ORIGINAL RESEARCH

Intensive Care Unit versus High-dependency Care Unit for COVID-19 Patients with Invasive Mechanical Ventilation

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Abstract

Rationale: High-dependency care units (HDUs), also termed “intermediate care units”, “step-down units”, or “respiratory HDUs”, are areas in which degrees of patient care and costs are between those of the intensive care unit (ICU) and the general ward. In general, patients requiring mechanical ventilation are treated in the ICU rather than in the HDU, except for the use of HDU beds as surge capacity beds during a massive strain; however, the HDU, as well as ICU, are used as the standard care units for mechanically ventilated patients with coronavirus disease (COVID-19) in Japan.

Objectives: To assess the outcomes of patients with COVID-19 with invasive mechanical ventilation treated in the HDU versus those treated in the ICU.

Methods: In this retrospective cohort study, we used a multicenter inpatient database in Japan to identify mechanically ventilated patients with COVID-19 in the ICU or HDU on the start day of invasive mechanical ventilation from February 10, 2020, to November 30, 2021. The primary outcome was in-hospital mortality within 30 days from the start of the first invasive mechanical ventilation. Propensity score matching was performed to compare the outcomes of patients treated in the ICU with those treated in the HDU.

Results: Of 1,985 eligible patients with COVID-19 with invasive mechanical ventilation, 1,303 (66%) were treated in the ICU, and 682 (34%) were treated in the HDU on the start day of invasive mechanical ventilation. After propensity score matching, patients treated in the ICU had significantly lower in-hospital mortality within 30 days than those treated in the HDU (18.3% vs. 24.2%; risk difference, −5.8%; 95% confidence interval, −10.9% to −0.8%).

Conclusions: This multicenter observational study in Japan suggests that care for mechanically ventilated patients with COVID-19 in the ICU may significantly reduce in-hospital mortality within 30 days compared with care in the HDU. Establishing a critical care system that would allow patients with COVID-19 requiring ventilators to be treated in the ICU is desirable. Because this study was an observational study, our finding represents an association, not causation. Further studies of different critical care systems are warranted to confirm our findings.

Keywords: coronavirus disease 2019; intensive care unit; high-dependency care unit; mechanical ventilation; propensity score

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The coronavirus disease 2019 (COVID-19) pandemic has put a tremendous strain on the critical care system, leading to a shortage of ventilators and critical care resources (1). In some areas, such as the United States and Europe, critically ill patients with COVID-19 overflowed from intensive care units (ICUs) into postanesthesia care units, emergency departments, operating rooms, and even temporary or tent facilities (2). A previous study in the United States showed that up to 25% of COVID-19 deaths could be attributed to increased hospital surge caseloads (3). Therefore, operational strategies against COVID-19 surges are needed to prevent crises in regional critical care systems.

One strategy against COVID-19 surges consists of using high-dependency care units (HDUs) for critically ill patients with COVID-19 (4, 5). HDUs, also termed "intermediate care units", "step-down units", or "respiratory high-dependency units", are areas in which degrees of patient care and costs are between those of the ICU and the general ward (5–7). HDUs may be used in different ways in the continuum of inpatient critical care worldwide. In general, patients requiring mechanical ventilation are treated in the ICU rather than in the HDU (8); however, in some countries, including Japan, a considerable number of mechanically ventilated patients are treated in the HDU (5, 9, 10). One study involving 400 acute care hospitals in Japan conducted between April 2010 and March 2012 showed that 46.4% of mechanically ventilated patients were treated in the HDUs, and those in the HDUs tended to be older, less likely to receive standard critical care (e.g., arterial line placement, enteral nutrition, and stress-ulcer prevention), and have higher mortality than those in the ICUs (9). This low prevalence of ICU services and the relatively high prevalence of HDU services in Japan stem from tradition, insufficient public and social awareness, inadequate government funding, and an underdeveloped educational system (11).

On April 18, 2020, during the first wave of the COVID-19 pandemic, the Japanese government officially issued a revision of the reimbursement that would double the normal reimbursement for treating patients with COVID-19 requiring invasive mechanical ventilation in ICUs as well as in HDUs (12). Therefore, in Japan, patients with COVID-19 requiring invasive mechanical ventilation were treated in HDUs as well as in ICUs as part of standard care.

