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Clinical paper

Changes in the neurological status from 30 to 90 days post-cardiac arrest by age: A nationwide retrospective observational study

Hiromi Miyoshi, Mitsuaki Nishikimi, Kazuya Kikutani, Shinichiro Ohshimo, Nobuaki Shime*

Abstract

Introduction: Few studies have investigated the changes in the neurological status after 30 days post-arrest in out-of-hospital cardiac arrest (OHCA) patients according to the patient age. The aim of this study was to investigate the differences in the mid-term (from 30 days to 90 days) neurological changes after CA according to the age group.

Methods: We retrospectively analysed the data of all OHCA patients aged ≥1 year who showed return of spontaneous circulation and survived until 30 days after CA. We compared the proportions of patients who showed neurological deterioration from 30 to 90 days post-CA by age group (1–17, 18–39, 40–64, 65–79, ≥80 years). The neurological outcome was assessed by the Cerebral Performance Category (CPC) or Pediatric Cerebral Performance Category (PCPC) scale.

Results: Of the 68,110 registered patients, we analysed the data of a total of 2,663 patients. The neurological deterioration rate and improvement rate from 30 to 90 days after CA in each age group were as follows: 1–17 years: 11.6% (8/69)/7.2% (5/69); 18–39 years: 8.3% (15/181)/6.1% (11/181); 40–64 years: 7.3% (72/982)/7.0% (69/982); 65–79 years: 13.5% (130/965)/8.1% (78/965); and ≥ 80 years: 24.2% (113/466)/4.9% (23/466). Multivariable logistic regression analysis showed a higher likelihood of mid-term neurological deterioration in patients aged ≥ 80 years than in those aged 1–17 years.

Conclusions: Most OHCA patients, irrespective of age, showed no change of the neurological status from 30 to 90 days after OHCA. However, a relatively large percentage of patients aged ≥80 years old showed significant neurological deterioration after 30 days post-OHCA.

Keywords: Post-cardiac arrest syndrome, Neurological prognosis, Mid-term neurological changes, Age, Out-of-hospital cardiac arrest

Introduction

The consensus statement of the American Heart Association recommends that out-of-hospital cardiac arrest (OHCA) patients be followed up for no less than 90 days to allow for a more precise assessment of the neurological outcomes after CA,[1] because most cognitive recovery occurs during the first 90 days.[2–3] But in actual clinical practice, assessment before 90 days post-cardiac arrest (post-CA), such as at 30 days, is rather common, because cardiac arrest patients are usually transferred out to a second hospital at around 30 days. However, as the choice of the second hospital could be substantially influenced by the potential for further neurological recovery in the patients, it is important to explore factors which could significantly influence the possibility of further changes of the neurological status after 30 days post-CA.

Patient age is one of the most important candidate variables that can influence changes of the neurological status after 30 days post-CA. For example, elderly OHCA patients may be at a higher risk of progressive cognitive decline even if they survive until 30 days post-CA.[4] Also, the capacity for compensation might be greater at a younger age, and it is easy to conceive why the probability of mid- to long-term neurological recovery after brain injury can vary with age. In fact, a previous study reported that only 7% of adult OHCA patients showed improvement in the Cerebral Performance Category (CPC) score between 30 and 90 days,[5] while another study

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reported that 16.6% of pediatric OHCA patients showed neurological improvement until several years after CA.[6] In the field of traumatic brain injury (TBI), advancing age has been reported as exerting a significant negative influence on the changes of the neurological outcomes post-TBI.[7] However, no studies to date have compared the changes in the neurological status after 30 days post-CA by age group in OHCA patients. Therefore, the aim of this study was to investigate the differences in the mid-term (from 30 days to 90 days) neurological changes after CA and to compare the proportions of patients who showed neurological deterioration from 30 to 90 days post-CA by age group.

