

## Comparison of Two Different Intensive Care Unit Systems for Severely Ill Children in Japan: Data from the JaRPAC Registry

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The importance of centralizing treatment services for severely ill children has been well established, but such centralization remains difficult in Japan. We aimed to compare the trauma and illness severity and mortality of children admitted to two common types of ICUs for children. According to the type of management and disposition of the medical provider, we classified ICUs as pediatric ICUs [PICUs] or general ICUs, and analyzed differences in endogenous and exogenous illness settings between them. Overall, 1,333 pediatric patients were included, with 1,143 patients admitted to PICUs and 190 patients to general ICUs. The Pediatric Cerebral Performance Category score (PCPC) at discharge was significantly lower in the PICU group (adjusted OR: 0.45; 95%CI: 0.23-0.88). Death and unfavorable neurological outcomes occurred less often in the PICU group (adjusted OR: 0.29; 95%CI: 0.14-0.60). However, when limited to exogenous illness, PCPC scores (adjusted OR: 0.38; 95%CI: 0.07-1.99) or death/unfavorable outcomes (adjusted OR: 0.72; 95%CI: 0.08-6.34) did not differ between the groups. PCPC deterioration and overall sequelae/death rates were lower in PICUs for children with endogenous illnesses, although the outcomes of exogenous illness were similar between the 2 unit types. Further studies on the necessity of centralization are warranted.

**Key words:** kids, critical care, mortality, morbidity, centralization

The arrangement of emergency health care systems for children is an important consideration throughout the world. Many countries or regions develop systems specialized for or experienced in pediatric healthcare [1-3]. The importance of centralizing health care for severely ill children has been well established. Pearson *et al.* reported on the importance of centralizing health care for severely ill children, demonstrating substantial reductions in mortality by centralizing pediatric admission to large specialized pediatric intensive care units (PICUs) [2]. However,

centralizing care for severely ill children remains difficult in many regions, partly due to the small incidence of critically ill children. In Japan, mortality among patients aged < 18 was reported to account for 0.3% of all patient mortality. Similarly, critically ill children comprise only 2.2% of all transports of patients under the age of 18 <[https://www.fdma.go.jp/publication/rescue/items/kkkkg\\_h30\\_01\\_kyukyu.pdf](https://www.fdma.go.jp/publication/rescue/items/kkkkg_h30_01_kyukyu.pdf)>(accessed March, 2020). The Japanese transport system for ill children has not been sufficiently developed to permit the centralization of all severe cases, except in some areas in very large cities. A 2004 report showed that

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mortality for 1- to 4-year-old ill children was higher in Japan than in the US and Australia [4], suggesting the need for a centralized PICU system. However, data showing the efficacy of centralization in the Japanese ICU system are still lacking.

Twenty-four-hour pediatric critical care in-hospital physician coverage has been associated with shorter ICU stay in the US [5], demonstrating the need for pediatricians in the ICU or a specialized PICU. In Europe, there are 2.5 PICU beds per 100,000 child population [6]. In general, the number of Japanese ICU beds for children appears to be lower, but is not precisely known. Government grants can be obtained to promote the installation of specialized PICUs; nevertheless, the effect of such financial support is limited [3]. Presumably due to the lack of PICU beds in many Japanese districts, children with exogenous illnesses, especially those with trauma, are traditionally treated by non-pediatricians, such as emergency physicians, surgeons, or anesthesiologists in the general ICU or emergency ICU. On the other hand, severely ill children with endogenous illnesses are often treated by pediatricians at PICUs or general wards. The advantages of PICUs with around-the-clock pediatrician coverage over general ICUs in Japan have not been elucidated.

In this study, we aimed to compare the trauma and illness severity and mortality of children admitted to two different types of ICUs, PICUs and general ICUs, in both endogenous and exogenous illness settings in Japan.

## Methods

The study was approved by the Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences Institutional Review Board (Eki 853).

**Overview of the Japanese Registry of Pediatric Acute Care (JaRPAC).** JaRPAC is an observational, multicenter, prospective database that contains information about pediatric patients consecutively admitted to ICUs in Japan. The registry, led by the pediatric committee of the Japanese Society for Emergency Medicine ([www.jarpac.org](http://www.jarpac.org)), was started on October 1st, 2013. The JaRPAC includes data on patients admitted to ICUs or who died in emergency rooms. Patients in children's hospitals are all registered regardless of age, while those at other hospitals are registered

if they are under 16 years old. Subject data is collected; 23 variables are documented at ICU admission and 27 are documented at ICU discharge, including information on demographics, pre-hospital management, treatments, predictive death rate, and outcomes. Details of the registry have been described previously [7].