To date, whether patients with COVID-19 requiring invasive mechanical ventilation should be treated in the ICU or the HDU is unknown. Several societies have recommended that patients with COVID-19 with invasive mechanical ventilation be treated in the ICU rather than the HDU on the basis of an expert opinion without clear evidence (13, 14). Nevertheless, one previous observational study showed that mechanically ventilated patients with non–COVID-19 pneumonia treated in the HDU had higher mortality rates than those treated in the ICU (15). However, because that study was conducted before the COVID-19 pandemic, whether this association is true among mechanically ventilated patients with COVID-19 remains unclear. To the best of our knowledge, no studies have compared the outcomes of mechanically ventilated patients with COVID-19 treated in the ICU with those treated in the HDU. Therefore, the present study aimed to assess the outcomes of patients with COVID-19 with invasive mechanical ventilation treated in the HDU versus those treated in the ICU, using data from multicenter acute care hospitals in Japan, where mechanically ventilated patients with COVID-19 are routinely treated in HDUs.

Methods

Data Source

For this study, we used a commercially available database containing routinely collected administrative data and discharge summaries at multicenter acute care hospitals in Japan. The database was built by the Medical Data Vision Co., Ltd. and consists of inpatient and outpatient data from over 350 voluntarily participating acute care hospitals (16). Participating hospitals provided data on all patients during the participation period. The database includes age, sex, diagnoses recoded with the ICD-10 (International Classification of Diseases, Tenth Revision) codes, daily procedures, and medications recorded using Japanese medical fee codes, as well as admission and discharge status. A previous validation study of Japanese administrative data and discharge summaries showed high specificity and moderate sensitivity for diagnoses and high specificity and sensitivity for procedures (17).

This study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) Statement: guidelines for reporting observational studies (18). The Institutional Review Board of The University of Tokyo approved this study (approval number: 2020310NI; January 20, 2021). Because the data were anonymized before the researchers received them, the requirement for informed consent was waived.

Study Population

We identified hospitalized patients with COVID-19 in the database from February 10, 2020, to November 30, 2021. We defined hospitalized patients with COVID-19 as those with a diagnosis of COVID-19 (ICD-10 code: U071) as the admission-precipitating diagnosis listed in the discharge abstract. We excluded patients with a suspected diagnosis of COVID-19. We then limited the study population to those who received invasive mechanical ventilation during hospitalization. We also excluded patients aged less than 15 years, those discharged to another hospital on the day of first invasive mechanical ventilation, and patients who were not admitted to either the ICU or HDU on the day of first invasive mechanical ventilation. We followed up on all eligible patients from hospitalization to discharge in the hospital in which they received invasive mechanical ventilation.

Treatment Groups

The ICU group was defined as those admitted to the ICU on the start day of the first invasive mechanical ventilation. The HDU group was defined as those admitted to the HDU on the start day of the first invasive mechanical ventilation. The definition of an ICU in this study was a separate unit providing critical care services with at least one physician on site 24 hours per day, at least two intensivists working full-time, around-the-clock nursing, the equipment necessary to care for critically ill patients, and a nurse-to-patient ratio of 1:2. The definition of an HDU in this study was consistent with that of an ICU, except that HDUs were not required to employ intensivists, and the requirement for the nurse-to-patient ratio was reduced to 1:4 or 1:5. The Japanese medical fee codes used to define ICUs and HDUs are presented in Table E1 in the online supplement.

Outcomes and Covariates

The primary outcome was in-hospital mortality within 30 days from the start of the first invasive mechanical ventilation. The secondary outcomes were ICU/HDU mortality, length of hospital stay from the start of first invasive mechanical ventilation, length of ICU/HDU stay from the start of first invasive mechanical ventilation, the total length of invasive mechanical ventilation, and total hospitalization costs. Total hospitalization costs were calculated on the basis of reference prices in the Japanese national fee schedule that determine item-by-item prices for surgical, pharmaceutical, laboratory, and other inpatient services (19).

