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Interhospital transports and mortality in patients with critical COVID-19: a single-centre cohort study

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ABSTRACT

Objectives

This study aimed to compare mortality rates and length of hospital stay between patients with critical COVID-19 who were transferred to another hospital due to capacity constraints and those who remained at their initial admission hospital.

Design

Single-centre cohort study

Setting and participants

Six hundred and sixty-five patients treated for SARS-CoV-2 at two intensive care units (ICU) in X from 1 March 2020 to 30 June 2021. Data on interhospital transfers were retrieved from medical records and patient data management systems according to pre-defined protocols.

Main outcome measures

The outcomes were 30- and 90-day mortality, days alive and out of ICU. Hazard ratios (HR) with 95% confidence intervals (CI) were calculated using Cox proportional hazard models with adjustments for age, sex, body mass index, severity of illness, comorbidity, invasive ventilation, treatment limitations and pandemic waves.

Results

Of 665 patients, 133 (20%) were transferred to another hospital. The mortality rate for transferred patients compared to non-transferred patients at 30 days was 19% versus 26% (p=0.13), and at 90 days 26% versus 30% (p = 0.43). In the adjusted Cox regression analysis,

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interhospital transfer was associated with a lower mortality risk at 30 days (HR 0.47, 95% CI: 0.30–0.76) and 90 days (HR 0.52, 95% CI: 0.34–0.79). However, the number of days alive and out of ICU was significantly lower for the IHT group at 30 and 90 days.

Conclusion

This study indicates that interhospital transfer due to capacity constraints among patients with critical COVID-19 was associated with lower mortality but an extended length of ICU stay. The latter was probably due to the need for invasive ventilation among transferred patients, not the transfer per se. Suitability for transfer may be associated with lower mortality, but residual confounding cannot be excluded.

Strengths and limitations of this study

- The strengths are the comprehensive data collection conducted by dedicated researchers during the three pandemic waves and validated by independent researchers.
- The low proportion of missing data, and the adjustment for known confounders in the analyses.
- The main weaknesses are the single-centre non-randomised design.
- There may be a risk of selection bias in the study since it is likely that stable patients with recovery potential were selected for transport.
- Information about the severity of illness immediately before transport was not readily available in our cohort.

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BACKGROUND

Transports of critically ill patients between intensive care units (ICUs) across hospitals are relatively common. The primary reasons include the need to transfer to a hospital with specialised competence, as well as capacity constraints at the transferring hospital (1-3). Regardless of the reason for the transport, studies have shown that patient transfers entail direct risks related to the transport itself and can be linked to delayed diagnostics or treatments (1, 4-8). In X, where the ICU beds per capita are among the lowest in Europe (9), approximately 600 ICU patients are transported between hospitals each year due to a lack of resources at the sending ICU (10). During the COVID-19 pandemic, the influx of patients requiring ICU treatment significantly increased interhospital transfers (IHTs) (10). Studies investigating the risk of IHT during the COVID-19 pandemic have shown conflicting results. Some studies indicate that IHT is not associated with an increased mortality risk (2, 11-14) or may even be associated with a lower risk of death (15), whereas others have shown that IHT is associated with a longer duration of mechanical ventilation (11-13), ICU stay (12) and length of hospital stay (2, 12, 13). None of these studies were randomised controlled trials, and many were limited by a small sample size (2, 11, 14). Despite the large increase in ICU beds in Sweden during the pandemic, a substantial proportion of critically ill patients were transferred between hospitals. To the best of our knowledge, no study has so far studied the influence of IHTs on patient outcomes during the COVID-19 pandemic in X. Therefore, we aimed to compare mortality rates and length of hospital stay between patients who were transferred to another hospital due to capacity constraints and those who remained at their initial admission hospital.

METHODS

Study design

This study included all adult patients (age \geq 18 years) with confirmed SARS-CoV-2, as verified by polymerase chain reaction test, requiring intensive care at X Hospital (X) in X, X, between 1 March 2020 and 30 June 2021. The hospital is a secondary referral centre with a large emergency department and a total capacity of 600 beds. Normally, there are 18 beds dedicated to intensive care. However, during the COVID-19 pandemic, the ICUs expanded to accommodate a total of 60 ICU beds. The study was approved by the Regional Ethical Review Board X, X (Dnr: 2023-01778-01-380347, amendment 2023-01778-01), and the requirement for written informed consent from patients was waived. The reporting of the study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology evic (STROBE) guidelines (16).

Cohort

Adult patients admitted to the ICU due to SARS-CoV-2 as the primary diagnosis (ICD codes JA36 and U07.1) were eligible for the study. Patients who were transported for reasons other than capacity constraints (e.g. repatriation or clinical transfers) were excluded from the study. Patients were identified using the patient data management system. Clinical data were automatically and manually extracted from medical records and the patient data management system using a pre-defined data collection protocol to ensure consistency and uniformity of the data collection. Cross-validation of data from randomly selected patients was performed separately by two independent researchers.

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Exposure

The exposure was IHT, defined as unit-to-unit capacity transfer, with the patient discharged from the ICU at X Hospital and admitted to an ICU at another hospital. The IHTs adhered to the transport recommendations issued by the X Society for Anaesthesia and Intensive Care (17). The selection of patients for transfer due to capacity constraints was commonly done in dialogue with the admitting ICU. The decision was based on whether the patient's physiological status allowed for safe transport, and on the admitting hospital's ability to provide the required care. The actual transport was prepared according to local routines for transports, and handover was reported by telephone. ICU patients in X are commonly transported between hospitals using a mobile intensive care unit (MICU). A MICU is staffed with one ambulance nurse, one paramedic and one physician from the departing intensive care unit. The MICU transporter is more spacious than a standard ambulance, and is equipped with continuous electrocardiography monitoring, invasive hemodynamic monitoring and advanced ventilatory support. Information about the date, time and reasons for transfer was obtained from the patients' medical records and the patient data management system.

Outcomes

The outcomes were mortality at days 30 and 90 from ICU admission and days alive and out of ICU. Length of ICU stay was measured from the date of ICU admission to the date of discharge from ICU at X Hospital or the admitting hospital.

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Statistical analysis

Continuous variables are presented as medians with interquartile ranges (IQRs), and categorical variables are expressed as numbers and proportions (percentages). The distribution of continuous variables was tested with the Shapiro-Wilk test. Differences between groups were analysed using the Mann-Whitney U test and the Chi² test for continuous and categorical variables, respectively.

In the survival analyses, patients were followed up from the date of ICU admission until the date of death or until 30 and 90 days had passed since admission. Kaplan–Meier curves were used to estimate the cumulative risk of death, and the log-rank test was employed to compare patients with exposure to IHT versus those without IHT. Cox proportional hazards regression was used to estimate hazard ratios (HR) with corresponding 95% confidence intervals (CI) for death within 30 and 90 days from ICU admission. Multivariate models were adjusted for age (continuous), sex (male/female), body mass index ($<30/\geq30$ kg/m²), Simplified Acute Physiology Score III (SAPS III) (>50/50–59/≥60), Charlson Comorbidity Index (categorised as 0/1/2) (18), invasive mechanical ventilation (yes/no), treatment limitations (yes/no), COVID waves (first wave, March to September 2020 versus second and third waves, October 2020 to January 2021 and February to June 2021 (19)) and IHT (yes/no). Both crude and multivariable models were investigated with no IHT as the reference group. Scaled Schoenfeld residuals were regressed against survival time to assess the proportional hazard assumptions, and Martingale residual plots, together with the Grambsch-Therneau test, were used to assess evidence of non-linearity. Variance inflation factors were used when investigating multicollinearity. All variables were complete except for SAPS and BMI

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which were missing for 105 and 6 patients, respectively. This was handled by a separate category for patients with missing values.

To assess the robustness of the findings and potential variations in the data, we performed sensitivity analyses on subgroups of patients based on length of ICU stay (more than 6, 8, 10 and 12 days), mechanical ventilation and COVID waves. Comparisons of days alive free from ICU were conducted using the Mann-Whitney U test and presented as medians with interquartile ranges (IQRs).

A two-sided p-value less than 0.05 was considered statistically significant. The analysis followed a predefined protocol and was conducted using the IBM SPSS Statistics version 29 statistical software and R version 4.3.3 (R Core, 2017. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria). All analyses were discussed and confirmed with an experienced biostatistician.

RESULTS

Patient cohort

Of 2622 critically ill patients admitted to the two ICUs during the study period, 679 had a confirmed SARS-CoV-2 diagnosis. Nine patients were transported to other hospitals for tertiary care (e.g. ECMO) and five were repatriated to their home region. In total, 665 SARS-CoV-2 patients were included in the study, of which 133 (20%) underwent interhospital transports due to capacity constraints (Figure 1). All patients (n=133) were transported to a hospital within a 30-kilometer radius or maximum of 30 minutes.

The median age of included patients was 64 years, and most were men (72%). Patients who were transferred were more often on mechanical ventilation (98%) compared with the non-transferred patients (40%), and fewer had limitations in terms of life-sustaining treatment (4% versus 15%). Otherwise, the groups were balanced regarding patient and clinical characteristics (Table 1). The median day of IHT from admission was 6 (IQR: 3–11).

Interhospital capacity transfer and mortality

Analyses of IHT and mortality in patients with critical COVID-19 are shown in Table 2. Mortality rates did not differ between groups at either 30 days (19% vs. 26%, p = 0.13) or 90 days (26% vs. 30%, p = 0.43). This was consistent across the log-rank test for survival for 30 days (Supplementary figure 1, p = 0.06) and 90 days (Supplementary figure 2, p = 0.2), as well as the HR of the univariate Cox regression of 0.66 (95% CI: 0.43–1.02) for 30-day mortality and 0.79 (95% CI: 0.54–1.14) for 90-day mortality. When the exposure of IHT was

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analysed in the multivariate model, it was associated with a lower risk of mortality for both 30 days (HR 0.47, 95% CI: 0.30–0.76) and 90 days (HR 0.52, 95% CI: 0.34–0.79) (Table 2).

As the assumptions of proportional hazards were violated when scaled Schoenfeld residuals were regressed against survival time (p < 0.001 for the multivariate model for 30- and 90-day mortality), sensitivity analyses were performed. When splitting the time and analysing by different lengths of stay (LOS) at the ICU, the assumptions were fulfilled for patients with a LOS of eight days and above (p = 0.14 for 30-day mortality and p = 0.09 for 90-day mortality). The results did not differ from the original models except for IHT being associated with lower 30-day mortality, including in the univariate analyses for patients with an ICU LOS of more than six and eight days (Table 3). Schoenfeld residuals indicated violations of proportional hazard assumptions, including for the covariates of mechanical ventilation, treatment limitations and COVID-19 wave in the multivariate models for 30 and 90 days. This issue was addressed by examining the various categories within these variables as subgroups. The reason for the violation of the variables of mechanical ventilation and treatment limitations was a small number of patients/events in the groups of patients without mechanical ventilation exposed to IHT and the group with treatment limitations exposed to IHT. When analysing the subgroup of only mechanically ventilated patients, the results changed in the univariate models, showing a lower risk of mortality for 30 days (19.3% versus 32.9%, p=0.008) and 90 days (26.0% versus 38.0%, p=0.029) in the IHT group compared to the non-IHT group. In the multivariate models, the decrease in mortality for the IHT group at 30 and 90 days remained unchanged. Excluding patients with treatment limitations did not change the results.

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The results differed between patients treated in the first COVID-19 wave and those treated in the second or third waves. For patients in the first wave, all models – both univariate and multivariate – showed that IHT was associated with lower HR of mortality at 30 and 90 days. By contrast, no significant differences in mortality were observed between the IHT exposure groups in the second and third COVID-19 waves for any of the models. More details regarding the subgroup analyses can be found in Supplementary Files 4-6.

Interhospital transfer and days alive free of ICU

Compared with non-IHT patients, IHT patients had in median fewer days alive and free from the ICU at 30 days (5, IQR: 0–18 versus 22, IQR: 0–27, p<0.001) and 90 days (64, IQR: 27–78 versus 81, IQR: 6–87, p=0.86) respectively (Supplementary figure 3). However, for mechanically ventilated patients, there were no statistically significant median differences between the groups at 30 days (5, IQR: 0–18 versus 2, IQR: 0–16, p=0.31) or 90 days (63, IQR: 24–78 versus 60, IQR: 0–75, p=0.14).