**Data collection.** Our inclusion criteria were patients under 16 years old treated at the ICU from January 2014 to December 2015. Exclusion criteria were patients with a Pediatric Cerebral Performance Category score (PCPC)  $\geq 2$  before admission and patients whose admission sources were operating rooms. The following variables were obtained from the data: sex, age in months, type of ICU (PICU/general ICU), admission shift time, source of ICU admission, disease category (endogenous/exogenous), Pediatric Index of Mortality 2 (PIM2) [8], and PCPC [9] before admission to and at discharge from the ICU. Injury Severity Score (ISS) and Trauma and Injury Severity Score (TRISS) [10] were obtained to predict the mortality for patients with trauma. The JaRPAC codifies admission sources into 5 categories: emergency departments; other hospitals; operating rooms; wards; and others. Allowable values for admission shift time in the JaRPAC are defined using four categories: weekdays daytime; weekdays nighttime, holidays daytime, and holidays nighttime.

**Measures.** According to the type of management and disposition of the medical provider, we classified the ICUs into 2 types: PICUs and general ICUs. Specifically, we defined the two types of ICUs as follows: PICU = the ICU of a hospital that generally treats ill children under 16 years old, general ICU = the ICU of a hospital that admits both adults and children. We analyzed differences in both endogenous and exogenous illness settings between the PICUs and general ICUs. The primary outcome was worsening of neurological status, defined as an increase in PCPC. The secondary outcome was death, and sequelae were defined as the total number of patients with PCPC  $\geq 3$  at discharge or death.

**Statistical analysis.** Continuous variables are described using means and standard deviations (SD). Categorical variables are described using percentages. We performed univariable logistic regression for comparison between groups. Then we conducted a multivariable logistic regression using the primary and secondary outcomes as dependent variables and age,

gender, admission year, admission shift time, admission source, and severity as independent variables. Results of multivariable logistic regressions were expressed using odds ratios (ORs) with 95% confidence intervals (CIs). Stata SE version 15 (StataCorp, College Station, TX, USA) was used for all analyses.

## Results

A total of 3,478 patients were admitted during the study period. After excluding patients aged > 16 years of age (n=199), those with PCPC scores  $\geq 2$  (n=1,077), and patients admitted to the ICU for elective surgery (n=869), 1,333 patients were enrolled in the final analysis (Figure 1), with 1,143 of these patients admitted to PICUs and 190 patients to general ICUs.

Patient characteristics are shown in Table 1. Patient age was higher in the general ICU group (PICU: 3.5 years old; general ICU: 5.2 years old); and the general ICU group had a higher proportion of exogenous illnesses (PICU: 16.6%; general ICU: 41.6%). There were more admissions on weekdays compared with weekend days or holidays in both groups (weekdays: PICU 69.8%, general ICU 73.6%; weekend days or holidays: PICU 30.3%, general ICU 26.4%). The proportion of emergency admissions was higher in the general ICU group (PICU: 36.1%; general ICU: 58.4%). PIM2 scores were higher in the general ICU group (PICU: 5.3; general ICU: 7.7); however, the proportions of patients with PIM2  $\geq 20$  were similar (PICU: 6.3%; general ICU: 6.3%). Severity scores for

trauma (predicted mortality using TRISS) were higher in the PICU groups (PICU: 7.9%; ICU: 2.2%); the proportion of patients with predicted mortality  $\geq 10\%$  was higher in the PICU group (PICU: 13.9%; general ICU: 3.0%).

Table 2 shows a comparison of overall outcomes for the 2 types of ICUs in multivariable logistic regression. PCPC at discharge was significantly lower in the PICU group (adjusted OR: 0.45; 95% CI: 0.23-0.88). Mortality did not differ between the groups (adjusted OR: 0.67; 95% CI: 0.13-3.45). Death and unfavorable neurological outcomes occurred less in the PICU group (adjusted OR: 0.29; 95% CI: 0.14-0.60).