The covariates consisted of the number of hospital beds (less than 500 or 500 or more), teaching or nonteaching hospital, pandemic waves at hospital admission used in Japan (first wave, February 10, 2020–June 13, 2020; second wave, June 14, 2020–October 9, 2020; third wave, October 10, 2020–February 29, 2021; fourth wave, March 1, 2021–June 20, 2021; fifth wave, June 21, 2021–November 31, 2021) (20, 21), a national estimate of invasive mechanical ventilation bed occupancy in Japan on the start day of invasive mechanical ventilation reported by Japan ECMOnet for COVID-19 (a web-based real-time nationwide registry and surveillance system from over 600 hospitals with 6,600 ICU beds in Japan [accounting for more than 80% of all ICU beds in Japan]) (22), age (continuous), sex, smoking history (nonsmoker, current/past smoker, or unknown), body mass index at admission (<18.5, 18.5–24.9, 25.0–29.9, ⩾30.0 kg/m^2, or missing), Japan Coma Scale at admission (23), Charlson comorbidity index score (continuous) (24), physical function at admission measured by the Barthel Index (BI) score (25), cognitive function before admission (no dementia, mild dementia, or moderate/severe dementia), home medical care before admission, ambulance use, admission on a weekend (i.e., Saturday or Sunday), length of hospital stay before invasive mechanical ventilation (26), place before hospitalization (home, another hospital, or nursing home), ICU/HDU admission before invasive mechanical ventilation, noninvasive mechanical ventilation before invasive mechanical ventilation, organ support therapies on the day of invasive mechanical ventilation (noradrenaline, dobutamine, chest compression, red blood cell transfusion, renal replacement therapy, and extracorporeal membrane oxygenation), and drug managements for COVID-19 before invasive mechanical ventilation (corticosteroids, corticosteroid pulse therapy, anticoagulant injection, oral anticoagulant, tocilizumab, baricitinib, ciclesonide, hydroxychloroquine, and antibiotics).

A national estimate of invasive mechanical ventilation bed occupancy was calculated by dividing the actual number of patients with COVID-19 with invasive mechanical ventilation by the acceptable number of patients with COVID-19 with invasive mechanical ventilation reported in the participating hospitals of Japan ECMOnet for COVID-19 (22). The Japan Coma Scale is well correlated with the Glasgow Coma Scale and is categorized as alert consciousness, confusion, somnolence, and coma (23). The Charlson comorbidity index was scored using the diagnosis for each patient after a previous study (24). Physical function at admission was categorized as total/severe dependence (BI, 0–60), slight/moderate dependence (BI, 61–99), independent (BI, 100), and missing (25).

Statistical Analysis

We performed a propensity score-matched analysis as our primary approach to compare the outcomes between the ICU and HDU groups (27). A multivariable logistic regression model using all the covariates was employed to compute the propensity scores for patients admitted to the ICU on the day of invasive mechanical ventilation. One-to-one nearest-neighbor matching without replacement was performed for the estimated propensity scores using a caliper width of 20% of the standard deviation of the propensity scores (28). To assess the performance of the matching, the covariates were compared using standardized mean differences, with an absolute standardized mean difference of 10% or less denoting a negligible imbalance between the two groups (28). C-statistics were measured by the area under the receiver operating characteristic curve for estimated propensity scores.

After propensity score matching, risk differences and their 95% confidence intervals of the outcomes between the two groups were assessed through a generalized linear model using the identity link function, irrespective of outcome types. For in-hospital mortality within 30 days, we also generated Kaplan-Meier curves and performed log-rank tests in the matched cohort. The number needed to treat was calculated as the inverse of the absolute risk reduction.