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DISCUSSION

In this study, transfers solely due to capacity constraints during the COVID-19 pandemic were not associated with a higher risk of 30- and 90-day mortality among patients with critical COVID-19. Our results indicated that such transfers may even be associated with a reduced mortality risk, especially for mechanically ventilated patients. Interhospital transfer was associated with a longer ICU LOS compared with patients who remained in the admitting ICU. This was probably explained by the higher prevalence of invasive ventilation among transferred patients.

The risk of interhospital transfer has been investigated to some extent in observational studies, albeit with conflicting results. A Swedish register-based study of 2,912 capacitytransferred ICU patients before the pandemic found that transportation was associated with a lower risk of death within 90 days (odds ratio 0.71, 95% CI: 0.65–0.79) (20). Conversely, another Swedish study including 11,176 ICU patients showed a higher risk of 30-day mortality after capacity transfers (odds ratio 1.25, 95% CI: 1.06–1.49) and clinical transfers (odds ratio 1.17, 95% CI: 1.02–1.36) (21). However, the reference consisted of repatriated patients. While we excluded such patients in our study, other studies have confirmed that clinical transfer to a higher level of care is associated with better patient outcomes (22, 23). A French cohort study of 18,348 COVID-19 patients in the ICU found that transferred patients had a lower mortality rate than non-transferred patients, concluding that this might be due to a rigorous selection process of patients eligible for transfer (15). However, the study only included patients from the first wave of the pandemic. This finding resembles ours, where the results were driven by lower mortality in IHT patients during the first COVID wave. A retrospective cohort study including 5,207 patients mostly with SARS-CoV-2 during

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wave 3 of the pandemic in Australia found no association between IHT and mortality (12). Combining the findings of the present study with the previous literature makes it reasonable to argue that IHT of ICU patients does not appear to increase mortality. Nevertheless, there may be other drawbacks to IHTs, such as hospital-acquired infections, discontinued care, information gaps or patients being intubated to ensure safe transport, which may prolong the hospital stay (24, 25).

The observed absence of increased mortality risk associated with the transfer may be explained by the fact that patients with recovery potential were carefully selected to be stable enough to tolerate transport safely. This aligns with the results from the abovementioned French study (15). Furthermore, the technical difficulties associated with transporting patients with high-flow oxygen therapy with high oxygen fractions most likely contributed to the decision to avoid such transfers, which was reflected in our study where mechanical ventilation was more common in the transferred group.

The main methodological strengths of this study were the comprehensive data collection conducted by dedicated researchers during the three pandemic waves and validated by independent researchers, the low proportion of missing data, and the adjustment for known confounders in the analyses. Among the main weaknesses are the single-centre design and the non-randomised design. There may be a selection bias in the study, with patients on invasive ventilation and therefore with a secured airway and having limitations of care to a lesser extent, such as do not resuscitate orders, in the transferred group. This might explain the lower OR for mortality in the adjusted analysis and also the longer ICU LOS, as the treatments were not discontinued. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

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> Assessing illness during transport and comparing different patient groups presents several challenges. Information about the severity of illness immediately before transport, which might be more appropriate to include in the analyses than the severity of illness at ICU admission, was not readily available. We did not find sufficient and reliable data to analyse this in our cohort. Furthermore, we have not investigated patients' functional status after ICU discharge, which is of high importance for evaluating surviving patients' wellbeing.

Differences in mortality between countries may depend on variations in healthcare structure and the degree of burden that the country and the healthcare organisation experienced during the pandemic. Well-established routines for transport, availability of advanced medical transport equipment, and access to the same electronic patient data management systems for transferring and admitting centres may also influence the safety of transport. However, taken together, the findings of this study may be somewhat generalisable to countries with similar demographics, pandemic situations and healthcare to X. Future studies should focus on whether certain patient characteristics are predictive of safe transfers, and should study the effects of transfers on surviving patients' ability to recover. Furthermore, it is important to explore various types of complications related to IHT and long-term outcomes to identify factors that may influence treatment outcomes and thereby improve care.

CONCLUSIONS

This study indicates that interhospital transfer due to capacity constraints among patients with critical COVID-19 was associated with lower mortality but an extended length of ICU stay, probably due to the need for invasive ventilation among transferred patients and not

the transfer per se. Suitability for transfer is probably associated with lower mortality, and residual confounding cannot be excluded.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualisation, methodology, design: X, X, X, X, X, X. Analysis: X, X and X. Writing of the original draft: X, X, X. Review and editing: All authors. Final approval of submitted manuscript: All authors.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

PATIENT AND PUBLIC INVOLVEMENT

Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

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Table 1. Characteristics of patients admitted to an ICU for SARS-CoV-2	2
	-

All patients	Non-IHT patients	IHT patients	p-value
665	532 (80)	133 (20)	
64 (55–72)	64 (55–72)	65 (57–71)	ns
		× ,	ns
479 (72)	376 (71)	103 (77.4)	
186 (28)	156 (29)	30 (23)	
			ns
253(38)	202 (38)	51 (38)	
406 (62)	324 (61)	82 (62)	
	58 (47-67)	57 (49-65)	ns
		<u> </u>	ns
248 (37)	197 (37)	51 (38)	
250 (38)	198 (37)	52 (39)	
167 (25)	137 (26)	30 (23)	
			<0.001*
344 (52)	213 (40)	131 (98)	
321 (48)	319 (60)	2 (2)	
			0.001*
	10		
83 (12)	78 (15)	5 (4)	
582 (88)	454 (85)	128 (96)	
			ns
265 (40)	218 (41)	47 (35)	
400 (60)	314(59)	86 (65)	
()	()		1
	665 64 (55–72) 479 (72) 186 (28) 253(38) 406 (62) 248 (37) 250 (38) 167 (25) 344 (52) 321 (48) 83 (12) 582 (88) 265 (40)	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

Table 2. Risk of death 30 days and 90 days after interhospital transfer among critically ill patients with SARS-CoV-2 presented as hazard ratios with 95% CI (Non-IHT as reference)

	Exposure	Mor	tality	30-day m	ortality	90-day m	ortality
Variables	No (%)	30 days	90 days	Unadjusted model	Adjusted model	Unadjusted model	Adjusted model
		No (%)	No (%)	Hazard ratios 95% Cl	Hazard ratios 95% Cl	Hazard ratios 95% Cl	Hazard ratios 95% Cl
All patients		D,					
Non-IHT	532 (80)	136 (26)	157 (30)	1.0 (referent)	1.0 (referent)	1.0 (referent)	1.0 (referent)
IHT	133 (20)	25 (19)	34 (26)	0.66 (0.43– 1.02)	0.47 (0.30– 0.76) *	0.79 (0.54– 1.14)	0.52 (0.34– 0.78) *

The models were adjusted for age, sex, BMI categories (<30 or >30), SAPS, Charlson Comorbidity Index (0, 1, >2), mechanical ventilation (yes/no), treatment limitations (yes/no) and SARS-CoV-2 wave (wave 1/waves 2–3). *Statistically significant differences between groups, p<0.05

Abbreviations: IHT: inter-hospital transport; CI: confidence interval.

able 3. Sen azard ratio	sitivity analyse s with 95% Cl	es regarding th (Non-IHT as re	ie risk of 30-day ference	v and 90-day mortality af	ter interhospital trans	feuding for	Bength of ICU stay p	resented as
				Risk of death for IHT by le	ength of ICU stay	use use		
	Exposure	Mort	ality	, 30-day mortality	HR with 95% Cl	s re	90-day mortality	HR with 95% Cl
ICU LOS	· · · · · · · · · · · · · · · · · · ·		,	Unadjusted	Adjusted	ate	Unadjusted	Adjusted
>6 days				,	,	d d e	ў	,
, Non-IHT	241 (65)	70 (29)	83 (34)	1.0 (referent)	1.0 (referent)	ont s	1.0 (referent)	1.0 (referent)
IHT	127 (35)	25 (20)	34 (27)	0.62 (0.39–0.97)*	0.42 (0.26–0.68) *		0.70 (0.47–1.05)	0.45 (0.29–0.69)
>8 days		. ,		. ,		and		
Non-IHT	187	57(31)	69 (37)	1.0 (referent)	1.0 (referent)	da ur d	1.0 (referent)	1.0 (referent)
IHT	118	24(20)	33 (28)	0.61 (0.38–0.98)*	0.40 (0.24–0.67)*		0.69 (0.45–1.04)	0.43 (0.28–0.67)
>10 days						nin		
, Non-IHT	161	49 (30)	61 (38)	1.0 (referent)	1.0 (referent)	ng.	1.0 (referent)	1.0 (referent)
IHT	106	22 (21)	31 (29)	0.63 (0.38-1.05)	0.46 (0.27–0.78)*	2	0.71 (0.46–1.09)	0.49 (0.31–0.77)
>12 days		× ,			•	trai		
Non-IHT	147 (60)	44 (30)	55 (37)	1.0 (referent)	1.0 (referent)	nin	1.0 (referent)	1.0 (referent)
IHT	94 (40)	21 (22)	30 (32)	0.71 (0.42–1.19)	0.48 (0.28–0.85)*	9, a	0.80 (0.51–1.25)	0.53 (0.33-0.85)
						nd		
<0.05	ns: LOS: length	of stay; ICU: i	ntensive care u	nit; IHT: inter-hospital tr	ansfer; HR: hazard rati	technologies.	onfidence interval	



Supplementary figure 1. Kaplan-Meier curve showing survival to day 30 from ICU admission for patients with SARS-CoV-2 infection in Sweden between 1 March 2020 and 30 June 2021.

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Supplementary figure 2. Kaplan-Meier curve showing survival to day 90 from ICU admission for patients with SARS-CoV-2 infection in Sweden between 1 March 2020 and 30 June 2021.



Supplementary figure 3. Days alive and free of ICU within 30 and 90 days.



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Supplementary Figure 4. Patient distribution of 90 days mortality by ICU day of

transfer

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For the group without mechanical ventilation (total 321, 319 without IHT and two with IHT), neither of the two patients with exposure to IHT died within either 30 or 90 days compared to the 66 patients (21%) in the group without mechanical ventilation in the group not exposed to IHT. Due to the small number of patients and no event in the group without mechanical ventilation and IHT, the analyses were neither of interest nor statistically appropriate.

When analysing only the subgroup of patients with mechanical ventilation (total 344, 213 without IHT and 131 with IHT), the results showed a reduced risk of death in both the univariate model, HR 0.51 (95% CI 0.32–0.81) for 30-day mortality and HR 0.60 (95% CI 0.40–0.89) for 90-day mortality, and the multivariate model, HR 0.40 (95% CI 0.25–0.65) for 30-day mortality and HR 0.45 (95% CI 0.30–0.68) for 90-day mortality.

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For the group with treatment limitations (total 83, 78 without IHT and five with IHT), three patients (60 %) with exposure to IHT died within 30 and 90 days compared to the 55 (66%) and 58 (70%) with no exposure to IHT in 30 and 90 days, respectively. Even though the percentage was about the same in the two groups, the analysis was not carried out due to the small number of patients exposed to IHT with treatment limitations. For the patient group without treatment limitations (total 582, 454 without IHT and 128 with IHT), the results were the same as in the original models, showing no difference between patients without exposure to IHT compared to patients with exposure in the univariate model, HR 0.92 (0.58-1.48) for 30-day mortality and HR 1.08 (95% CI 0.72–1.60) for 90-day mortality, and a difference in the multivariate model, HR 0.38 (95% CI 0.23–0.62) for 30-day mortality and HR 0.45 (95% CI 0.29–0.68) for 90-day mortality.