Materials and methods

Study design

This study was conducted using data from the OHCA registry of the Japanese Association for Acute Medicine (JAAM), a nationwide, prospective registry of OHCA patients transported to critical care medical centres or hospitals with an emergency care department across Japan (137 institutions). The design and data collection methods used in the JAAM-OHCA registry have been described in detail previously.[8] Briefly, emergency medical service personnel collect prehospital data based on the Utstein-style template,[9] and physicians at the participating institutions collect in-hospital data, including the presumed aetiology of the OHCA and data on the patients' treatments and outcomes. We included the data of OHCA patients registered in the database between June 1, 2014, and December 31, 2020, for this study. The study was conducted with the approval of the Institutional Review Boards of all the participating institutions, which waived the requirement for obtaining of informed consent from the study participants so as to ensure participant anonymity as stipulated in the Japanese government guidelines. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement for this study (Supplementary Table 1).

Population

OHCA patients from the JAAM-OHCA registry who had the potential at 30 days for further changes of the neurological outcome, namely, patients with CPC scores of 1–4 or Pediatric Cerebral Performance Category (PCPC) scores of 1–5, were included. Patients for whom the neurological outcome data at either 30 or 90 days were not available were excluded. Patients under 1 year old were also excluded due to their different clinical profiles, namely, the cause of cardiac arrest is almost always non-cardiac cause in this age group (in fact, there was no patient aged less than 1 year old who showed a shockable initial rhythm in the database).

Outcome measurement

The primary outcome was change of the neurological status, defined as a decrease or increase of the CPC score by $\geq$ 1 point in patients aged $\geq$ 18 years old or of the PCPC score by $\geq$ 1 point in patients aged 1–17 years old, from 30 to 90 days post-CA. The CPC or PCPC scores of the survivors recorded in our database were based on evaluation by the medical staff at each institution. Our database did not mandate follow-up on the outcomes by telephone. As a quality control measure, if the data form of the registry was incomplete, the registry committee, composed of specialists in emergency medicine and epidemiology, returned the form to the respective institutions with a request that the form be filled as completely as possible.

Statistical analysis

Categorical variables were compared using the Chi-squared test, and continuous variables using Student's *t*-test. We evaluated the proportion of patients in each age category (1–17 years [children and adolescents], 18–39 years [young adults], 40–64 years [middle-aged adults], 65–79 years [older adults], $\geq$80 years [elderly]) who showed deterioration of the CPC or PCPC score between 30 and 90 days post-CA. Multivariable logistic regression analysis with adjustments for 7 variables (sex,[10] presence/absence of witness,[11] presence/absence of emergency medical service (EMS) witness,[12] presence/absence of bystander chest compressions,[13] initial rhythm,[14] percutaneous coronary intervention (PCI),[15] targeted temperature management (TTM)[16] was performed to evaluate the association between the age category and neurological improvement over the mid-term. The seven variables have been identified in previous studies as potentially exerting a significant influence on the neurological outcome in post cardiac arrest syndrome (PCAS) patients. To evaluate the association between the age and neurological deterioration from 30 to 90 days after OHCA more closely, we plotted an adjusted spline curve demonstrating how the estimated logarithm of the odds ratio for deterioration of the neurological outcome varied depending on the age. As a subgroup analysis, we also plotted another adjusted spline curve only for patients with a cardiac cause of the cardiac arrest or only for patients with a non-cardiac cause of the cardiac arrest. All the reported P values were two-sided, and $p < 0.05$ was regarded as denoting a statistically significant difference. All analyses were conducted using the JMP pro, version 17.0.0. (SAS Institute Inc., Cary, NC).[17–18]

Results

Among the 68,110 OHCA patients registered in the JAAM-OHCA registry between June 2014 and December 2020, the data of 7,761 patients were not in conformity with the Utstein template, 40,164 cases did not achieve ROSC, and 15,887 died within 30 days. Of the remaining 4,298 patients, 1,635 were excluded because they were <1 year old (n = 31) or there was no information available on the outcome (n = 1,604). Finally, the data of a total of 2,663 patients were analysed in this study (Fig. 1). The baseline characteristics of the patients with and without data on the 90-day outcomes are summarised in Supplementary Table 2. The age (in years) distribution in the study population was as follows: 1–17 years (n = 69); 18–39 years (n = 181); 40–64 years (n = 982); 65–79 years (n = 965); and $\geq$ 80 years (n = 466). The baseline characteristics of the analysed patients divided into five age categories are shown in Table 1.