All analyses were performed using Stata/SE 17.0 software (StataCorp). Continuous variables were presented as means and standard deviations or the median and interquartile range. Categorical variables were described using numbers

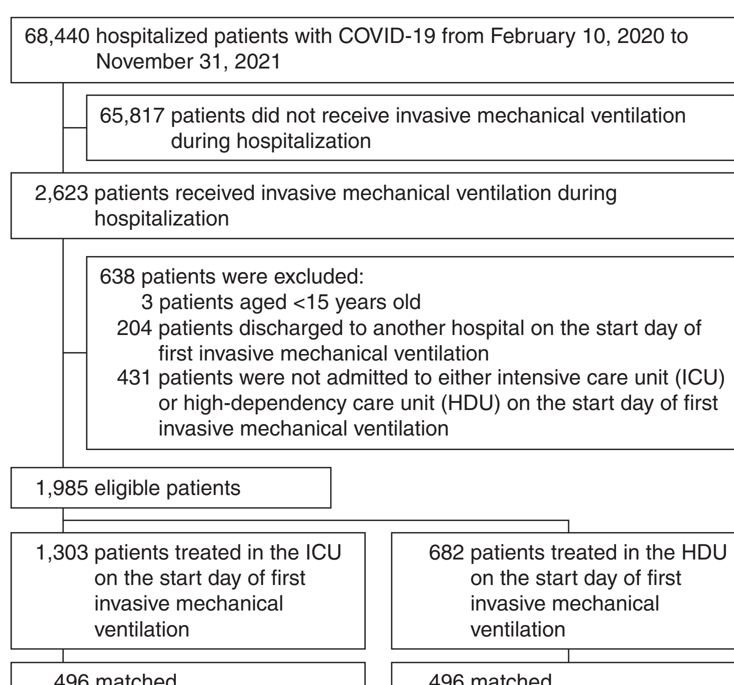

Figure 1. Flowchart of patient selection. COVID-19 = coronavirus disease; HDU = high-dependency care unit; ICU = intensive care unit.