For the group of patients treated during the first COVID-19 wave (total 265, 218 without IHT and 47 with IHT), the results showed a reduced risk of death in the univariate analyses for 30-day mortality, HR 0.26 (95% CI 0.10-0.73). For the univariate analyses for 90-day mortality and the multivariate analyses for both the 30and 90-day mortality, the results were unchanged, HR 0.44 (95% CI 0.20-0.96), HR 0.24 (95% CI 0.08-0.66) and HR 0.38 (95% CI 0.17-0.85). For the group treated during COVID waves 2 and 3 (total of 400, 314 without IHT and 86 with IHT), the results also differed from the original multivariate models. In this subgroup, there was still no difference between patients with and without exposure to IHT in the univariate models, with HR 0.95 (95% CI 0.58 to 1.54) for 30-day mortality and HR 1.01 (95% CI 0.65–1.54) for 90-day mortality. However, contrary to the findings in the whole cohort, there was no longer a difference in the associated risk of 30- and 90-day mortality in the multivariate models, HR 0.68 (95% CI 0.38-1.18) and HR 0.63 (95% CI 0.38-1.04)

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Supplementary Table 6. Characteristics of mechanically ventilated patients admitted to an	۱
ICU for SARS-CoV-2 (non-invasive ventilated patients were excluded)	

	All patients	Non-IHT patients	IHT patients	p-value
Total number (%)	344	213	131	
Age, median (IQR)	64 (55–71)	64 (55–71)	65 (57–72)	ns
Sex, n (%)				ns
Men	258 (75)	157 (74)	101 (77)	
Women	86 (25)	56 (26)	30 (23)	
BMI, n (%)	(n=341)	(n=210)		ns –
>30	139 (41)	89 (42)	50 (38)	rot
<30	202 (59)	121 (58)	81 (62)	ect
SAPS 3, median (IQR)	57 (53–63)	57 (53–63)	57 (53–63)	ns e
CCI category, n (%)				ns y co
0	132 (38)	82 (39)	50 (38)	руг
1	133 (39)	81 (38)	52 (40)	Ign
≥ 2	70 (23)	50 (23)	29 (22)	, II
Limitations on life-				ns c
sustaining treatments, n (%)	0			guipi
Yes	16 (5)	11 (5)	5 (4)	lor
No	328 (95)	202 (95)	126 (96)	us
COVID-19 period, n (%)				0.003* 3
Wave 1	160 (47)	113 (53)	47 (36)	ea
Waves 2–3	184 (53)	100 (47)	84 (64)	ted
				6
				tex

Abbreviations: BMI: body mass index; SAPS 3: Simplified Acute Physiology Score 3; CCI: Charlson Comorbidity Index score; SD: standard deviation; ns=no statistically significant differences, *p<0.05 statistically significant differences

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Interhospital transports and mortality in patients with critical COVID-19: a single-centre cohort study

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ABSTRACT

2 Objectives

- 3 This study aimed to compare mortality rates and length of hospital stay between patients
- 4 with critical COVID-19 transferred to another hospital due to capacity constraints and those
- 5 who remained at their initial admission hospital.
- 6 Design
- 7 Single-centre cohort study
- 8 Setting and participants

9 Six hundred and sixty-five patients treated for SARS-CoV-2 at two intensive care units (ICU)
10 in Stockholm, Sweden from 1 March 2020 to 30 June 2021. Data on interhospital transfers
11 were retrieved from medical records and patient data management systems according to

12 pre-defined protocols.

13 Main outcome measures

The outcomes were 30- and 90-day mortality, days alive and out of ICU. Hazard ratios (HR)
with 95% confidence intervals (CI) were calculated using Cox proportional hazard models
with adjustments for age, sex, body mass index, severity of illness, comorbidity, invasive
ventilation, treatment limitations and pandemic waves.

18 Results

19 Of 665 patients, 133 (20%) were transferred to another hospital. The mortality rate for

20 transferred patients compared to non-transferred patients at 30 days was 19% versus 26%

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(p=0.13) and at 90 days 26% versus 30% (p = 0.43). In the adjusted Cox regression analysis,

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interhospital transfer was associated with a lower mortality risk at 30 days (HR 0.47, 95% CI: 0.30-0.76) and 90 days (HR 0.52, 95% CI: 0.34-0.79). However, the number of days alive and out of ICU was significantly lower for the IHT group at 30 and 90 days. Conclusion In our study, interhospital transfer due to capacity constraints among critically ill COVID-19 patients was not associated with a higher mortality risk. The suitability for transfer was likely associated with lower mortality, although residual confounding cannot be ruled out. The requirement for invasive ventilation among transferred patients might account for the extended length of ICU stay, rather than the transfer itself. However, the difficulty in studying this issue lies in the fact that while patients are likely exposed to risks during transfer, they are simultaneously the patients stable enough to be transported. Strengths and limitations of this study The strengths are the comprehensive data collection conducted by dedicated researchers during the three pandemic waves and validated by independent researchers. The low proportion of missing data, and the adjustment for known confounders in the analyses. The main weakness is the single-centre non-randomised design. There may be a risk of selection bias in the study since it is likely that respiratory – and hemodynamic-stable patients with recovery potential were selected for transport.

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 Information about the severity of illness immediately before transport was not readily available in our cohort.

45 BACKGROUND

Transports of critically ill patients between intensive care units (ICUs) across hospitals are relatively common. The primary reasons include the need to transfer to a hospital with specialised competence, as well as capacity constraints at the transferring hospital ¹⁻³. Regardless of the reason for the transport, studies have shown that patient transfers entail direct risks related to the transport itself and can be linked to delayed diagnostics or treatments ¹⁴⁻⁸. In the years before the COVID-19 pandemic, around 600 ICU patients (1.8%) were transported between hospitals in Sweden each year due to resource shortages at the sending ICU. However, during the pandemic, the influx of patients requiring ICU treatment significantly increased interhospital transfers (IHTs) to 3.5% 9.

Studies investigating the risk of IHT during the COVID-19 pandemic have shown conflicting results. Some studies indicate that IHT is not associated with an increased mortality risk ^{2 10-} ¹³ or may even be associated with a lower risk of death ¹⁴, whereas others have shown that IHT is associated with a longer duration of mechanical ventilation ¹⁰⁻¹², ICU stay ¹¹ and length of hospital stay ²¹¹¹². None of these studies were randomised controlled trials, and many were limited by a small sample size ^{2 10 13}. Despite the large increase in ICU beds in Sweden during the pandemic, a substantial proportion of critically ill patients were transferred between hospitals. To the best of our knowledge, no study has so far studied the influence of IHTs on patient outcomes during the COVID-19 pandemic in Sweden. Therefore, we aimed to compare mortality rates and length of hospital stay between patients transferred to
METHODS

Study design

This study included all adult patients (age \geq 18 years) with confirmed SARS-CoV-2, as verified by polymerase chain reaction test, requiring intensive care at Södersjukhuset, Sweden, between 1 March 2020 and 30 June 2021. The hospital is a secondary referral centre, serving a diverse range of medical and surgical patients in Stockholm, a city with 2.5 million inhabitants. The hospital has a total capacity of 600 beds and houses a large emergency department with a continuous inflow of acutely ill patients. Healthcare in Sweden is predominantly funded by taxes, ensuring access to medical services for all citizens. Normally, there are 18 beds dedicated to intensive care. However, during the COVID-19 pandemic, the ICUs expanded to accommodate a total of 60 ICU beds. The study was approved by the Swedish Ethical Review Authority (Dnr: 2023-01778-01-380347, amendment 2023-01778-01), and the requirement for written informed consent from patients was waived. The reporting of the study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines ¹⁵. Cohort All adult patients with a SARS-CoV-2 diagnosis and initial admission at the study hospital's ICU were eligible for inclusion in the study. Patients first admitted to other ICUs and

subsequently transferred to the study hospital were excluded. Additionally, patients transferred due to reasons other than capacity constraints, such as repatriation (return to a

local ICU near the patient's home) and clinical transfers (requiring specialized care not

available at the admitting hospital) were excluded from the study.

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Patients were identified using the patient data management system. Clinical data were automatically and manually extracted from medical records and the patient data management system using a pre-defined data collection protocol to ensure consistency and uniformity of the data collection. Cross-validation of data from randomly selected patients was performed separately by two independent researchers. Exposure The exposure was Interhospital Transfer (IHT), specifically defined as the transfer of patients from the Intensive Care Unit (ICU) at the index hospital to another hospital's ICU due to capacity constraints. These constraints typically involve a shortage of staffed ICU beds at the referring hospital, necessitating the transfer of patients to ensure they receive the critical care they need. The interhospital transfers were conducted in accordance with the transport recommendations provided by the Swedish Society for Anaesthesia and Intensive Care. These guidelines ensure that transfers are carried out safely and efficiently, minimising risks to the patient during transport. The guidelines cover various aspects, such as patient stability before the transfer, necessary medical equipment during the transfer, and the qualifications of the medical personnel accompanying the patient. The transfers were crucial for managing ICU capacity and ensuring that patients continue to receive appropriate care without delay ¹⁶. The selection of patients for transfer was commonly carried out in consultation with the admitting ICU. The decision was based on the patient's physiological status to ensure safe transport and the receiving hospital's capacity to provide the required care. This process did not adhere to a standardized protocol or guideline; rather, it relied on the clinical judgment of senior physicians, who made joint decisions about which patient was most suitable for

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112	transfer, based on various clinical factors and the urgency of the situation. The decision-
113	making process involved assessing the patient's condition, stability, and the potential risks
114	and benefits of transfer aiming to ensure that the patient most in need of ICU care at
115	another facility was selected for transfer, taking into consideration the overall capacity and
116	resources of both the referring and receiving hospitals. The lack of a standardized protocol
117	meant that decisions were tailored to individual cases relying of clinical expertise and
118	teamwork in managing ICU capacity and patient care.
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119	The transport was prepared according to local routines, and handover was reported by
120	telephone. ICU patients in Stockholm are commonly transported between hospitals using a
121	mobile intensive care unit (MICU). A MICU is staffed with one ambulance nurse, one
122	paramedic and one physician from the departing intensive care unit. The MICU transporter is
123	more spacious than a standard ambulance and is equipped with continuous
124	electrocardiography monitoring, invasive hemodynamic monitoring and advanced
125	ventilatory support. Information about the date, time and reasons for transfer was obtained
126	from the patient's medical records and the patient data management system.
127	Outcomes
128	The outcomes were mortality at days 30 and 90 from ICU admission and days alive and out
129	of ICU. The length of ICU stay was measured from the date of ICU admission to the date of
130	discharge from the ICU at Södersjukhuset or the admitting hospital.
131	
132	Statistical analysis

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Continuous variables are presented as medians with interguartile ranges (IQRs), and categorical variables are expressed as numbers and proportions (percentages). The distribution of continuous variables was tested with the Shapiro-Wilk test. Differences between groups were analysed using the Mann-Whitney U test and the Chi² test for continuous and categorical variables, respectively. In the survival analyses, patients were followed up from the date of ICU admission until the date of death or until 30 and 90 days had passed since admission. Kaplan–Meier curves were used to estimate the cumulative risk of death, and the log-rank test was employed to compare patients with exposure to IHT versus those without IHT. Cox proportional hazards regression was used to estimate hazard ratios (HR) with corresponding 95% confidence intervals (CI) for death within 30 and 90 days from ICU admission. Multivariate models were adjusted for age (continuous), sex (male/female), body mass index ($<30/\geq30$ kg/m²), Simplified Acute Physiology Score III (SAPS III) (>50/50–59/≥60), Charlson Comorbidity Index (categorised as 0/1/2) ¹⁷, invasive mechanical ventilation (yes/no), treatment limitations (yes/no), COVID waves (first wave, March to September 2020 versus second and third waves, October 2020 to January 2021 and February to June 2021¹⁸) and IHT (yes/no). Both crude and multivariable models were investigated with no IHT as the reference group. Scaled Schoenfeld residuals were regressed against survival time to assess the proportional hazard assumptions, and Martingale residual plots, together with the Grambsch-Therneau test, were used to assess evidence of non-linearity. Variance inflation factors were used when investigating multicollinearity. All variables were complete except for SAPS and BMI which were missing for 105 and 6 patients, respectively. This was handled by a separate category

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for patients with missing values.

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Since the proportional hazards assumption in the Cox regression was not met, indicating that the effect of the variables could vary over time, we performed sensitivity analyses on subgroups of patients based on length of ICU stay (more than 6, 8, 10 and 12 days), COVID waves, mechanical ventilation and treatment limitations. Comparisons of days alive free from ICU were conducted using the Mann-Whitney U test and presented as medians with interquartile ranges (IQRs).

