terms of prevention, we suggest raising awareness and preserving renal function among middle-aged individuals based on their eGFR, an easily understood index. Nevertheless, eGFR should not be used as an indicator for decision-making in OHCA patients with initial non-shockable rhythm.

Strengths

The unique aspect of this study is that it explored the association between renal function and prognosis in OHCA patients based on initial CA rhythm at the scene, considering the clinical applicability. The large sample size and subgroup

analysis by age are the other strengths. The finding that eGFR was not associated with neurological prognosis in the older age subgroup, even in patients with initial shockable rhythm, is novel and clinically relevant. Overall, the inclusion of a diverse patient population and the examination of subgroups make this study generalizable to clinical practice.

Limitations

The first limitation concerns the validity of the measurements, including the accuracy of cardiac rhythm analysis, lack of a protocol for the timing of blood sampling, lack of uniformity in laboratory equipment at each participating facility, and other factors that may have caused a measurement bias. Second, we were unable to determine each patient's medical history and pre-OHCA renal function. Third, potentially unmeasured confounders may have influenced our results. For example, the quality of daily living activities before OHCA and the quality of CPR may have affected our results. Fourth, it is possible that the outcome among OHCA patients with non-shockable rhythm was too poor to detect the association between renal function and prognosis. Fifth, this was a hospital-based cohort study and did not include all OHCA patients in Japan, which could have resulted in a selection bias. Moreover, the generalizability of these JAAM-OHCA registry-based results to countries outside Japan is unclear. Further studies are required to eliminate these potential biases.

CONCLUSIONS

This study found an association between eGFR and neurological prognosis in OHCA patients with initial shockable rhythm at the scene but not in those with initial PEA or asystole.

ACKNOWLEDGMENTS

We appreciate the contributions of all members of the JAAM-OHCA Registry group.

FUNDING INFORMATION

Author Y.O. was supported by grants from the ZOLL Foundation and overseas scholarships from the FUKUDA Foundation for Medical Technology and the International Medical Research Foundation. The funding for this study was provided by scientific research grants from the JSPS KAKENHI of Japan (JP22K21143 to YO) and from Zoll foundation (2022 to YO). The funding source had no role in the design, practice, or analysis of this study.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interests for this article.

DATA AVAILABILITY STATEMENT

The JAAM-OHCA Registry data are not publicly available because the ethics committee does not permit it.


ETHICS STATEMENT

The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. Ethics Committee of the Japanese Red Cross Society Kyoto Daini Hospital and each participating hospital, Approval No. S29-32. The requirement for consent was waived by the Ethics Committee of the Japanese Red Cross Society Kyoto Daini Hospital and each participating hospital.

ORCID

Kenji Kandori  <https://orcid.org/0000-0003-0026-7437>

Asami Okada  <https://orcid.org/0000-0001-8112-1397>

Tasuku Matsuyama  <https://orcid.org/0000-0003-4068-0306>

Tetsuhisa Kitamura  <https://orcid.org/0000-0003-0107-0580>

REFERENCES

- Andrew E, Nehme Z, Bernard S, Smith K. The influence of comorbidity on survival and long-term outcomes after out-of-hospital cardiac arrest. *Resuscitation*. 2017;110:42–7.
- Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function — measured and estimated glomerular filtration rate. *N Engl J Med*. 2006;354:2473–83.
- Lim HJ, Jeong J, Kim J, Ro YS, Shin SD. Effect of estimated glomerular filtration rate (eGFR) on incidence of out-of-hospital cardiac arrests: a case-control study. *Resuscitation*. 2019;142:38–45.
- Tamura T, Suzuki M, Hayashida K, Sasaki J, Yonemoto N, Sakurai A, et al. Renal function and outcome of out-of-hospital cardiac arrest - multicenter prospective study (SOS-KANTO 2012 study). *Circ J*. 2018;83:139–46.
- Kandori K, Okada Y, Okada A, Nakajima S, Okada N, Matsuyama T, et al. Association between cardiac rhythm conversion and neurological outcome among cardiac arrest patients with initial shockable rhythm: a nationwide prospective study in Japan. *Eur Heart J Acute Cardiovasc Care*. 2021;10:119–26.
- Havranek S, Fingrova Z, Rob D, Smalcova J, Kavalkova P, Franek O, et al. Initial rhythm and survival in refractory out-of-hospital cardiac arrest. Post-hoc analysis of the Prague OHCA randomized trial. *Resuscitation*. 2022;181:289–96.
- Kürkciyan I, Meron G, Sterz F, Domanovits H, Tobler K, Lagner AN, et al. Spontaneous subarachnoid haemorrhage as a cause of out-of-hospital cardiac arrest. *Resuscitation*. 2001;51:27–32.
- Kitamura T, Iwami T, Atsumi T, Endo T, Kanna T, Kuroda Y, et al. The profile of Japanese Association for Acute Medicine – out-of-hospital cardiac arrest registry in 2014–2015. *Acute Med Surg*. 2018;5:249–58.
- Matsuo S, Imai E, Horio M, Yasuda Y, Tomita K, Nitta K, et al. Revised equations for estimated GFR from serum creatinine in Japan. *Am J Kidney Dis*. 2009;53:982–92.
- Castro P, Azevedo E, Rocha I, Sorond F, Serrador JM. Chronic kidney disease and poor outcomes in ischemic stroke: is impaired cerebral autoregulation the missing link? *BMC Neurol*. 2018;18:21.
- Sundgreen C, Larsen FS, Herzog TM, Knudsen GM, Boesgaard S, Aldershvile J. Autoregulation of cerebral blood flow in patients resuscitated from cardiac arrest. *Stroke*. 2001;32:128–32.
- Ruilope LM, van Veldhuisen DJ, Ritz E, Luscher TF. Renal function: the Cinderella of cardiovascular risk profile. *J Am Coll Cardiol*. 2001;38:1782–7.
- Fang Y, Gong AY, Haller ST, Dworkin LD, Liu Z, Gong R. The ageing kidney: molecular mechanisms and clinical implications. *Ageing Res Rev*. 2020;63:101151.

14. Hang CC, Li CS, Wu CJ, Yang J. Acute kidney injury after cardiac arrest of ventricular fibrillation and asphyxiation swine model. *Am J Emerg Med.* 2014;32:208–15.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Kandori K, Okada A, Nakajima S, Matsuyama T, Kitamura T, Narumiya H, et al. Association between eGFR and neurological outcomes among patients with out-of-hospital cardiac arrest: A nationwide prospective study in Japan. *Acute Med Surg.* 2024;11:e952. <https://doi.org/10.1002/ams2.952>