Table 1. Baseline characteristics before and after propensity score matching

	Before Matching			After Matching		
Baseline characteristics	**ICU (*n* = 1,303)**	**HDU (*n* = 682)**	**SMD**	**ICU (*n* = 496)**	**HDU (*n* = 496)**	**SMD**
Hospital characteristics, *n* (%)						
Number of total hospital beds						
<500 beds	335 (26)	348 (51)	54	214 (43)	190 (38)	−10
⩾500 beds	968 (74)	334 (49)		282 (57)	306 (62)	
Teaching hospital	1,221 (94)	569 (83)	33	445 (90)	450 (91)	−3
Pandemic waves at hospital admission, *n* (%)						
First, Feb 10, 2020–Jun 13, 2020	71 (5)	37 (5)	0	21 (4)	29 (6)	−7
Second, Jun 14, 2020–Oct 9, 2020	69 (5)	33 (5)	2	21 (4)	24 (5)	−3
Third, Oct 10, 2020–Feb 29, 2021	414 (32)	170 (25)	15	132 (27)	136 (27)	−2
Fourth, Mar 1, 2021–Jun 20, 2021	450 (35)	248 (36)	−4	191 (39)	174 (35)	7
Fifth, Jun 21, 2021–Nov 31, 2021	299 (23)	194 (28)	−13	131 (26)	133 (27)	−1
Percentage of IMV bed occupancy at IMV, *n* (%)						
3–9	53 (4)	21 (3)	5	10 (2)	17 (3)	−8
10–19	246 (19)	118 (17)	4	86 (17)	86 (17)	0
20–29	426 (33)	171 (25)	17	133 (27)	134 (27)	0
30–39	520 (40)	325 (48)	−16	236 (48)	229 (46)	3
40–44	58 (4)	47 (7)	−11	31 (6)	30 (6)	1
Age (yr), median (IQR)	65 (55–73)	65 (56–74)	−6	65 (55–73)	64 (55–73)	−2
Male sex, *n* (%)	969 (74)	517 (76)	−3	379 (76)	370 (75)	4
Smoking history, *n* (%)						
Nonsmoker	586 (45)	296 (43)	3	196 (40)	212 (43)	−7
Current/past smoker	342 (26)	221 (32)	−14	170 (34)	152 (31)	8
Unknown	375 (29)	165 (24)	10	130 (26)	132 (27)	−1
Body mass index at admission (kg/m^2), *n* (%)						
<18.5	21 (2)	20 (3)	−9	12 (2)	10 (2)	3
18.5–24.9	483 (37)	261 (38)	−3	179 (36)	185 (37)	−3
25.0–29.9	440 (34)	214 (31)	5	174 (35)	162 (33)	5
⩾30.0	247 (19)	101 (15)	11	76 (15)	85 (17)	−5
Missing data	112 (9)	86 (13)	−13	55 (11)	54 (11)	1
Japan Coma Scale at admission, *n* (%)						
Clear	867 (67)	506 (74)	−17	377 (76)	368 (74)	4
Confusion	133 (10)	70 (10)	0	41 (8)	42 (8)	−1
Somnolence	60 (5)	28 (4)	2	16 (3)	19 (4)	−3
Coma	243 (19)	78 (11)	20	62 (13)	67 (14)	−3
Charlson comorbidity index, median (IQR)	1 (1-3)	1 (1-3)	4	1 (0-2)	1 (1-2)	2
Physical function at admission, *n* (%)						
Total/severe dependence (BI 0–60)	696 (53)	333 (49)	9	246 (50)	255 (51)	−4
Slight/moderate dependence (BI 61–99)	59 (5)	58 (9)	−16	40 (8)	37 (7)	3
Independent (BI = 100)	285 (22)	227 (33)	−26	161 (32)	146 (29)	7
Missing	263 (20)	64 (9)	31	49 (10)	58 (12)	−5
Cognitive function before admission, *n* (%)						
No dementia	1,207 (93)	587 (86)	21	439 (89)	437 (88)	1
Mild dementia	58 (4)	59 (9)	−17	39 (8)	40 (8)	−1
Moderate/severe dementia	38 (3)	36 (5)	−12	18 (4)	19 (4)	−1
Home medical care before admission, *n* (%)	8 (1)	7 (1)	−5	4 (1)	4 (1)	0
Ambulance use, *n* (%)	950 (73)	408 (60)	28	300 (60)	312 (63)	−5
Admission at weekend, *n* (%)	277 (21)	159 (23)	−5	117 (24)	118 (24)	−1
Length of hospital stay before IMV, *n* (%)						
Same day of hospital admission	684 (52)	276 (40)	24	204 (41)	220 (44)	−7
2–3 d	250 (19)	168 (25)	−13	111 (22)	111 (22)	0
4–7 d	241 (18)	162 (24)	−13	122 (25)	112 (23)	5
⩾8 d	128 (10)	76 (11)	−4	59 (12)	53 (11)	4
Place before hospitalization, *n* (%)						
Home	719 (55)	457 (67)	−24	335 (68)	322 (65)	5
Another hospital	583 (45)	214 (31)	28	160 (32)	172 (35)	−5
Nursing home	1 (0)	11 (2)	−17	1 (0)	2 (0)	−2
ICU/HDU admission before IMV, *n* (%)	396 (30)	290 (43)	−25	195 (39)	184 (37)	5
NIMV before IMV, *n* (%)	4 (0)	1 (0)	3	1 (0)	1 (0)	0
Organ support therapies, *n* (%)						
Noradrenaline	575 (44)	189 (28)	35	136 (27)	162 (33)	−10
Dobutamine	30 (2)	7 (1)	10	7 (1)	7 (1)	0

(*Continued*)

Table 1. (*Continued*)

Baseline characteristics	Before Matching ICU (*n* = 1,303)	Before Matching HDU (*n* = 682)	Before Matching SMD	After Matching ICU (*n* = 496)	After Matching HDU (*n* = 496)	After Matching SMD
Chest compression	14 (1)	15 (2)	−9	8 (2)	6 (1)	3
Red blood cell transfusion	35 (3)	20 (3)	−2	21 (4)	16 (3)	6
Renal replacement therapy	61 (5)	22 (3)	8	22 (4)	19 (4)	3
Extracorporeal membrane oxygenation	58 (4)	20 (3)	8	18 (4)	19 (4)	−1
Drug managements for COVID-19, *n* (%)						
Corticosteroids	715 (55)	425 (62)	−15	294 (59)	296 (60)	−1
Corticosteroid pulse therapy	128 (10)	82 (12)	−7	60 (12)	60 (12)	0
Anticoagulant injection	1,202 (92)	574 (84)	25	430 (87)	436 (88)	−4
Oral anticoagulant	128 (10)	87 (13)	−9	62 (13)	54 (11)	5
Tocilizumab	107 (8)	137 (20)	−35	71 (14)	65 (13)	4
Baricitinib	137 (11)	87 (13)	−7	59 (12)	52 (10)	4
Ciclesonide	26 (2)	12 (2)	2	7 (1)	9 (2)	−3
Hydroxychloroquine	8 (1)	5 (1)	−2	1 (0)	2 (0)	−3
Antibiotics	684 (52)	369 (54)	−3	247 (50)	259 (52)	−5