A two-sided p-value less than 0.05 was considered statistically significant. The analysis followed a predefined protocol and was conducted using the IBM SPSS Statistics version 29 statistical software and R version 4.3.3 (R Core, 2017. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria). All analyses were discussed and confirmed with an experienced biostatistician.

RESULTS

Patient cohort

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Of 2622 critically ill patients admitted to the two ICUs during the study period, 674 had a

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48	184
49 50	105
51	185
52	107
53	186
54 55	107
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confirmed SARS-CoV-2 diagnosis. Nine patients were transported to other hospitals for
tertiary care (e.g. ECMO) and five patients had been transferred to the study hospital from
other hospitals/regions. In total, 665 SARS-CoV-2 patients were included in the study, of
which 133 (20%) underwent interhospital transports due to capacity constraints (Figure 1).
All patients (n=133) were transported to a hospital within a 30-kilometer radius or maximum
of 30 minutes.
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The median age of included patients was 64 years, and most were men (72%). Patients who
were transferred were more often on mechanical ventilation (98%) compared with the non-
transferred patients (40%), and fewer had limitations in terms of life-sustaining treatment
(4% versus 15%). Otherwise, the groups were balanced regarding patient and clinical
characteristics (Table 1). The median day of IHT from admission was 6 (IQR: 3–11).
Interhospital capacity transfer and mortality

33 Analyses of IHT and mortality in patients with critical COVID-19 are shown in Table 2. Mortality rates did not differ between groups at either 30 days (19% vs. 26%, p = 0.13) or 90 34 35 days (26% vs. 30%, p = 0.43). This was consistent across the log-rank test for survival for 30 6 days (Figure 2, p = 0.06) and 90 days (Figure 3, p = 0.2), as well as the HR of the univariate 37 Cox regression of 0.66 (95% CI: 0.43–1.02) for 30-day mortality and 0.79 (95% CI: 0.54–1.14) 88 for 90-day mortality. When the exposure of IHT was analysed in the multivariate model, it

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189 was associated with a lower risk of mortality for both 30 days (HR 0.47, 95% CI: 0.30–0.76)
190 and 90 days (HR 0.52, 95% CI: 0.34–0.79) (Table 2).

As the assumptions of proportional hazards were violated when scaled Schoenfeld residuals were regressed against survival time (p <0.001 for the multivariate model for 30- and 90-day mortality), sensitivity analyses were performed. When splitting the time and analysing by different lengths of stay (LOS) at the ICU, the assumptions were fulfilled for patients with a LOS of eight days and above (p = 0.14 for 30-day mortality and p = 0.09 for 90-day mortality). The results did not differ from the original models except for IHT being associated with lower 30-day mortality, including in the univariate analyses for patients with an ICU LOS of more than six and eight days (Table 3). Schoenfeld residuals indicated violations of proportional hazard assumptions, including for the covariates of mechanical ventilation, treatment limitations and COVID-19 wave in the multivariate models for 30 and 90 days. This issue was addressed by examining the various categories within these variables as subgroups. The reason for the violation of the variables of mechanical ventilation and treatment limitations was a small number of patients/events in the groups of patients without mechanical ventilation exposed to IHT and the group with treatment limitations exposed to IHT. When analysing the subgroup of only mechanically ventilated patients, the results changed in the univariate models, showing a lower risk of mortality for 30 days (19.3% versus 32.9%, p=0.008) and 90 days (26.0% versus 38.0%, p=0.029) in the IHT group compared to the non-IHT group. In the multivariate models, the decrease in mortality for the IHT group at 30 and 90 days remained unchanged. Excluding patients with treatment limitations did not change the results.

211 Interhospital capacity transfer and mortality by COVID-19 wave

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2 3	212	For the group of patients treated during the first COVID-19 wave, the univariate analyses for
4 5	212	20 down and the showed a reduced risk of death with a horizont ratio (UD) of 0.20 (000 Ch
6 7	213	30-day mortality showed a reduced risk of death, with a hazard ratio (HR) of 0.26 (95% CI:
8 9	214	0.10–0.73). The univariate analyses for 90-day mortality and the multivariate analyses for
10 11	215	both 30- and 90-day mortality remained consistent, with HRs of 0.44 (95% CI: 0.20–0.96),
12 13 14	216	0.24 (95% CI: 0.08–0.66), and 0.38 (95% CI: 0.17–0.85), respectively (Table 4).
15 16	217	For the group treated during the second and third COVID-19 waves, the results differed from
17 18	218	the original multivariate models. In this subgroup, there was still no significant difference
19 20 21	219	between patients with and without IHT in the univariate models, with HRs of 0.95 (95% CI:
22 23	220	0.58–1.54) for 30-day mortality and 1.01 (95% CI: 0.65–1.54) for 90-day mortality. However,
24 25	221	unlike the findings in the whole cohort, there was no longer a significant difference in the
26 27 28	222	associated risk of 30- and 90-day mortality in the multivariate models, with HRs of 0.68 (95%
29 30	223	CI: 0.38–1.18) and 0.63 (95% CI: 0.38–1.04), respectively (Table 4).
31 32		
33 34 35	224	More details regarding the subgroup analyses can be found in Supplementary files 1-3.
36 37 38 39	225	Interhospital transfer and days alive free of ICU
40 41	226	Compared with non-IHT patients, IHT patients had in median fewer days alive and free from
42 43 44	227	the ICU at 30 days (5, IQR: 0–18 versus 22, IQR: 0–27, p<0.001) and 90 days (64, IQR: 27–78
45 46	228	versus 81, IQR: 6–87, p=0.86) respectively (Figure 4). However, for mechanically ventilated
47 48	229	patients, there were no statistically significant median differences between the groups at 30
49 50 51	230	days (5, IQR: 0–18 versus 2, IQR: 0–16, p=0.31) or 90 days (63, IQR: 24–78 versus 60, IQR: 0–
52 53	231	75, p=0.14).
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56 57	232	DISCUSSION
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In this study, transfers solely due to capacity constraints during the COVID-19 pandemic were not associated with a higher risk of 30- and 90-day mortality among patients with critical COVID-19. Our results indicated that such transfers may even be associated with a lower mortality risk, especially for mechanically ventilated patients. Interhospital transfer was associated with a longer ICU LOS compared with patients who remained in the admitting ICU. This was probably explained by the higher prevalence of invasive ventilation among transferred patients.

The risk of interhospital transfer has been investigated to some extent in observational studies, albeit with conflicting results. A Swedish register-based study of 2,912 capacity-transferred ICU patients before the pandemic found that transportation was associated with a lower risk of death within 90 days (odds ratio 0.71, 95% CI: 0.65–0.79)¹⁹. Conversely, another Swedish study including 11,176 ICU patients showed a higher risk of 30-day mortality after capacity transfers (odds ratio 1.25, 95% CI: 1.06–1.49) and clinical transfers (odds ratio 1.17, 95% CI: 1.02–1.36)²⁰. However, the reference consisted of repatriated patients. While we excluded such patients in our study, other studies have confirmed that clinical transfer to a higher level of care is associated with better patient outcomes ^{21 22}. A French cohort study of 18,348 COVID-19 patients in the ICU found that transferred patients had a lower mortality rate than non-transferred patients, concluding that this might be due to a rigorous selection process of patients eligible for transfer ¹⁴. However, the study only included patients from the first wave of the pandemic. This finding resembles ours, where the results were driven by lower mortality in IHT patients during the first COVID wave. A retrospective cohort study including 5,207 patients mostly with SARS-CoV-2 during wave 3 of the pandemic in Australia found no association between IHT and mortality ¹¹. The difference

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3 4	257	in outcomes between the pandemic waves may be attributed to changes in healthcare
5 6 7	258	conditions among patients and the accumulated experience in managing the disease.
7 8 9	259	Although capacity constraints remained high during the pandemic waves, the outcomes
10 11	260	improved due to the learning curve in treating COVID-19 patients and the implementation of
12 13 14	261	standardized treatments.
15 16 17	262	Combining the findings of the present study with the previous literature makes it
18 19	263	reasonable to argue that IHT of ICU patients does not appear to increase mortality.
20 21 22	264	Nevertheless, there may be other drawbacks to IHTs, such as hospital-acquired infections,
23 24	265	discontinued care, information gaps or patients being intubated to ensure safe transport,
25 26 27	266	which may prolong the hospital stay ^{23 24} .
28 29 30	267	The observed absence of increased mortality risk associated with the transfer may be
31 32	268	explained by the fact that patients with recovery potential were carefully selected to be
33 34 35	269	stable enough to tolerate transport safely. This aligns with the results from the above-
36 37	270	mentioned French study ¹⁴ . Furthermore, the technical difficulties associated with
38 39	271	transporting patients with high-flow oxygen therapy with high oxygen fractions most likely
40 41 42	272	contributed to the decision to avoid such transfers, which was reflected in our study where
43 44 45	273	mechanical ventilation was more common in the transferred group.
46 47 48	274	
49 50 51	275	The main methodological strengths of this study were the comprehensive data collection
52 53	276	conducted by dedicated researchers during the three pandemic waves and validated by
54 55	277	independent researchers, the low proportion of missing data, and the adjustment for known
56 57 58 59	278	confounders in the analyses. Among the main weaknesses are the single-centre design and
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3	279	the non-randomised design.
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, 8	281	lesser extent such as do not
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42	295	national context. However
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50	298	leading to a gap at one of th
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52	299	than patient-related factors
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54 55	300	characteristics and diagnose
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57	301	assumption that the missing
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There may be a selection bias in the study, with patients on refore with a secured airway and having limitations of care to a t resuscitate orders, in the transferred group. This difference for mortality in the adjusted analysis and also the longer ICU e not discontinued. In this study, we selected mortality and days ne of the outcome measures. However, we acknowledge that Ild have been another valuable parameter to assess the impact measure could provide additional insights into the safety of ssing illness during transport and comparing different patient llenges. Information about the severity of illness immediately the more appropriate to include in the analyses than the nission, was not readily available. We did not find sufficient and in our cohort. Furthermore, we used SAPS III to assess illness commonly used systems like APACHE II or IV. SAPS III is the intensive care patients in Sweden and is utilised for reporting to Register (SIR), ensuring consistency and accuracy within the this choice may limit the direct comparability of our results with systems. Fourteen per cent of SAPS data were missing. The ue to manual documentation processes during the pandemic, e ICUs. This gap was likely caused by work-related issues rather . Patients across the two ICUs were similar in clinical es, and all other variables were complete, supporting the data were random. We also conducted a sensitivity analysis

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3	02	with complete cases and the results remained unchanged. Another issue was that lifestyle
3	03	factors such as smoking, physical activity, and alcohol consumption, as well as socio-
3	04	economic variables like deprivation, education, and employment status, were not available
3	05	in our dataset. As such, we were unable to adjust for these variables in the analysis.
3	06	Furthermore, we have not investigated patients' functional status after ICU discharge, which
3	07	is of high importance for evaluating surviving patients' well-being.
3	08	Differences in mortality between countries may depend on variations in healthcare structure
3	09	and the degree of burden that the country and the healthcare organisation experienced
3	10	during the pandemic. Well-established routines for transport, availability of advanced
3	11	medical transport equipment, and access to the same electronic patient data management
3	12	systems for transferring and admitting centres may also influence the safety of transport.
3	13	The findings of this study may be somewhat representative to countries with comparable
3	14	population structures, healthcare systems, and pandemic responses. The use of standardised
3	15	healthcare protocols ensures consistency in patient care and treatment, which can make the
3	16	results of this study applicable to other regions facing similar challenges. Future studies
3	17	should focus on whether certain patient characteristics are predictive of safe transfers and
3	18	should study the effects of transfers on surviving patients' ability to recover. Furthermore, it
3	19	is important to explore various types of complications related to IHT and long-term
3	20	outcomes to identify factors that may influence treatment outcomes and thereby improve
3	21	care.
3	22	CONCLUSIONS
3	23	In our study interhospital transfer due to capacity constraints among critically ill COVID-19

⁸ 324 patients was not associated with a higher mortality risk. The suitability for transfer was likely