The CPC and PCPC scores at 30 and 90 days, both overall and by age group, are shown in Table 2. The percentages (number) of patients in the different age groups who showed neurological deterioration/neurological improvement from 30 to 90 days after CA were as follows: 1–17 years: 11.6% (8/69)/7.2% (5/69); 18–39 years: 8.3% (15/181)/6.1% (11/181); 40–64 years: 7.3% (72/982)/7.0% (69/982); 65–79 years: 13.5% (130/965)/8.1% (78/965); $\geq$80 years: 24.2% (113/466)/4.9% (23/466). The summary of the percentages of patients who showed mid-term changes of the neurological status is shown by the 30-day CPC score category and age group in Fig. 2. In the majority of patients, irrespective of the age group, the CPC or PCPC scores remained unchanged from 30 days to 90 days. The results of multivariable logistic regression analysis indicated a lower likelihood of mid-term neurological deterioration in patients

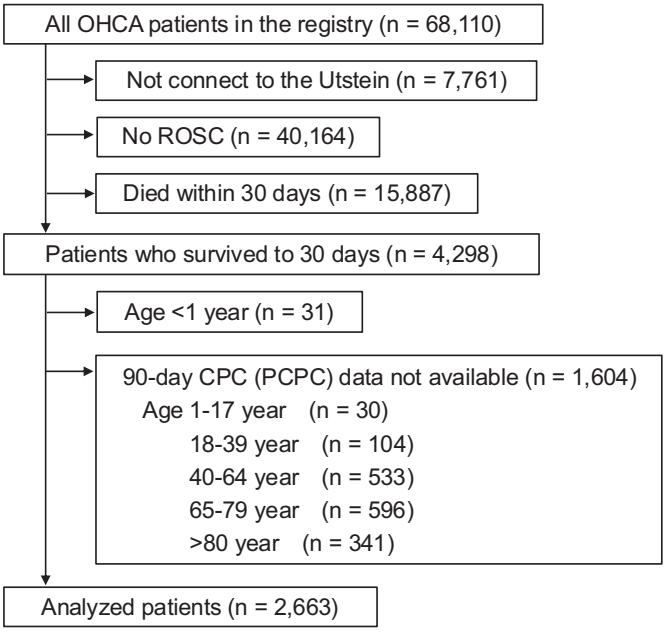

Fig. 1 – Flow diagram of patients. OHCA = out-of-hospital cardiac arrest; ROSC = return of spontaneous circulation; CPC = Cerebral Performance Category; PCPC = Pediatric Cerebral Performance Category.

aged 1–79 years old (odds ratio [OR]: 1–17 years: 0.49 [0.22–1.08], p = 0.077; 18–39 years: OR, 0.39 [0.22–0.71], p = 0.002; 40–64 years: OR, 0.40 [0.28–0.57], p < 0.001; and 65–79 years: OR, 0.69 [0.51–3.11], p = 0.016) than in those ≥ 80 years old (Table 3).

We also plotted the adjusted spline curve depicting the correlation between the age and likelihood of neurological improvement over the mid-term, which showed that patients aged ≥ 80 years had a higher probability of neurological deterioration after 30 days post-CA as compared with younger patients (sFig. 2A). On the other hand, the neurological status in patients aged 1–17 years was not expected to improve as much as that in other adult OHCA patients. A similar trend was observed in the adjusted spline curve plotted only for patients with a cardiac cause of the cardiac arrest and only for those with a non-cardiac cause of the cardiac arrest (sFig. 2B and C). The baseline characteristics of these patients are summarised in Supplementary Table 3 and 4, respectively.

Discussion

In this observational study, while the majority of patients, irrespective of the age group, showed no changes of the CPC or PCPC scores from 30 to 90 days after OHCA, older OHCA patients aged ≥ 80 years showed a significantly higher likelihood of neurological deterioration over this period. The adjusted spline curve revealed that while young to older adults showed a progressively higher likelihood of mid-term neurological deterioration with increasing age, patients aged 1–17 years tended to show a higher likelihood of mid-term neurologic improvement with increasing age.