Definition of abbreviations: BI = Barthel Index; COVID-19 = coronavirus disease; HDU = high-dependency care unit; ICU = intensive care unit; IMV = invasive mechanical ventilation; IQR = interquartile range; NIMV = noninvasive mechanical ventilation; SMD = standardized mean difference.

and percentages. All reported *P* values were two-sided, and $P < 0.05$ was considered statistically significant.

Results

A total of 1,985 patients were eligible. Of these, 1,303 (66%) were treated in the ICU, and 682 (34%) were treated in the HDU on the start day of the first invasive mechanical ventilation (Figure 1). Of the 1,303 patients treated in the ICU on the start day of invasive mechanical ventilation, 346 (27%) were subsequently transferred to the HDU after the second day of invasive mechanical ventilation. Of the 682 patients treated in the HDU on the start day of invasive mechanical ventilation, 47 (7%) were subsequently transferred to the ICU after the second day of invasive mechanical ventilation.

Table 1 shows the baseline characteristics before and after propensity score matching. The median age was 65 years (interquartile range, 55–73), and 75% were men. Before propensity score matching, patients in the ICU group tended to have been admitted to a teaching hospital with a high total number of hospital beds; they also had poor consciousness at admission, had been transferred from another hospital, received noradrenaline, and received an anticoagulant injection. Meanwhile, patients in the HDU group tended to have been admitted during the fifth pandemic wave; they received invasive mechanical ventilation at higher invasive mechanical ventilation bed

Figure 2. Balance of the covariates before and after propensity score (PS) matching. HDU = high-dependency care unit; ICU = intensive care unit; IMV = invasive mechanical ventilation; JCS = Japan Coma Scale; NIMV = noninvasive mechanical ventilation.

Table 2. Outcomes before and after propensity score matching

Outcomes	Before Matching ICU (*n* = 1,303)	Before Matching HDU (*n* = 682)	After Propensity Score Matching ICU (*n* = 496)	After Propensity Score Matching HDU (*n* = 496)	Risk difference (95% CI)	*P* value
In-hospital mortality within 30 d, *n* (%)	261 (20.0)	165 (24.2)	91 (18.3)	120 (24.2)	−5.8 (10.9 to –0.8)	0.024
ICU/HDU mortality, *n* (%)	201 (15.4)	131 (19.2)	66 (13.3)	96 (19.4)	−6.0 (–10.6 to –1.5)	0.010
Length of hospital stay (d), mean (SD)	28 (24)	25 (22)	29 (25)	26 (23)	2.6 (−0.4 to 5.7)	0.087
Length of ICU/HDU stay (d), mean (SD)	16 (12)	14 (10)	16 (13)	15 (10)	0.7 (−0.8 to 2.2)	0.33
Length of IMV (d), mean (SD)	15 (19)	12 (12)	15 (20)	12 (13)	2.8 (0.8 to 4.9)	0.008
Hospitalization cost (10 × 4 yen), mean (SD)	744 (564)	497 (351)	729 (610)	529 (376)	200 (137 to 263)	<0.001

Definition of abbreviations: CI = confidence interval; HDU = high-dependency care unit; ICU = intensive care unit; IMV = invasive mechanical ventilation; SD = standard deviation.

occupancy in Japan, had dementia, underwent longer length of hospital stay before invasive mechanical ventilation, had been admitted to the ICU/HDU before invasive mechanical ventilation, had received corticosteroids, and received tocilizumab. The C-statistic was 0.766. The distributions of propensity scores before and after matching are shown in Figures E1 and E2. One-to-one propensity score matching created 496 matched pairs. After matching, patient characteristics were well balanced between the two groups (Table 1 and Figure 2).