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3 4	325	associated with lower mortality, although residual confounding cannot be ruled out. The
5 6 7	326	requirement for invasive ventilation among transferred patients might account for the
7 8 9	327	extended length of ICU stay, rather than the transfer itself. However, the difficulty in
10 11	328	studying this issue lies in the fact that while patients are likely exposed to risks during
12 13 14 15	329	transfer, they are simultaneously the patients stable enough to be transported.
16 17 18	330	ACKNOWLEDGEMENTS
19 20 21	331	Special thanks to MD Jacob Litorell for developing, validating, and maintaining the COVID-19
21 22 23	332	database we used in this study.
24 25 26 27	333	FUNDING
28 29 30	334	The study was supported by grants from the Swedish patient insurance company (LÖF). The
31 32 33	335	funders had no role in the design or conduct of the study.
34 35 36	336	CONFLICT OF INTEREST STATEMENT
37 38 39 40	337	The authors declare no conflict of interest.
41 42 43	338	AUTHOR CONTRIBUTIONS
44 45 46	339	KB: Conceptualisation, methodology, design, analysis, writing the original draft, review and
47 48 40	340	editing. LTA: Conceptualisation, methodology, design, writing the original draft, review and
50 51	341	editing. PS: conceptualisation, methodology, design, review and editing. MC:
52 53	342	Conceptualisation, methodology, design, review and editing. SJ: conceptualisation,
55 56 57 58 59	343	methodology, design, analysis, review and editing. EJA: conceptualisation, methodology,

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3 4	344	design, review and editing. AS: conceptualisation, methodology, design, analysis, writing the
5 6 7	345	original draft, review and editing. AS: are responsible for the overall content as guarantor.
8 9 10 11	346	DATA AVAILABILITY STATEMENT
12 13 14	347	The data that support the findings of this study are available from the corresponding author
15 16 17	348	upon reasonable request.
17 18 19 20	349	PATIENT AND PUBLIC INVOLVEMENT
21 22 23	350	Patients and/or the public were not involved in the design, conduct, reporting or
24 25 26	351	dissemination plans of this research.
27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 9 50 51 52 53 54	352	
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Table 1. Characteristics of patients admitted to an ICU for SARS-CoV-2

Table 2. Risk with 95% CI (	of death 30 Non-IHT as	days and 90 day reference)	ys after interho	BMJ Open ospital transfer among cri	itically ill patients with	by copyright, incading for u	CoV-2 presented as	hazard ratios
				Risk of death after interh	ospital transfers	Ses		
	Exposure	Mort	ality	30-day m	ortality	reig	90-day m	ortality
All patients	No (%)	30-day No (%)	90-day No (%)	Unadjusted HR with 95% CI	Adjusted HR with 95% Cl	Inemer	Unadjusted HR with 95% CI	Adjusted HR with 95% Cl
Non-IHT	532 (80)	136 (26)	157 (30)	1.0 (referent)	1.0 (referent)	te S	1.0 (referent)	1.0 (referent)
IHT	133 (20)	25 (19)	34 (26)	0.66 (0.43-1.02)	0.47 (0.30-0.76)*	upe Xt a	0.79 (0.54–1.14)	0.52 (0.34-0.78)*
						nd		

The models were adjusted for age, sex, BMI categories (<30 or >30), SAPS, Charlson Comorbidity Index (2), mechanical ventilation (yes/no), treatment limitations (yes/no) and SARS-CoV-2 wave (wave 1/waves 2–3). *Statistically significant differences between groups, Al training, and similar technologies bmjopen.bmj.com/ on June 11, 2025 at Agence Bibliographique de l p<0.05

Abbreviations: IHT: inter-hospital transfer; HR: hazard ratio; CI: confidence interval hc

BMJ Open Table 3. The sensitivity analysis presents the risk of 30-day and 90-day mortality following interhospital grants for (IHT), categorised by the length of ICU stay from admission to the day of transfer. The analyses are presented as hazard ratios (H) with 95% confidence intervals (CI), using non-IHT natients as the reference group using non-IHT patients as the reference group. for u Fe

				Risk of death for IHT by the	length of ICU stay	Ses		
	Exposure	Mort	ality	30-day mortality		reig	90-day mortality	
ICU LOS		30-day	90-day	Unadjusted	Adjusted	ner ate	S Unadjusted	Adjusted
	No (%)	No (%)	No (%)	HR with 95% Cl	HR with 95% Cl	d to r	HR with 95% Cl	HR with 95% Cl
>6 days						te te		
Non-IHT	241 (65)	70 (29)	83 (34)	1.0 (referent)	1.0 (referent)	t a	1.0 (referent)	1.0 (referent)
IHT	127 (35)	25 (20)	34 (27)	0.62 (0.39–0.97)*	0.42 (0.26–0.68) *	nd	0.70 (0.47–1.05)	0.45 (0.29–0.69)*
>8 days						dat	<u>,</u>	
Non-IHT	187 (61)	57(31)	69 (37)	1.0 (referent)	1.0 (referent)	AB	1.0 (referent)	1.0 (referent)
IHT	118 (39)	24(20)	33 (28)	0.61 (0.38-0.98)*	0.40 (0.24–0.67)*		0.69 (0.45–1.04)	0.43 (0.28–0.67)*
>10 days						ŋġ, :		
Non-IHT	161 (60)	49 (30)	61 (38)	1.0 (referent)	1.0 (referent)	Alt	1.0 (referent)	1.0 (referent)
IHT	106 (40)	22 (21)	31 (29)	0.63 (0.38–1.05)	0.46 (0.27–0.78)*	rain	0.71 (0.46–1.09)	0.49 (0.31–0.77)*
>12 days			·		0	ling		
Non-IHT	147 (60)	44 (30)	55 (37)	1.0 (referent)	1.0 (referent)	, a	1.0 (referent)	1.0 (referent)
IHT	94 (40)	21 (22)	30 (32)	0.71 (0.42–1.19)	0.48 (0.28-0.85)*	nd :	0.80 (0.51–1.25)	0.53 (0.33–0.85)*
						sim		

The models were adjusted for age, sex, BMI categories (<30 or >30), SAPS, Charlson Comorbidity Index (a), 1% >2), mechanical ventilation (yes/no), treatment limitations (yes/no) and SARS-CoV-2 wave (wave 1 or waves 2/3). *Statistically sign and the set wave set wave groups, p<0.05 ies.

Abbreviations: LOS: length of stay; ICU: intensive care unit; IHT: inter-hospital transfer; HR: hazard ratio; CI: and the care unit; IHT: inter-hospital transfer; HR: hazard ratio; CI:

nce Bibliographique de

 BMJ Open Table 4. The sensitivity analysis presents the risk of 30-day and 90-day mortality following interhospital data by pandemic waves. The analyses are presented as hazard ratios (HR) with 95% confidence intervals (CI), using non-IH patients as the reference group.

				Risk of death for IHT by	COVID-19 wave	gne		
	Exposure	Mortality		30-day mortality		ed	90-day m	ortality
Waves		30-day	90-day	Unadjusted	Adjusted		<b>V</b> nadjusted	Adjusted
	No (%)	No (%)	No (%)	HR with 95% CI	HR with 95% CI	Sup	HR with 95% Cl	HR with 95% Cl
Wave 1						beri		
Non-IHT	218 (82)	61 (28)	64 (29)	1.0 (referent)	1.0 (referent)	eur d da	1.0 (referent)	1.0 (referent)
IHT	47 (18)	4 (9)	7 (15)	0.26 (0.10-0.73)*	0.24 (0.08–0.66)*	ata	0.44 (0.20–0.96)*	0.38 (0.17–0.85)*
Wave 2-3						min		
Non-IHT	314 (78)	75 (24)	93 (30)	1.0 (referent)	1.0 (referent)	ing	1.0 (referent)	1.0 (referent)
IHT	86 (22)	21(24)	27 (31)	0.95 (0.58-1.54)	0.68 (0.38–1.18)	, A	1.01 (0.65–1.54)	0.63 (0.38–1.04)
						<del>.</del>		

The models were adjusted for age, sex, BMI categories (<30 or >30), SAPS, Charlson Comorbidity Index 🕃 1, 22) mechanical ventilation (yes/no), treatment limitations (yes/no) and SARS-CoV-2 wave (wave 1/wave 2-3). *Statistically significant differences between groups, p<0.05

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Abbreviations: IHT: inter-hospital transfer; HR: hazard ratio; CI: confidence interval

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Figure 2. Kaplan-Meier curve showing survival to day 30 from ICU admission for patients with SARS-CoV-2 infection in Sweden between 1 March 2020 and 30 June 2021.

Abbreviations: IHT: Interhospital transport

Figure 3. Kaplan-Meier curve showing survival to day 90 from ICU admission for patients with SARS-CoV-2 infection in Sweden between 1 March 2020 and 30 June 2021.

Abbreviations: IHT: Interhospital transport

Figure 4. Days alive and free of ICU within 30 and 90 days among transferred and non-transferred patients.

Abbreviations: IHT: Interhospital transport

File 1. Mortality distribution among transferred patients in relation to the day of transfer.









Page 310 day mortality by ICU day of transport



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#### SUPPLEMENTARY FILES

#### Supplementary File 2

For the group without mechanical ventilation (total 321, 319 without IHT and two with IHT), neither of the two patients with exposure to IHT died within either 30 or 90 days compared to the 66 patients (21%) in the group without mechanical ventilation in the group not exposed to IHT. Due to the small number of patients and no event in the group without mechanical ventilation and IHT, the analyses were neither of interest nor statistically appropriate. When analysing only the subgroup of patients with mechanical ventilation (total 344, 213 without IHT and 131 with IHT), the results showed a reduced risk of death in both the univariate model, HR 0.51 (95% CI 0.32–0.81) for 30-day mortality and HR 0.60 (95% CI 0.40–0.89) for 90-day mortality, and the multivariate model, HR 0.40 (95% CI 0.25–0.65) for 30-day mortality and HR 0.45 (95% CI 0.30–0.68) for 90-day mortality.

For the group with treatment limitations (total 83, 78 without IHT and five with IHT), three patients (60 %) with exposure to IHT died within 30 and 90 days compared to the 55 (66%) and 58 (70%) with no exposure to IHT in 30 and 90 days, respectively. Even though the percentage was about the same in the two groups, the analysis was not carried out due to the small number of patients exposed to IHT with treatment limitations. For the patient group without treatment limitations (total 582, 454 without IHT and 128 with IHT), the results were the same as in the original models, showing no difference between patients without exposure to IHT compared to patients with exposure in the univariate model, HR 0.92 (0.58-1.48) for 30-day mortality and HR 1.08 (95% CI 0.72–1.60) for 90-day mortality, and a difference in the multivariate model, HR 0.38 (95% CI 0.23–0.62) for 30-day mortality and HR 0.45 (95% CI 0.29–0.68) for 90-day mortality.

# SUPPLEMENTARY FILES

Supplementary file 3 Characteristics of mechanically ventilated patients admitted to a	an ICU
for SARS-CoV-2 (non-invasive ventilated patients were excluded)	

	All patients	Non-IHT patients	IHT patients	p-value
Total number (%)	344	213	131	
Age, median (IQR)	64 (55–71)	64 (55–71)	65 (57–72)	ns
Sex, n (%)				ns
Men	258 (75)	157 (74)	101 (77)	
Women	86 (25)	56 (26)	30 (23)	
BMI, n (%)	(n=341)	(n=210)		ns -
>30	139 (41)	89 (42)	50 (38)	
<30	202 (59)	121 (58)	81 (62)	
SAPS 3, median (IQR)	57 (53–63)	57 (53–63)	57 (53–63)	ns c
CCI category, n (%)				ns
0	132 (38)	82 (39)	50 (38)	3
1	133 (39)	81 (38)	52 (40)	L L L L L L L L L L L L L L L L L L L
≥2	70 (23)	50 (23)	29 (22)	,
Limitations on life- sustaining treatments, n (%)	30			ns
Yes	16 (5)	11 (5)	5 (4)	<u> </u>
No	328 (95)	202 (95)	126 (96)	
COVID-19 period, n (%)			× /	0.003*
Wave 1	160 (47)	113 (53)	47 (36)	
Waves 2–3	184 (53)	100 (47)	84 (64)	
				5

Abbreviations: BMI: body mass index; SAPS 3: Simplified Acute Physiology Score 3; CCI: Charlson Comorbidity Index score; SD: standard deviation; ns=no statistically significant differences, *p<0.05 statistically significant differences. **BMJ** Open

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# Interhospital transports and mortality in patients with critical COVID-19: a single-centre cohort study

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#### 

# ABSTRACT

2 Objectives

- 3 This study aimed to compare mortality rates and length of hospital stay between patients
- 4 with critical COVID-19 transferred to another hospital due to capacity constraints and those
- 5 who remained at their initial admission hospital.
- 6 Design
- 7 Single-centre cohort study
- 8 Setting and participants

9 Six hundred and sixty-five patients treated for SARS-CoV-2 at two intensive care units (ICU)
10 in Stockholm, Sweden from 1 March 2020 to 30 June 2021. Data on interhospital transfers
11 were retrieved from medical records and patient data management systems according to

12 pre-defined protocols.