Table 3 shows comparison of outcomes for the 2 types of ICUs in endogenous vs. exogenous illness settings. In the endogenous illness setting, PCPC was better in the PICU group compared to the general ICU group (adjusted OR: 0.45; 95% CI: 0.21-0.95). Mortality did not differ between the groups (adjusted OR: 0.58; 95% CI: 0.11-2.98). Overall rates of death and unfavorable outcomes were better in the PICU group (adjusted OR: 0.26; 95% CI: 0.12-0.56). In the exogenous illness setting, PCPC did not differ between the groups (adjusted OR: 0.38; 95% CI: 0.07-2.00). Since the number of deaths was very small, we could not statistically compare mortality between the groups. Overall rates of death and unfavorable outcomes did not differ between the groups (adjusted OR: 0.72; 95% CI: 0.08-6.34).

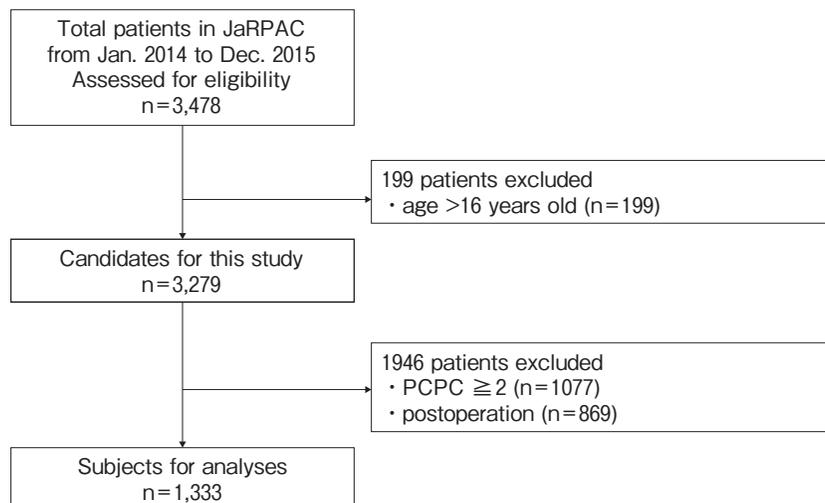


Fig. 1 Patient flow diagram.

**Table 1** Demographic characteristics of participants separated by the type of ICU

	General ICUs	PICUs
Female, n (%)	64/174 (36.8)	479/1,143 (41.9)
Age, years, mean (SD)	5.2 (4.8)	3.5 (4.0)
Age category, year, n (%)		
0	43/190 (22.6)	451/1,139 (39.6)
1	32/190 (16.8)	177/1,139 (15.5)
2 to 5	41/190 (21.6)	239/1,139 (21.0)
6 to 15	74/190 (39.0)	272/1,139 (23.9)
Hospital admission year, n (%)		
2014	66/190 (34.7)	590/1,143 (51.6)
2015	124/190 (65.3)	553/1,143 (48.4)
Disease category, n (%)		
Endogenous causes	111/190 (58.4)	947/1,135 (83.4)
Exogenous causes	79/190 (41.6)	188/1,135 (16.6)
Hospital admission time, n (%)		
Weekday daytime	51/174 (29.3)	342/1,142 (30.0)
Weekday night-time	77/174 (44.3)	455/1,142 (39.8)
Weekend daytime	20/174 (11.5)	148/1,142 (13.0)
Weekend night-time	26/174 (14.9)	197/1,142 (17.3)
Hospital admission type, n (%)		
Direct transfer to the hospitals	111/190 (58.4)	412/1,143 (36.1)
Referral from other hospitals	69/190 (36.3)	579/1,143 (50.7)
Transfer from wards in the hospital	10/190 (5.3)	149/1,143 (13.0)
Others	0/190 (0)	3/1,143 (0.3)
Predicted mortality (by PIM2), mean (SD) <sup>a</sup>	7.7 (18.3)	5.3 (12.9)
PIM2 ≥ 20, n (%) <sup>a</sup>	7/111 (6.3)	60/947 (6.3)
Predicted mortality (by TRISS), mean (SD) <sup>a</sup>	2.2 (7.6)	7.9 (20.9)
Predicted mortality (by TRISS) ≥ 10%, n (%) <sup>a</sup>	2/66 (3.0)	19/137 (13.9)

ICU, intensive care unit; PICU, pediatric intensive care unit; PIM2, pediatric index of mortality 2; SD, standard deviation; TRISS, trauma injury severity score.

<sup>a</sup>, PIM2 is used for participants suffering from endogenous causes and TRISS is used for those suffering from exogenous causes.