Our study identified advancing age, excluding patients aged <18 years, as an important clinical factor associated with an increased probability of neurological deterioration between 30 and 90 days after OHCA. One potential mechanism that could explain this finding is the higher risk of co-existence of dementia in OHCA patients of more advanced ages. A previous study reported that CA survivors were more likely to develop dementia after hospital discharge as compared with the general population.[19] Because advanced age and the risk of dementia are known to be closely associated,[20] it is quite conceivable that older OHCA patients are more likely to show functional decline during the mid-term post-OHCA because of the higher risk of co-existence of dementia. Our data suggest that we may have to take the risk of functional decline in older patients into consideration when predicting further changes in the neurological status at 30 days post-OHCA. A future study is warranted to investigate the relationship between functional decline over the mid-term post-OHCA and co-existence of dementia.

On the other hand, younger OHCA patients showed a lower risk for deterioration of the neurological status over the mid-term post-CA. Several studies have suggested that early follow-up, screening, and intervention, including rehabilitation, for post-CA patients can potentially improve the probability of neurological recovery over the long term.[21–23] Younger patients may be more responsive to these interventions. It would be of great interest to investigate the effects of early interventions, such as cognitive rehabilitation, focusing on younger patients, who may have a higher probability of neurological recovery.

A possible reason for the lower likelihood of improvement of the neurological status among patients aged 1–17 years is that this group might have a relatively higher proportion of patients with severe brain injury, making neurological improvement less likely. In pediatric cardiac arrest patients, the decision to withhold or terminate treatment is often challenging, even if the probability of a good neurological outcome is low [24]. This may delay the decision to withhold or terminate treatment, leading to more survivors with such poor neurological outcome at 30 days in whom further neurological outcome improvement cannot be expected. Our data may suggest the importance of establishing a consensus to guide medical providers and family members in joint decision-making about the future treatment options available to OHCA patients, including withholding or termination of treatment. However, since our study was a retrospective study

Table 1 – Baseline characteristics of patients. Data are presented as absolute frequencies with percentages.

		Age categories				
	Total	1–17 yr	18–39 yr	40–64 yr	65–79 yr	80 yr-
Variable	n = 2663	n = 69	n = 181	n = 982	n = 965	n = 466
Sex, female, n (%)	737 (27.7)	18 (26.1)	59 (32.6)	206 (21.0)	240 (24.9)	214 (45.9)
Witness, n (%)	2182 (81.9)	49 (71.0)	143 (79.0)	809 (82.4)	803 (83.2)	378 (81.1)
Witness by EMS, n (%)	457 (17.2)	5 (7.2)	18 (9.9)	160 (16.3)	190 (19.7)	84 (18.0)
Chest compression by bystander, n (%)	1322 (49.6)	44 (63.8)	101 (55.8)	519 (52.9)	454 (47.0)	204 (43.8)
Non-cardiac cause CA, n (%)	590 (22.2)	30 (43.5)	49 (27.1)	135 (13.7)	188 (19.5)	188 (40.3)
Initial rhythm, n (%)						
Shockable	1202 (45.1)	18 (26.1)	109 (60.2)	542 (55.2)	436 (45.2)	97 (20.8)
Non-shockable	987 (37.1)	30 (43.5)	50 (27.6)	257 (26.2)	351 (36.4)	299 (64.2)
Unknown	474 (17.8)	21 (30.4)	22 (12.2)	183 (18.6)	178 (18.4)	70 (15.0)
PCI, n (%)	712 (26.7)	0 (0)	10 (5.5)	339 (34.5)	302 (31.3)	61 (13.1)
TTM, n (%)	1255 (47.1)	29 (42.0)	121 (66.9)	541 (55.1)	444 (46.0)	120 (25.8)
90-day survival, n (%)	2369 (89.0)	64 (92.8)	167 (92.3)	917 (93.4)	852 (88.3)	369 (79.2)
30-day good neurological outcome (CPC $\leq$ 2 or PCPC $\leq$ 2), n (%)*	1533 (57.6)	30 (43.5)	131 (72.4)	686 (69.9)	535 (55.4)	151 (32.4)
90-day good neurological outcome (CPC $\leq$ 2 or PCPC $\leq$ 2), n (%)*	1547 (58.1)	32 (46.4)	131 (72.4)	684 (69.7)	549 (56.9)	151 (32.4)
90-day CPC (PCPC) scores improved, n (%)	186 (7.0)	5 (7.2)	11 (6.1)	69 (7.0)	78 (8.1)	23 (4.9)
90-day CPC (PCPC) scores worsened, n (%)	338 (12.7)	8 (11.6)	15 (8.3)	72 (7.3)	130 (13.5)	113 (24.2)

EMS; emergency medical services, CA; cardiac arrest, PCI; percutaneous coronary intervention, TTM; target temperature management, CPC; Cerebral Performance Category, PCPC; Pediatric Cerebral Performance Category.