13 Main outcome measures

The outcomes were 30- and 90-day mortality, days alive and out of ICU. Hazard ratios (HR)
with 95% confidence intervals (CI) were calculated using Cox proportional hazard models
with adjustments for age, sex, body mass index, severity of illness, comorbidity, invasive
ventilation, treatment limitations and pandemic waves.

18 Results

19 Of 665 patients, 133 (20%) were transferred to another hospital. The mortality rate for

20 transferred patients compared to non-transferred patients at 30 days was 19% versus 26%

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21	(p=0.13) and at 90 days 26% versus 30% (p = 0.43). In the adjusted Cox regression analysis,
22	interhospital transfer was associated with a lower mortality risk at 30 days (HR 0.47, 95% CI:
23	0.30–0.76) and 90 days (HR 0.52, 95% CI: 0.34–0.79). However, the number of days alive and
24	out of ICU was significantly lower for the IHT group at 30 days.
25	Conclusion
26	In our study, interhospital transfer due to capacity constraints among critically ill COVID-19
27	patients was not associated with a higher mortality risk. The suitability for transfer was likely
28	associated with lower mortality, although residual confounding cannot be ruled out. The
29	requirement for invasive ventilation among transferred patients might account for the
30	extended length of ICU stay, rather than the transfer itself. However, the difficulty in
31	studying this issue lies in the fact that while patients are likely exposed to risks during
32	transfer, they are simultaneously the patients stable enough to be transported.
33	Strengths and limitations of this study
34	The strengths are the comprehensive data collection conducted by dedicated
35	researchers during the three pandemic waves and validated by independent
36	researchers.
37	• The low proportion of missing data, and the adjustment for known confounders in
38	the analyses.
39	• The main weakness is the single-centre non-randomised design.
40	• There may be a risk of selection bias in the study since it is likely that respiratory –
41	and hemodynamic-stable patients with recovery potential were selected for
42	transport.

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 Information about the severity of illness immediately before transport was not readily available in our cohort.

# 45 BACKGROUND

Transports of critically ill patients between intensive care units (ICUs) across hospitals are relatively common. The primary reasons include the need to transfer to a hospital with specialised competence, as well as capacity constraints at the transferring hospital ¹⁻³. Regardless of the reason for the transport, studies have shown that patient transfers entail direct risks related to the transport itself and can be linked to delayed diagnostics or treatments ¹⁴⁻⁸. In the years before the COVID-19 pandemic, around 600 ICU patients (1.8%) were transported between hospitals in Sweden each year due to resource shortages at the sending ICU. However, during the pandemic, the influx of patients requiring ICU treatment significantly increased interhospital transfers (IHTs) to 3.5% 9.

Studies investigating the risk of IHT during the COVID-19 pandemic have shown conflicting results. Some studies indicate that IHT is not associated with an increased mortality risk ^{2 10-} ¹³ or may even be associated with a lower risk of death ¹⁴, whereas others have shown that IHT is associated with a longer duration of mechanical ventilation ¹⁰⁻¹², ICU stay ¹¹ and length of hospital stay ²¹¹¹². None of these studies were randomised controlled trials, and many were limited by a small sample size ^{2 10 13}. Despite the large increase in ICU beds in Sweden during the pandemic, a substantial proportion of critically ill patients were transferred between hospitals. To the best of our knowledge, no study has so far studied the influence of IHTs on patient outcomes during the COVID-19 pandemic in Sweden. Therefore, we aimed to compare mortality rates and length of hospital stay between patients transferred to

# **METHODS**

# 68 Study design

This study included all adult patients (age ≥18 years) with confirmed SARS-CoV-2, as verified by polymerase chain reaction test, requiring intensive care at Södersjukhuset, Sweden, between 1 March 2020 and 30 June 2021. The hospital is a secondary referral centre, serving a diverse range of medical and surgical patients in Stockholm, a city with 2.5 million inhabitants. The hospital has a total capacity of 600 beds and houses a large emergency department with a continuous inflow of acutely ill patients. Healthcare in Sweden is predominantly funded by taxes, ensuring access to medical services for all citizens. Normally, there are 18 beds dedicated to intensive care. However, during the COVID-19 pandemic, the ICUs expanded to accommodate a total of 60 ICU beds. The study was approved by the Swedish Ethical Review Authority (Dnr: 2023-01778-01-380347, amendment 2023-01778-01), and the requirement for written informed consent from patients was waived. The reporting of the study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines ¹⁵. Cohort All adult patients with a SARS-CoV-2 diagnosis and initial admission at the study hospital's ICU were eligible for inclusion in the study. Patients first admitted to other ICUs and

85 subsequently transferred to the study hospital were excluded. Additionally, patients

86 transferred due to reasons other than capacity constraints, such as repatriation (return to a

87 local ICU near the patient's home) and clinical transfers (requiring specialized care not

88 available at the admitting hospital) were excluded from the study.
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Patients were identified using the patient data management system. Clinical data were
automatically and manually extracted from medical records and the patient data
management system using a pre-defined data collection protocol to ensure consistency and
uniformity of the data collection. Cross-validation of data from randomly selected patients
was performed separately by two independent researchers.

95 The exposure was Interhospital Transfer (IHT), specifically defined as the transfer of patients
96 from the Intensive Care Unit (ICU) at the index hospital to another hospital's ICU due to
97 capacity constraints. These constraints typically involve a shortage of staffed ICU beds at the
98 referring hospital, necessitating the transfer of patients to ensure they receive the critical
99 care they need.

recommendations provided by the Swedish Society for Anaesthesia and Intensive Care.

100 The interhospital transfers were conducted in accordance with the transport

These guidelines ensure that transfers are carried out safely and efficiently, minimising risks to the patient during transport. The guidelines cover various aspects, such as patient stability before the transfer, necessary medical equipment during the transfer, and the qualifications of the medical personnel accompanying the patient. The transfers were crucial for managing ICU capacity and ensuring that patients continue to receive appropriate care without delay ¹⁶. The selection of patients for transfer was commonly carried out in consultation with the admitting ICU. The decision was based on the patient's physiological status to ensure safe transport and the receiving hospital's capacity to provide the required care. This process did not adhere to a standardized protocol or guideline; rather, it relied on the clinical judgment of senior physicians, who made joint decisions about which patient was most suitable for

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	112	transfer, based on various clinical factors and the urgency of the situation. The decision-
	113	making process involved assessing the patient's condition, stability, and the potential risks
	114	and benefits of transfer aiming to ensure that the patient most in need of ICU care at
)	115	another facility was selected for transfer, taking into consideration the overall capacity and
<u>-</u> 	116	resources of both the referring and receiving hospitals. The lack of a standardized protocol
, ,	117	meant that decisions were tailored to individual cases relying of clinical expertise and
;	118	teamwork in managing ICU capacity and patient care.
) )	119	The transport was prepared according to local routines, and handover was reported by
; ;	120	telephone. ICU patients in Stockholm are commonly transported between hospitals using a
) ) ,	121	mobile intensive care unit (MICU). A MICU is staffed with one ambulance nurse, one
; )	122	paramedic and one physician from the departing intensive care unit. The MICU transporter is
)	123	more spacious than a standard ambulance and is equipped with continuous
}	124	electrocardiography monitoring, invasive hemodynamic monitoring and advanced
, ,	125	ventilatory support. Information about the date, time and reasons for transfer was obtained
;	126	from the patient's medical records and the patient data management system.
) <u>-</u> ;	127	Outcomes
 ;	128	The outcomes were mortality at days 30 and 90 from ICU admission and days alive and out
) , }	129	of ICU. The length of ICU stay was measured from the date of ICU admission to the date of
)	130	discharge from the ICU at Södersjukhuset or the admitting hospital.
2	131	
;	132	Statistical analysis
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Continuous variables are presented as medians with interquartile ranges (IQRs), and categorical variables are expressed as numbers and proportions (percentages). The distribution of continuous variables was tested with the Shapiro-Wilk test. Differences between groups were analysed using the Mann-Whitney U test and the Chi² test for continuous and categorical variables, respectively. In the survival analyses, patients were followed up from the date of ICU admission until the date of death or until 30 and 90 days had passed since admission. Kaplan–Meier curves were used to estimate the cumulative risk of death, and the log-rank test was employed to compare patients with exposure to IHT versus those without IHT. Cox proportional hazards regression was used to estimate hazard ratios (HR) with corresponding 95% confidence intervals (CI) for death within 30 and 90 days from ICU admission. Multivariate models were adjusted for age (continuous), sex (male/female), body mass index (< $30/\geq 30$  kg/m²), Simplified Acute Physiology Score III (SAPS III) (>50/50–59/≥60), Charlson Comorbidity Index (categorised as 0/1/2) ¹⁷, invasive mechanical ventilation (yes/no), treatment limitations (yes/no), COVID waves (first wave, March to September 2020 versus second and third waves, October 2020 to January 2021 and February to June 2021¹⁸) and IHT (yes/no). Both crude and multivariable models were investigated with no IHT as the reference group. Scaled Schoenfeld residuals were regressed against survival time to assess the proportional hazard assumptions, and Martingale residual plots, together with the Grambsch-Therneau test, were used to assess evidence of non-linearity. Variance inflation factors were used when investigating multicollinearity. All variables were complete except for SAPS and BMI which were missing for 105 and 6 patients, respectively. This was handled by a separate category for patients with missing values.

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Since the proportional hazards assumption in the Cox regression was not met, indicating that the effect of the variables could vary over time, we performed sensitivity analyses on subgroups of patients based on length of ICU stay (more than 6, 8, 10 and 12 days), COVID waves, mechanical ventilation, and treatment limitations. Comparisons of days alive free from ICU were conducted using the Mann-Whitney U test and presented as medians with interquartile ranges (IQRs).

A two-sided p-value less than 0.05 was considered statistically significant. The analysis followed a predefined protocol and was conducted using the IBM SPSS Statistics version 29 statistical software and R version 4.3.3 (R Core, 2017. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria). All analyses were discussed and confirmed with an experienced biostatistician. 

RESULTS

Patient cohort

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48	184
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55 54	100
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# 70 Of 2622 critically ill patients admitted to the two ICUs during the study period, 674 had a 71 confirmed SARS-CoV-2 diagnosis. Nine patients were transported to other hospitals for 72 tertiary care (e.g. ECMO) and five patients had been transferred to the study hospital from 73 other hospitals/regions. In total, 665 SARS-CoV-2 patients were included in the study, of 74 which 133 (20%) underwent interhospital transports due to capacity constraints (Figure 1). '5 All patients (n=133) were transported to a hospital within a 30-kilometer radius or maximum 76 of 30 minutes. 77 The median age of included patients was 64 years, and most were men (72%). Patients who 78 were transferred were more often on mechanical ventilation (98%) compared with the non-9 transferred patients (40%), and fewer had limitations in terms of life-sustaining treatment 30 (4% versus 15%). Otherwise, the groups were balanced regarding patient and clinical characteristics (Table 1). The median day of IHT from admission was 6 (IQR: 3–11). 81 32 Interhospital capacity transfer and mortality 33 Analyses and distribution of IHT and mortality in patients with critical COVID-19 are shown in 34 Table 2 and Supplementary file 1. Mortality rates did not differ between groups at either 30 35 days (19% vs. 26%, p = 0.13) or 90 days (26% vs. 30%, p = 0.43). This was consistent across the log-rank test for survival for 30 days (Figure 2, p = 0.06) and 90 days (Figure 3, p = 0.2), as 36 37 well as the HR of the univariate Cox regression of 0.66 (95% CI: 0.43–1.02) for 30-day 88 mortality and 0.79 (95% CI: 0.54–1.14) for 90-day mortality. When the exposure of IHT was

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> 189 analysed in the multivariate model, it was associated with a lower risk of mortality for both 190 30 days (HR 0.47, 95% CI: 0.30–0.76) and 90 days (HR 0.52, 95% CI: 0.34–0.79) (Table 2).