Table 2 shows the outcomes before and after propensity score matching. After propensity score matching, patients in the ICU group had significantly lower in-hospital mortality within 30 days than those in the HDU group (18.3% vs. 24.2%; risk difference, −5.8%; 95% confidence interval, −10.9% to −0.8%). Kaplan-Meier analysis with the log-rank test showed a statistically significant difference in in-hospital mortality within 30 days between the two groups ($P = 0.018$) (Figure 3). The estimated number needed to treat was 17 (95% confidence interval, 9–125). Compared with patients in the HDU group, those in the ICU group had significantly lower ICU/HDU mortality, longer lengths of invasive mechanical ventilation, and higher hospitalization costs (7,290,000 yen vs. 5,290,000 yen; risk difference, +2,000,000 yen; 95% confidence interval, +1,370,000 yen to +2,630,000 yen). There were no statistically significant differences between the two groups in the length of hospital stay or ICU/HDU stay.

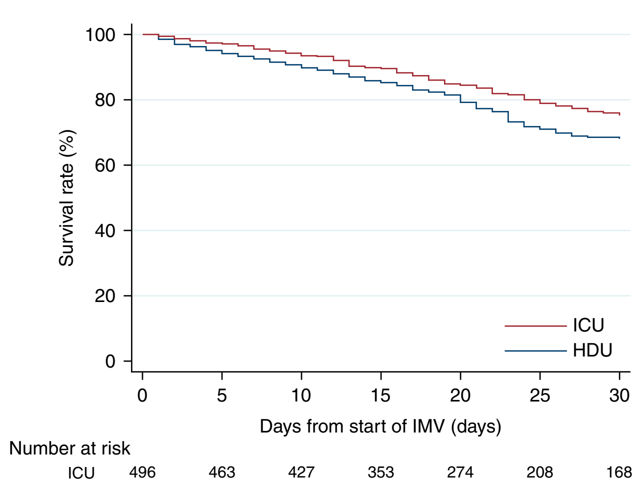

Figure 3. Kaplan-Meier survival plots for mechanically ventilated patients with COVID-19 treated in the ICU versus HDU in propensity score-matched cohorts. There is a statistically significant difference in in-hospital mortality within 30 days between the two groups (log-rank test, $P = 0.021$). COVID-19 = coronavirus disease; HDU = high-dependency care unit; ICU = intensive care unit; IMV = invasive mechanical ventilation.

Discussion

In this multicenter study of mechanically ventilated patients with COVID-19, care in the ICU was associated with lower in-hospital mortality within 30 days than care in the HDU. Notably, the results of this study apply directly to Japan, where treating mechanically ventilated patients with COVID-19 in either the ICU or HDU is the standard of care.

Consistent with the recommendation from several societies and a previous study of patients without COVID-19, mechanically ventilated patients with COVID-19 treated in the ICU had lower mortality than those treated in the HDU (13–15, 29). Considering the definition of ICU and HDU in Japan, the difference in mortality between the two units in our study may be explained by two factors: higher nurse-to-patient ratios and the presence of intensivists in the ICU. Mechanically ventilated patients, particularly those with COVID-19, require a high workload from physicians and nursing staff (30, 31). Evidence suggests that inadequate nurse staffing and increased nurse workload may affect the delivery of care and increase the risk of mortality (32). In addition, a large body of evidence supports the superiority of a high-intensity intensivist staffing model, in which an intensivist is responsible for day-to-day patient management (33). In critical care facilities without intensivists, a lack of knowledge of rapidly changing COVID-19 treatments may delay the implementation of evidence-based interventions.