There is no missing value.

* CPC1/PCPC1 and CPC2/PCPC2 are considered as representing a good neurological outcome.

Table 2 – CPC or PCPC scores at 30 and 90 days overall and by age group. Data are presented as absolute frequencies with percentages.

	All patients	1–17 yr	18–39 yr	40–64 yr	65–79 yr	80 yr-
Variable	n = 2663	n = 69	n = 181	n = 982	n = 965	n = 466
30 days neurological outcome						
CPC/PCPC 1	1214 (45.6)	24 (34.8)	112 (61.9)	581 (59.2)	400 (41.5)	97 (20.8)
CPC/PCPC 2	319 (12.0)	6 (8.7)	19 (10.5)	105 (10.7)	135 (14.0)	54 (11.6)
CPC/PCPC 3	424 (15.9)	7 (10.1)	14 (7.7)	121 (12.3)	177 (18.3)	105 (22.5)
CPC/PCPC 4	689 (25.9)	15 (21.7)	36 (19.9)	175 (17.8)	253 (26.2)	210 (45.1)
PCPC 5	17 (0.6)	17 (24.6)	–	–	–	–
90 days neurological outcome						
CPC/PCPC 1	1309 (49.2)	26 (37.7)	120 (66.3)	612 (62.3)	443 (45.9)	108 (23.2)
CPC/PCPC 2	238 (8.9)	6 (8.7)	11 (6.1)	72 (7.3)	106 (11.0)	43 (9.2)
CPC/PCPC 3	314 (11.8)	4 (5.8)	13 (7.2)	101 (10.3)	121 (12.5)	75 (16.1)
CPC/PCPC 4	497 (18.7)	12 (17.4)	24 (13.3)	133 (13.5)	183 (19.0)	145 (31.3)
CPC/PCPC 5	300 (11.3)	16 (23.2)	13 (7.2)	64 (6.5)	112 (11.6)	95 (20.4)
PCPC 6	5 (0.2)	5 (7.2)	–	–	–	–

CPC; Cerebral Performance Category, PCPC; Pediatric Cerebral Performance Category.

There is no missing value.

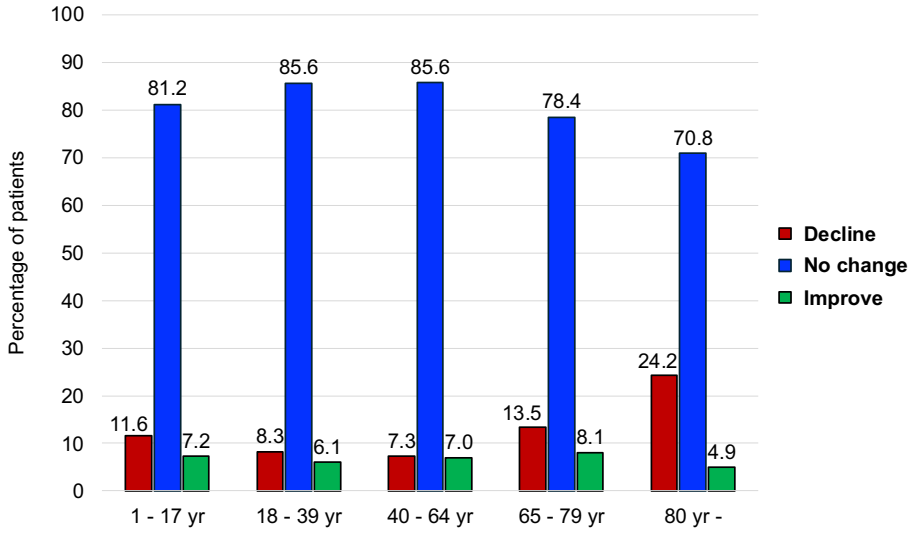

Fig. 2 – Change in the CPC or PCPC scores from 30 to 90 days post-OHCA in different age groups. The graph shows the percentages of patients in each age category in whom the CPC or PCPC score changed from 30 to 90 days after OHCA. Patients with declined scores are shown in red, those with no change of the score in blue, and those with improved scores in green. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 3 – Multivariable regression analysis for 30- to 90-day CPC(PCPC) deterioration.