191 As the assumptions of proportional hazards were violated when scaled Schoenfeld residuals 192 were regressed against survival time (p <0.001 for the multivariate model for 30- and 90-day 193 mortality), sensitivity analyses were performed. When splitting the time and analysing by 194 different lengths of stay (LOS) at the ICU, the assumptions were fulfilled for patients with an 195 LOS of eight days and above (p = 0.14 for 30-day mortality and p = 0.09 for 90-day mortality). 196 The results did not differ from the original models except for IHT being associated with lower 197 30-day mortality, including in the univariate analyses for patients with an ICU LOS of more 198 than six and eight days (Table 3). Schoenfeld residuals indicated violations of proportional 199 hazard assumptions, including for the covariates of mechanical ventilation, treatment 200 limitations and COVID-19 wave in the multivariate models for 30 and 90 days. This issue was 201 addressed by examining the various categories within these variables as subgroups. The 202 reason for the violation of the variables of mechanical ventilation and treatment limitations 203 was a small number of patients/events in the groups of patients without mechanical 204 ventilation exposed to IHT and the group with treatment limitations exposed to IHT (See 205 details in Supplementary file 2 and 3). When analysing the subgroup of only mechanically 206 ventilated patients, the results changed in the univariate models, showing a lower risk of 207 mortality for 30 days (19.3% versus 32.9%, p=0.008) and 90 days (26.0% versus 38.0%, 208 p=0.029) in the IHT group compared to the non-IHT group. In the multivariate models, the 209 decrease in mortality for the IHT group at 30 and 90 days remained unchanged. Excluding 210 patients with treatment limitations did not change the results. 211 Interhospital capacity transfer and mortality by COVID-19 wave

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2 3	212	For the group of patients treated during the first COVID-19 wave, the univariate analyses for
4 5 6	213	30-day mortality indicated a reduction in deaths for the IHT group, with a hazard ratio (HR)
7 8	214	of 0.26 (95% CI: 0.10–0.73). The univariate analyses for 90-day mortality and the
9 10	211	
10 11 12	215	multivariate analyses for both 30- and 90-day mortality remained consistent, with HRs of
13 14	216	0.44 (95% CI: 0.20–0.96), 0.24 (95% CI: 0.08–0.66), and 0.38 (95% CI: 0.17–0.85), respectively
15 16	217	(Table 4).
17 18 19	218	For the group treated during the second and third COVID-19 waves, the results differed from
20 21	219	the original multivariate models. In this subgroup, there was still no significant difference
22 23	220	between patients with and without IHT in the univariate models, with HRs of 0.95 (95% CI:
24 25 26	221	0.58–1.54) for 30-day mortality and 1.01 (95% CI: 0.65–1.54) for 90-day mortality. However,
27 28	222	unlike the findings in the whole cohort, there was no longer a significant difference in the
29 30 31	223	associated risk of 30- and 90-day mortality in the multivariate models, with HRs of 0.68 (95%
32 33	224	CI: 0.38–1.18) and 0.63 (95% CI: 0.38–1.04), respectively (Table 4).
34 35	225	
30 37 38	226	Interhospital transfer and days alive free of ICU
39 40		
41 42	227	In unadjusted analyses, IHT patients had a median of fewer days alive and free from the ICU
43 44	228	at 30 days compared to non-IHT patients (5, IQR: 0–18 versus 22, IQR: 0–27, p<0.001). At 90
45 46	229	days, there were no statistically significant differences (Figure 4). In the subgroup of
47 48 49	230	mechanically ventilated patients, no significant median differences were observed at either
50 51	231	30 or 90 days.
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In this study, transfers solely due to capacity constraints during the COVID-19 pandemic were not associated with a higher risk of 30- and 90-day mortality among patients with critical COVID-19. Our results indicated that such transfers may even be associated with a lower mortality risk, especially for mechanically ventilated patients. Interhospital transfer was associated with a longer ICU LOS compared with patients who remained in the admitting ICU. This was probably explained by the higher prevalence of invasive ventilation among transferred patients.

The risk of interhospital transfer has been investigated to some extent in observational studies, albeit with conflicting results. A Swedish register-based study of 2,912 capacity-transferred ICU patients before the pandemic found that transportation was associated with a lower risk of death within 90 days (odds ratio 0.71, 95% CI: 0.65–0.79)¹⁹. Conversely, another Swedish study including 11,176 ICU patients showed a higher risk of 30-day mortality after capacity transfers (odds ratio 1.25, 95% CI: 1.06–1.49) and clinical transfers (odds ratio 1.17, 95% CI: 1.02–1.36)²⁰. However, the reference consisted of repatriated patients. While we excluded such patients in our study, other studies have confirmed that clinical transfer to a higher level of care is associated with better patient outcomes ^{21 22}. A French cohort study of 18,348 COVID-19 patients in the ICU found that transferred patients had a lower mortality rate than non-transferred patients, concluding that this might be due to a rigorous selection process of patients eligible for transfer ¹⁴. However, the study only included patients from the first wave of the pandemic. This finding resembles ours, where the results were driven by lower mortality in IHT patients during the first COVID wave. A retrospective cohort study including 5,207 patients mostly with SARS-CoV-2 during wave 3 of the pandemic in Australia found no association between IHT and mortality ¹¹. The difference 

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3 4	257	in outcomes between the pandemic waves may be attributed to changes in healthcare
5 6 7	258	conditions among patients and the accumulated experience in managing the disease.
7 8 9	259	Although capacity constraints remained high during the pandemic waves, the outcomes
10 11	260	improved due to the learning curve in treating COVID-19 patients and the implementation of
12 13 14	261	standardized treatments.
15 16 17	262	Combining the findings of the present study with the previous literature makes it
18 19	263	reasonable to argue that IHT of ICU patients does not appear to increase mortality.
20 21 22	264	Nevertheless, there may be other drawbacks to IHTs, such as hospital-acquired infections,
23 24	265	discontinued care, information gaps or patients being intubated to ensure safe transport,
25 26 27	266	which may prolong the hospital stay ^{23 24} .
28 29 30	267	The observed absence of increased mortality risk associated with the transfer may be
31 32	268	explained by the fact that patients with recovery potential were carefully selected to be
33 34 35	269	stable enough to tolerate transport safely. This aligns with the results from the above-
36 37	270	mentioned French study ¹⁴ . Furthermore, the technical difficulties associated with
38 39	271	transporting patients with high-flow oxygen therapy with high oxygen fractions most likely
40 41 42	272	contributed to the decision to avoid such transfers, which was reflected in our study where
43 44 45	273	mechanical ventilation was more common in the transferred group.
46 47 48	274	
49 50 51	275	The main methodological strengths of this study were the comprehensive data collection
51 52 53	276	conducted by dedicated researchers during the three pandemic waves and validated by
54 55	277	independent researchers, the low proportion of missing data, and the adjustment for known
56 57 58 59 60	278	confounders in the analyses. Among the main weaknesses are the single-centre design and $14$
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2 3 4	279	the non-randomised design. There may be a selection bias in the study, with patients on
5 6 7	280	invasive ventilation and therefore with a secured airway and having limitations of care to a
7 8 9	281	lesser extent, such as do not resuscitate orders, in the transferred group. This difference
10 11	282	might explain the lower OR for mortality in the adjusted analysis and also the longer ICU
12 13 14	283	LOS, as the treatments were not discontinued. In this study, we selected mortality and days
15 16	284	alive and out of the ICU as one of the outcome measures. However, we acknowledge that
17 18 19	285	organ support-free days could have been another valuable parameter to assess the impact
20 21	286	of transfers. This alternative measure could provide additional insights into the safety of
22 23 24	287	interhospital transfers. Assessing illness during transport and comparing different patient
25 26	288	groups presents several challenges. Information about the severity of illness immediately
27 28 20	289	before transport, which might be more appropriate to include in the analyses than the
29 30 31	290	severity of illness at ICU admission, was not readily available. We did not find sufficient and
32 33	291	reliable data to analyse this in our cohort. Furthermore, we used SAPS III to assess illness
34 35 36	292	severity instead of the more commonly used systems like APACHE II or IV. SAPS III is the
37 38	293	standard scoring system for intensive care patients in Sweden and is utilised for reporting to
39 40 41	294	the Swedish Intensive Care Register (SIR), ensuring consistency and accuracy within the
42 43	295	national context. However, this choice may limit the direct comparability of our results with
44 45	296	studies using other scoring systems. Fourteen per cent of SAPS data were missing. The
40 47 48	297	missingness was primarily due to manual documentation processes during the pandemic,
49 50	298	leading to a gap at one of the ICUs. This gap was likely caused by work-related issues rather
51 52 53	299	than patient-related factors. Patients across the two ICUs were similar in clinical
54 55	300	characteristics and diagnoses, and all other variables were complete, supporting the
56 57 58	301	assumption that the missing data were random. We also conducted a sensitivity analysis
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302	with complete cases and the results remained unchanged. Another issue was that lifestyle
303	factors such as smoking, physical activity, and alcohol consumption, as well as socio-
304	economic variables like deprivation, education, and employment status, were not available
305	in our dataset. As such, we were unable to adjust for these variables in the analysis.
306	Furthermore, we have not investigated patients' functional status after ICU discharge, which
307	is of high importance for evaluating surviving patients' well-being.
308	Differences in mortality between countries may depend on variations in healthcare structure
309	and the degree of burden that the country and the healthcare organisation experienced
310	during the pandemic. Well-established routines for transport, availability of advanced
311	medical transport equipment, and access to the same electronic patient data management
312	systems for transferring and admitting centres may also influence the safety of transport.
313	The findings of this study may be somewhat representative to countries with comparable
314	population structures, healthcare systems, and pandemic responses. The use of
315	standardised healthcare protocols ensures consistency in patient care and treatment, which
316	can make the results of this study applicable to other regions facing similar challenges.
317	Future studies should focus on whether certain patient characteristics are predictive of safe
318	transfers and should study the effects of transfers on surviving patients' ability to recover.
319	Furthermore, it is important to explore various types of complications related to IHT and
320	long-term outcomes to identify factors that may influence treatment outcomes and thereby
321	improve care.
322	CONCLUSIONS

In our study interhospital transfer due to capacity constraints among critically ill COVID-19
 patients was not associated with a higher mortality risk. The suitability for transfer was likely
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3 4	325	associated with lower mortality, although residual confounding cannot be ruled out. The
5 6 7	326	requirement for invasive ventilation among transferred patients might account for the
7 8 9	327	extended length of ICU stay, rather than the transfer itself. However, the difficulty in
10 11	328	studying this issue lies in the fact that while patients are likely exposed to risks during
12 13 14 15	329	transfer, they are simultaneously the patients stable enough to be transported.
16 17 18	330	ACKNOWLEDGEMENTS
19 20 21	331	Special thanks to MD Jacob Litorell for developing, validating, and maintaining the COVID-19
21 22 23	332	database we used in this study.
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28 29 30	334	The study was supported by grants from the Swedish patient insurance company (LÖF). The
31 32 33	335	funders had no role in the design or conduct of the study.
34 35 36 27	336	CONFLICT OF INTEREST STATEMENT
37 38 39 40	337	The authors declare no conflict of interest.
41 42 43	338	AUTHOR CONTRIBUTIONS
44 45 46	339	KB: Conceptualisation, methodology, design, analysis, writing the original draft, review and
47 48 49	340	editing. LTA: Conceptualisation, methodology, design, writing the original draft, review and
50 51	341	editing. PS: conceptualisation, methodology, design, review and editing. MC:
52 53 54	342	Conceptualisation, methodology, design, review and editing. SJ: conceptualisation,
55 56 57 58 59	343	methodology, design, analysis, review and editing. EJA: conceptualisation, methodology,