Because of the lower mortality in the ICU group, patients in the ICU group had significantly longer lengths of invasive mechanical ventilation than those in the HDU group. The mean difference in total hospitalization cost between the ICU and HDU groups was 2,000,000 yen, and the median estimated number needed to treat was 17 in this study. A previous study of 258 acute respiratory failure survivors with mechanical ventilation (median age 64 yr and 67% men) showed that the mean predicted lifetime quality-adjusted life years was 15.4 (34). On the basis of the above figures, the incremental cost-effectiveness ratio for ICU admission with reference to HDU admission was approximately 2,200,000 yen per quality-adjusted life year. Because the benchmark for willingness-to-pay threshold in Japan is 5,000,000 yen per quality-adjusted life year (35), ICU use may be cost-effective and justified in terms of health economics.

Our results have important clinical implications. First, this study provides evidence that mechanically ventilated patients with COVID-19 be treated in the ICU rather than in the HDU as the standard of care. Therefore, establishing a critical care system that would allow patients with COVID-19 requiring ventilators to be treated in the ICU is desirable. Second, as a contingency/crisis strategy for surge response, treating mechanically ventilated patients with COVID-19 outside the ICU should happen later, and other operational strategies such as scaling up staffing or patient transfer should be the priority (4). Our results will influence healthcare providers, hospital administrators, and policymakers to provide better critical care services in the future.

Limitations

The present study had several limitations. First, because this was not a clinical trial, no causation could be inferred. Second, we used a multicenter, real-world database in Japan, and no standard protocol for critical care admission in Japan had been established. Therefore, admission to the HDU rather than the ICU for mechanical ventilation was not random but rather on the basis of the decisions of the attending physician or hospital, which may have led to confounding by indication. We attempted to control for measured confounders in the adjusted analyses, but there still may have been unmeasured residual confounders. Specifically, patients in the ICU appeared to have more severe illnesses than those in the HDU. Moreover, unmeasured illness severities could bias even larger differences in mortality between the ICU and HDU groups. Therefore, these unmeasured confounders would not change the direction of our results and can be disregarded. Third, because of the variations in the definition of ICU and HDU, the results of this study may not be generalizable to other countries. For example, the nurse-to-patient ratios of the ICU and HDU in Japan are 1:2 and 1:4, respectively, whereas those in the United Kingdom are 1:1 and 1:2 (36), and in the United States are 1:1–1:2 and 1:3–1:4, respectively (37). Fourth, we were not able to obtain data on withholding or withdrawing invasive mechanical ventilation, which might affect a patient's prioritization for admission to the ICU rather than the HDU (38). However, because all patients in the present study received invasive mechanical ventilation on the day they were admitted to the ICU or HDU, these patients would not have been at the end-of-life stage at the time of treatment allocation. Therefore, the lack of data on withholding or withdrawing life-sustaining therapy may not have caused serious bias in our study.

Fifth, although the national calculation indicated that the COVID-19 surge did not exceed ICU capacity in Japan (22, 39), some individual hospitals may have increased their critical care capacity by deploying surge capacity beds (i.e., ICU or HDU beds newly created in response to the COVID-19 pandemic) (39). We were not able to obtain data regarding surge capacity beds from our database. However, as a previous study showed that admission to a surge capacity bed was not associated with increased mortality (40), bias from this unmeasured variable would be negligible. Sixth, because hospital participation in the database built by the Medical Data Vision Co., Ltd. was voluntary, this study may have a selection bias when considering all ICUs in Japan as a source population. A previous descriptive study using a national ICU registry database in Japan showed that the median age was 68 years, with 77% being men, and the in-hospital mortality of mechanically ventilated patients in the ICU was 17% (41). These similar patient characteristics and outcomes between the two databases suggested acceptable internal validity of our study. Seventh, we were unable to obtain the vaccination status in the dataset. Finally, because information on hospital identification was not available from the dataset, hospital clustering was considered when calculating the propensity score, which might cause bias (42).

Conclusions

This multicenter observational study in Japan suggests that care for mechanically ventilated patients with COVID-19 in the ICU may be associated with decreased in-hospital mortality within 30 days compared with care in the HDU. Because this study was an observational study, our finding represents an association, not causation. Further studies of different critical care systems are warranted to confirm our findings. ■

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