**Table 2** Comparison of outcomes for the two types of ICUs

	n (%)	Crude OR (95% CI)	Adjusted OR (95% CI) <sup>a</sup>
Deterioration of PCPC			
ICUs	19/190 (10)	1 (Ref)	1 (Ref)
PICUs	99/1,143 (8.7)	0.85 (0.51–1.43)	0.45 (0.23–0.88)
Sequela or death			
ICUs	17/190 (8.9)	1 (Ref)	1 (Ref)
PICUs	74/1,143 (6.5)	0.70 (0.41–1.22)	0.29 (0.14–0.60)
Death			
ICUs	5/190 (2.6)	1 (Ref)	1 (Ref)
PICUs	35/1,143 (3.1)	1.17 (0.45–3.02)	0.67 (0.13–3.45)

CI, confidence interval; ICU, intensive care unit; OR, odds ratio; PICU, pediatric intensive care unit.

<sup>a</sup>, Adjusted for age category, sex, admission year, disease category, admission time, admission type, and severity of disease.

**Table 3** Comparison of outcomes for the two types of ICUs in endogenous vs. exogenous illness settings

	Endogenous causes			Exogenous causes		
	n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)	n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Deterioration of PCPC						
ICUs	13/111 (11.7)	1 (Ref)	1 (Ref)	6/79 (7.6)	1 (Ref)	1 (Ref)
PICUs	66/947 (7.0)	0.56 (0.30–1.06)	0.45 (0.21–0.95)	26/188 (13.8)	1.95 (0.77–4.95)	0.38 (0.07–2.00)
Sequela or death						
ICUs	13/111 (11.7)	1 (Ref)	1 (Ref)	4/79 (5.1)	1 (Ref)	1 (Ref)
PICUs	47/947 (5.0)	0.39 (0.21–0.75)	0.26 (0.12–0.56)	20/188 (10.6)	2.23 (0.74–6.76)	0.72 (0.08–6.34)
Death						
ICUs	3/111 (2.7)	1 (Ref)	1 (Ref)	2/79 (2.5)	1 (Ref)	1 (Ref)
PICUs	19/947 (2.0)	0.74 (0.21–2.53)	0.58 (0.11–2.98)	12/188 (6.4)	2.63 (0.57–12.01)	NE

CI, confidence interval; ICU, intensive care unit; NE, not estimable; OR, odds ratio; PICU, pediatric intensive care unit.

<sup>a</sup>, Adjusted for age category, sex, admission year, disease category, admission time, admission type, and severity of disease.

## Discussion

The number of PICUs in Japan remains insufficient, so children with severely ill emergent conditions are generally transported to general emergency units and not ICUs specialized for them. However, no study has yet compared the outcomes between general ICUs and specialized PICUs in Japan. In our present analysis, increase in PCPC scores at discharge, which is used as an index of sequelae of critical illness, was better in PICUs compared to general ICUs in the endogenous illness setting. However, in the exogenous illness setting, outcomes were similar between pediatric and general ICUs. Thus the installation of more PICUs or around-the-clock staffing of general ICUs with pediatric specialists is required nationally.

In this study, outcomes for endogenous illnesses were better in PICUs; however, installation of ICUs, including PICUs, is largely dependent on regional numbers of children and healthcare systems, and the regional economy. In Japan in 2014, PICUs for critically ill children were available in only 29 facilities with 200 beds, which is one PICU bed per 100,000 pediatric population. This was far less than the number of European PICU beds per population (2.5 beds per 100,000 pediatric population in 2002 [6]). In 2017, the Japanese PICUs bed number increased to 280 in a total of 28 facilities (2 facilities combined the PICU with the adult critical care unit) [11]. This is approximately two PICU beds per 100,000 pediatric populations, which may be comparable to European countries. The PICU bed numbers have increased; however, another factor, the decreasing number of children in the general Japanese population, may also play an important role

(the child population is currently decreasing at 23.9/10<sup>4</sup> child population/year). Since 2009, government grants have been provided to promote installation of specialized PICUs <<https://www.mhlw.go.jp/shingi/2009/03/s0304-7.html>>(accessed March, 2020). Simultaneously, since 2010, the Japanese government has accelerated efforts to centralize severely ill children in nationally certified Emergency and Critical Care Center ICU beds, to offset the lack of PICUs <<https://www.mhlw.go.jp/file/05-Shingikai-12401000-Hokenkyoku-Soumuka/0000096262.pdf>>(accessed March, 2020). Traditionally, in many Japanese districts, children with exogenous illnesses (which account for 1/3 of pediatric deaths in Japan), especially those with trauma, are transported to certified Emergency and Critical Care Centers and treated in general ICUs in these facilities [12]. Both the PICU and general ICU systems (supported by Emergency Critical Care Centers) currently seem inadequate for centralization and need comprehensive advancement to cover regional severely ill pediatric care.