Variables	OR (95%CI)	P
Age		
1–17 yr	0.49 (0.22–1.08)	0.077
18–39 yr	0.39 (0.22–0.71)	0.002
40–64 yr	0.40 (0.28–0.57)	< 0.001
65–79 yr	0.69 (0.51–3.11)	0.016
80 yr-	Reference	
Sex, female	1.10 (0.85–1.42)	0.465
Witness	0.92 (0.68–1.26)	0.616
EMS-Witness	0.85 (0.60–1.22)	0.388
Chest compression by bystander	0.71 (0.55–0.93)	0.012
Initial rhythm		
Shockable	Reference	
Non-shockable	2.71 (2.00–3.69)	<0.001
Unknown	1.05 (0.68–1.63)	0.828
PCI	0.57 (0.40–0.82)	0.003
TTM	0.99 (0.76–1.28)	0.934

Abbreviations: PCI, percutaneous coronary intervention; TTM, targeted temperature management; OR, odds ratio; 95% CI, 95% confidence interval.

conducted in a single country, further prospective studies conducted in different regions of the world or global studies are needed to validate our findings.

The results of our multivariable regression analysis identified bystander CPR as being associated with a decreased OR for neurological status deterioration from 30 to 90 days. This result may highlight the importance of bystander CPR. However further study is needed to validate this notion.

There were some limitations of this study. First, it was an observational study, and we could not completely exclude selection bias. We excluded 37% (1,604/4,298) of patients from our analysis because of missing 90-day outcome data; the percentage of patients excluded for this reason was especially high in the ≥ 80 years age group (42.3% [341/807]), which could have influenced our results. We identified that patients with missing 90-day outcome data tended to show poorer outcomes (as shown in Supplementary Table 2); our findings should be confirmed in a large-scale prospective study. Second, in the present study, we used the CPC or PCPC scales to evaluate the neurological outcomes of OHCA patients. These scores are known to be reliable to evaluate the overall brain function, but do not include items specific for cognitive or memory functions. The proportions of patients showing a favourable neurological outcome post-OHCA are known to differ according to the scales used to evaluate the neurological outcome.[25] Third, the lack of discrimination by using CPC or PCPC scales and the ceiling effect are also limitation of our study.[26] Fourth, variations in the EMS resuscitation rates between Japan and other countries could have influenced our results. In fact, the percentage of patients with a favourable neurological outcome

after OHCA appears to be moderately higher in Japan as compared with that reported from other countries [27]. Finally, although no studies have been conducted to investigate the differences in post-discharge care for OHCA patients between Japan and other countries, post-discharge care could exert an influence on the changes of the neurological status of OHCA patients from 30 to 90 days post-OHCA.

Conclusion

We have reported the proportions of patients showing changes of the neurological status from 30 to 90 days post-CA by age group. Patients aged ≥80 years old showed a higher likelihood of significant neurological deterioration after 30 days post-CA. Most OHCA patients, irrespective of age, showed no change of the neurological status from 30 to 90 days after OHCA. However, a relatively large percentage of patients aged ≥80 years old showed significant neurological deterioration after 30 days post-OHCA.

CRediT authorship contribution statement

Hiromi Miyoshi: Writing – original draft, Conceptualization. **Mitsuaki Nishikimi:** Writing – original draft, Formal analysis, Data curation, Conceptualization. **Kazuya Kikutani:** Investigation. **Shinichiro Ohshimo:** Writing – review & editing, Data curation. **Nobuaki Shime:** Writing – review & editing, Supervision, Data curation.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resplu.2025.100917.

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