2 3	244	destructure to consider divisor <b>ac</b> onomical testing consultants and the second state of the sta
4	344	design, review and editing. As: conceptualisation, methodology, design, analysis, writing the
5 6 7	345	original draft, review and editing. AS: are responsible for the overall content as guarantor.
8 9 10 11	346	DATA AVAILABILITY STATEMENT
12 13 14	347	The data that support the findings of this study are available from the corresponding author
15 16 17	348	upon reasonable request.
17 18 19 20	349	PATIENT AND PUBLIC INVOLVEMENT
20 21 22	350	Patients and/or the public were not involved in the design, conduct, reporting or
23 24	351	dissemination plans of this research.
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# Table 1. Characteristics of patients admitted to an ICU for SARS-CoV-2

All patients Non-IHT patients	p-value
665 532 (80)	
64 (55–72) 64 (55–72)	ns
	ns
479 (72) 376 (71)	
186 (28) 156 (29)	
	ns
253(38) 202 (38)	
406 (62) 324 (61)	
58 (47–67)	ns
	ns
248 (37) 197 (37)	
250 (38) 198 (37)	
167 (25) 137 (26)	
	<0.001*
344 (52) 213 (40)	
321 (48) 319 (60)	
C	0.001*
83 (12) 78 (15)	
582 (88) 454 (85)	
	ns
265 (40) 218 (41)	
400 (60) 314(59)	
265 (40)218 (41)400 (60)314(59)body mass index; SAPS 3: Simplified Acute Phty Index score; SD: Standard deviation; ns=no5 statistically significant differences	l: nt

Table 2. Risk with 95% CI (	of death 30 Non-IHT as	days and 90 day reference)	ys after interho	BMJ Open ospital transfer among cri	itically ill patients with	by copyright, incading for u	CoV-2 presented as	hazard ratios
				Risk of death after interh	ospital transfers	Ses		
	Exposure	Mortality		30-day m	ortality	ම ලි.දි. 90-day mortality		ortality
All patients	No (%)	30-day No (%)	90-day No (%)	Unadjusted HR with 95% CI	Adjusted HR with 95% Cl	Inemer lated to	Unadjusted HR with 95% CI	Adjusted HR with 95% Cl
Non-IHT	532 (80)	136 (26)	157 (30)	1.0 (referent)	1.0 (referent)	te S	1.0 (referent)	1.0 (referent)
IHT	133 (20)	25 (19)	34 (26)	0.66 (0.43-1.02)	0.47 (0.30-0.76)*	upe Xt a	0.79 (0.54–1.14)	0.52 (0.34-0.78)*
						nd		

The models were adjusted for age, sex, BMI categories (<30 or >30), SAPS, Charlson Comorbidity Index (2), mechanical ventilation (yes/no), treatment limitations (yes/no) and SARS-CoV-2 wave (wave 1/waves 2–3). *Statistically significant differences between groups, Al training, and similar technologies bmjopen.bmj.com/ on June 11, 2025 at Agence Bibliographique de l p<0.05

Abbreviations: IHT: inter-hospital transfer; HR: hazard ratio; CI: confidence interval hc

BMJ Open Table 3. The sensitivity analysis presents the risk of 30-day and 90-day mortality following interhospital grants for (IHT), categorised by the length of ICU stay from admission to the day of transfer. The analyses are presented as hazard ratios (H) with 95% confidence intervals (CI), using non-IHT natients as the reference group using non-IHT patients as the reference group. for u Fe

Risk of death for IHT by the length of ICU stay								
	Exposure	xposure Mort		ality <b>30-day mo</b>		reig	90-day mortality	
ICU LOS		30-day	90-day	Unadjusted	Adjusted	ner ate	S Unadjusted	Adjusted
	No (%)	No (%)	No (%)	HR with 95% Cl	HR with 95% Cl	d to r	HR with 95% Cl	HR with 95% Cl
>6 days						te te		
Non-IHT	241 (65)	70 (29)	83 (34)	1.0 (referent)	1.0 (referent)	t a	1.0 (referent)	1.0 (referent)
IHT	127 (35)	25 (20)	34 (27)	0.62 (0.39–0.97)*	0.42 (0.26–0.68) *	nd	0.70 (0.47–1.05)	0.45 (0.29–0.69)*
>8 days						dat	<u>,</u>	
Non-IHT	187 (61)	57(31)	69 (37)	1.0 (referent)	1.0 (referent)	AB	1.0 (referent)	1.0 (referent)
IHT	118 (39)	24(20)	33 (28)	0.61 (0.38-0.98)*	0.40 (0.24–0.67)*		0.69 (0.45–1.04)	0.43 (0.28–0.67)*
>10 days						ŋġ, :		
Non-IHT	161 (60)	49 (30)	61 (38)	1.0 (referent)	1.0 (referent)	Alt	1.0 (referent)	1.0 (referent)
IHT	106 (40)	22 (21)	31 (29)	0.63 (0.38–1.05)	0.46 (0.27–0.78)*	rain	0.71 (0.46–1.09)	0.49 (0.31–0.77)*
>12 days			·		0	ling		
Non-IHT	147 (60)	44 (30)	55 (37)	1.0 (referent)	1.0 (referent)	, a	1.0 (referent)	1.0 (referent)
IHT	94 (40)	21 (22)	30 (32)	0.71 (0.42–1.19)	0.48 (0.28-0.85)*	nd :	0.80 (0.51–1.25)	0.53 (0.33–0.85)*
						sim		

The models were adjusted for age, sex, BMI categories (<30 or >30), SAPS, Charlson Comorbidity Index (a), 1% >2), mechanical ventilation (yes/no), treatment limitations (yes/no) and SARS-CoV-2 wave (wave 1 or waves 2/3). *Statistically sign and the set wave set wave groups, p<0.05 ies.

Abbreviations: LOS: length of stay; ICU: intensive care unit; IHT: inter-hospital transfer; HR: hazard ratio; CI: and the care unit; IHT: inter-hospital transfer; HR: hazard ratio; CI:

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 BMJ Open Table 4. The sensitivity analysis presents the risk of 30-day and 90-day mortality following interhospital data by pandemic waves. The analyses are presented as hazard ratios (HR) with 95% confidence intervals (CI), using non-IH patients as the reference group.

				Risk of death for IHT by	COVID-19 wave	elat		
	Exposure Mortality		30-day mortality		25. ed	90-day m	ortality	
Waves		30-day	90-day	Unadjusted	Adjusted	to t	<b>U</b> nadjusted	Adjusted
	No (%)	No (%)	No (%)	HR with 95% Cl	HR with 95% Cl	Sup	HR with 95% Cl	HR with 95% Cl
Wave 1						beri and		
Non-IHT	218 (82)	61 (28)	64 (29)	1.0 (referent)	1.0 (referent)	d da	1.0 (referent)	1.0 (referent)
IHT	47 (18)	4 (9)	7 (15)	0.26 (0.10-0.73)*	0.24 (0.08–0.66)*	ata	0.44 (0.20–0.96)*	0.38 (0.17–0.85)*
Wave 2-3						MIN		
Non-IHT	314 (78)	75 (24)	93 (30)	1.0 (referent)	1.0 (referent)	ing	1.0 (referent)	1.0 (referent)
IHT	86 (22)	21(24)	27 (31)	0.95 (0.58–1.54)	0.68 (0.38–1.18)	, A	1.01 (0.65–1.54)	0.63 (0.38–1.04)
						- <del>-</del>		

The models were adjusted for age, sex, BMI categories (<30 or >30), SAPS, Charlson Comorbidity Index 🕃 1, 22) mechanical ventilation (yes/no), treatment limitations (yes/no) and SARS-CoV-2 wave (wave 1/wave 2-3). *Statistically significant differences between groups, p<0.05

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Abbreviations: IHT: inter-hospital transfer; HR: hazard ratio; CI: confidence interval

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- Figure 1. Flowchart of study inclusion •
- Figure 2. Kaplan-Meier curve showing survival to day 30 from ICU admission for patients with SARS-CoV-2 infection in Sweden between 1 March 2020 and 30 June 2021. Abbreviations: IHT: Interhospital transport
- Figure 3. Kaplan-Meier curve showing survival to day 90 from ICU admission for patients • with SARS-CoV-2 infection in Sweden between 1 March 2020 and 30 June 2021. Abbreviations: IHT: Interhospital transport
- Figure 4. Days alive and free of ICU within 30 and 90 days among transferred and non-• transferred patients. Abbreviations: IHT: Interhospital transport
- Supplementary File 1. Figure displaying 90-day mortality by ICU day of transfer •
- J. Isplay. Jup analys. aracteristics of mec. Supplementary File 2. Subgroup analysis regarding mechanical ventilation and treatment • limitations.
- Supplementary File 3. Characteristics of mechanically ventilated patients











Mortality distribution among transferred patients in relation to the day of transfer.



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Supplementary File 2. Subgroup analysis regarding mechanical ventilation and treatment limitations.

For the group without mechanical ventilation (total 321, 319 without IHT and two with IHT), neither of the two patients with exposure to IHT died within either 30 or 90 days compared to the 66 patients (21%) in the group without mechanical ventilation in the group not exposed to IHT. Due to the small number of patients and no event in the group without mechanical ventilation and IHT, the analyses were neither of interest nor statistically appropriate. When analysing only the subgroup of patients with mechanical ventilation (total 344, 213 without IHT and 131 with IHT), the results showed a reduced risk of death in both the univariate model, HR 0.51 (95% CI 0.32–0.81) for 30-day mortality and HR 0.60 (95% CI 0.40–0.89) for 90-day mortality, and the multivariate model, HR 0.40 (95% CI 0.25–0.65) for 30-day mortality and HR 0.45 (95% CI 0.30–0.68) for 90-day mortality.

For the group with treatment limitations (total 83, 78 without IHT and five with IHT), three patients (60 %) with exposure to IHT died within 30 and 90 days compared to the 55 (66%) and 58 (70%) with no exposure to IHT in 30 and 90 days, respectively. Even though the percentage was about the same in the two groups, the analysis was not carried out due to the small number of patients exposed to IHT with treatment limitations. For the patient group without treatment limitations (total 582, 454 without IHT and 128 with IHT), the results were the same as in the original models, showing no difference between patients without exposure to IHT compared to patients with exposure in the univariate model, HR 0.92 (0.58-1.48) for 30-day mortality and HR 1.08 (95% CI 0.72–1.60) for 90-day mortality, and a difference in the multivariate model, HR 0.38 (95% CI 0.23–0.62) for 30-day mortality and HR 0.45 (95% CI 0.29–0.68) for 90-day mortality.

# Supplementary File 3. Characteristics of mechanically ventilated patients

Characteristics of mechanically ventilated patients admitted to an ICU for SARS-CoV-2 (noninvasive ventilated patients were excluded)

	All patients	Non-IHT patients	IHT patients	p-value
Total number (%)	344	213	131	
Age, median (IQR)	64 (55–71)	64 (55–71)	65 (57–72)	ns
Sex, n (%)				ns
Ven	258 (75)	157 (74)	101 (77)	
Vomen	86 (25)	56 (26)	30 (23)	
SMI, n (%)	(n=341)	(n=210)		ns
·30	139 (41)	89 (42)	50 (38)	
:30	202 (59)	121 (58)	81 (62)	
APS 3, median (IQR)	57 (53–63)	57 (53–63)	57 (53–63)	ns
CCI category, n (%)	6			ns
)	132 (38)	82 (39)	50 (38)	
1	133 (39)	81 (38)	52 (40)	
2	70 (23)	50 (23)	29 (22)	
imitations on life- sustaining treatments, n %)				ns
/es	16 (5)	11 (5)	5 (4)	
No	328 (95)	202 (95)	126 (96)	
COVID-19 period, n (%)				0.003*
Wave 1	160 (47)	113 (53)	47 (36)	
Waves 2–3	184 (53)	100 (47)	84 (64)	
		2		
bbreviations: BMI: body m harlson Comorbidity Index ifferences, *p<0.05 statisti	ass index; SAPS 3: Sin score; SD: standard c ically significant differ	nplified Acute Physiol leviation; ns=no stati ences.	ogy Score 3; CCI: stically significant	