Our results have shown that overall unfavorable outcomes, including PCPC deterioration (adjusted OR: 0.45; 95% CI: 0.23–0.88) and overall sequelae/death (adjusted OR: 0.29; 95% CI: 0.14–0.60) were lower in PICUs. When limited to endogenous illness, however, the unfavorable outcomes were similar between the two types of ICU. The superiority of PICUs for endogenous illnesses may indicate the effectiveness of the present system, in which PICUs are used for specific illnesses in children, such as congenital heart disease. However, when limited to exogenous illnesses, the outcomes of general ICUs were like those of PICUs. This might be due to the historical transportation of patients with exogenous illnesses to Emergency Critical Care Centers

(general ICUs) or some not fully-equipped PICUs staffed by trauma surgeons, orthopedic surgeons, or neurosurgeons.

Pearson *et al.* reported on the importance of centralizing health care for severely ill children, demonstrating substantial reductions in mortality by centralizing pediatric admission to large specialized pediatric intensive care units (PICUs) [2]. In 2004, Farrell *et al.* reported that mortality rates at PICUs were lower than for other types of hospitals [13], similarly highlighting the need for centralization to PICUs.

Centralization of severely ill children seems to be generalizable to Japanese systems. In urban areas with a sufficient pediatric population, further centralization to existing PICUs or installation of new PICUs may improve the outcomes of severely ill children. However, for regions that cannot accommodate PICUs due to economic limitations or a shortage of pediatric medical staff, we advocate using the existing adult general ICU system with increased pediatric medical staffing to accomplish the desired centralization.

Pediatricians have been shown to be capable of appropriately triaging severely ill children to regional ICUs [14], indicating centralization to adult mixed Emergency Critical Centers should be achievable. Full-time availability of intensivists was associated with improved outcomes in the PICU as well as in adult units (general ICU) [15]. If general ICUs could be equipped with full-time pediatricians, general ICUs could effectively function as PICUs, even in the endogenous illness setting. Implementation of full-time pediatric in-hospital critical care attending coverage has been associated with shorter mechanical ventilation duration and shorter length of ICU stay [5]. High-intensity physician staffing may be another choice to improve mortality as in adult cases [16,17]. Pediatric education programs in the ICU could improve outcomes [18]. Since active involvement of intensive care specialists enables the effective use of ICU resources and mortality improvement [15], more intensive care physicians are needed in general ICUs and also in PICUs. For improved mortality in Japanese ICU settings, experienced physicians (and pediatricians) are essential [19,20].

Due to the decreasing number of children in the population and economic issues, additional installation of PICUs is impractical in some regions of Japan. However, our analysis showed that the comprehensive

outcomes of children treated in PICUs were better compared to those of children treated in general ICUs, indicating the need for improvement in the Emergency Critical Care Center-based general ICU system. Our study may show an important pathway for regional medical care systems tasked with treating critically ill pediatric patients at the present levels of available resources. We may need to further consider the use of national emergency critical care center ICU beds already available in the current system for the treatment of children, but with the addition of around-the-clock staffing of pediatric practitioners.

**Limitations.** The study is not free from some limitations. First, the JaRPAC database does not cover all Japanese facilities, which may cause selection bias. The results of the study may not be generalizable to all facilities. Second, some facilities with PICUs treat very high volumes of patients, over 500 admitted children. Data from these facilities may largely contribute to better PICU outcomes. High-volume PICUs are increasing nationally; therefore, future studies are needed to elucidate the potency of high-volume PICUs. Third, we could not quantify the intensity of pediatrician involvement in general ICUs. Finally, we did not demonstrate long-term outcomes for PCPC, which may change, even after discharge from the hospital.

In conclusion, PCPC deterioration, defined as PCPC  $\geq 3$  at discharge, and overall rates of sequelae/death were lower in PICUs in the current Japanese critical care system for children with endogenous illnesses. However, in the exogenous illness setting, outcomes from both pediatric and general ICUs were similar. Future study of centralization is needed; moreover, expanding existing PICUs or around-the-clock staffing of pediatric practitioners in general ICUs is required nationally.

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