Outcomes for people admitted to Australian and New Zealand intensive care units with primary, exacerbating, or incidental SARS-CoV-2 infections, 2022–23: a retrospective analysis of ANZICS data

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The known: Early in the COVID-19 pandemic, outcomes for people admitted to hospital with other conditions were poorer if they had concomitant SARS-CoV-2 infections.

The new: During 2022–23, risk-adjusted in-hospital mortality was higher and median ICU length of stay longer for people admitted to intensive care in Australia or New Zealand with SARS-CoV-2 infections, even when the infection was not the primary or a contributing reason for the ICU admission.

The implications: Despite improved treatments and widespread vaccination in Australia and New Zealand, SARS-CoV-2 infections are still associated with poorer clinical outcomes for people admitted to ICUs.

Abstract

Objectives: To compare in-hospital mortality and intensive care unit (ICU) length of stay for people admitted to Australian and New Zealand ICUs during 2022–23 with coronavirus disease 2019 (COVID-19) pneumonitis, incidental or exacerbating severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections, or without SAR-CoV-2 infections.

Study design: Retrospective cohort study; analysis of Australian and New Zealand Intensive Care Society (ANZICS) Adult Patient Database data.

Setting, participants: Adults (16 years or older) admitted to participating ICUs in Australia or New Zealand, 1 January 2022 – 30 June 2023.

Major outcome measures: The primary outcome was in-hospital mortality, the secondary outcome ICU length of stay, each by SARS-CoV-2 infection attribution classification: primary COVID-19; exacerbating SARS-CoV-2 infection (SARS-CoV-2 infection was a contributing factor to the primary cause of ICU admission); incidental SARS-CoV-2 infections (SARS-CoV-2 infection detected during ICU admission but did not contribute to admission diagnosis); no SARS-CoV-2 infection.

Results: A total of 207 684 adults were admitted to 195 Australian and New Zealand ICUs during 2022–23; 2674 people (1.3%) had incidental SARS-CoV-2 infections, 4923 (2.4%) exacerbating infections, and 3620 (1.7%) primary COVID-19. Unadjusted in-hospital mortality for people with incidental SARS-CoV-2 infections (288 deaths, 10.8%) was lower than for those with exacerbating infections (928 deaths, 18.8%) or primary COVID-19 (830 deaths, 22.9%), but higher than for patients without SARS-CoV-2 infections (15 486 deaths, 7.9%). After adjusting for illness severity, frailty, geographic region, and type of hospital, mortality was higher for patients with incidental SARS-CoV-2 infections (adjusted odds ratio [aOR], 1.28; 95% confidence interval [CI], 1.10–1.50), exacerbating infections (aOR, 1.35; 95% CI, 1.22–1.48), or primary COVID-19 (aOR, 2.54; 95% CI, 2.30–2.81) than for patients without SARS-CoV-2 infections. After adjusting for diagnosis and illness severity, ICU stays were longer for people with incidental (mean difference, 3.3 hours; 95% CI, 2.4–4.2 hours) or exacerbating infections (0.8 hours; 95% CI, 0.2–1.5 hours) than for those without SARS-CoV-2 infections.

Conclusion: Risk-adjusted in-hospital mortality and ICU length of stay are higher for people admitted to intensive care who have concomitant SARS-CoV-2 infections than for people who do not.

The coronavirus disease 2019 (COVID-19) pandemic has been a worldwide public health emergency.[1,2] During the early waves of the pandemic, many people infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) developed critical illnesses, and short and long term mortality was high.[2,3] Those admitted to hospital often required prolonged mechanical ventilation and long intensive care unit (ICU) stays.[4] In addition, concurrent or recent SARS-CoV-2 infection was associated with increased risk of death for people with myocardial infarction or undergoing surgical procedures.[5,6]

While the pandemic progressed, novel therapeutic strategies helped reduce mortality.[7-9] At the same time, vaccines were developed that reduced transmission of SARS-CoV-2 and the severity of critical illness in people with SARS-CoV-2 infections.[10,11] Further, the Omicron SARS-CoV-2 variants that have dominated since early 2022 are more transmissible than earlier variants, but are less pathogenic.[12,13]

The number of COVID-19 cases in Australia was low prior to the emergence of the Omicron variant of concern in mid-December 2021,[14] by which point 88.1% of people aged 16 years or older had received two or more COVID-19 vaccine doses.[14] Following the relaxation of highly restrictive public health policies for suppressing transmission,[15] the incidence of SARS-CoV-2 infections increased during 2022, as did worldwide community levels of natural immunity.[16-18] Consequently, a rising number of people admitted to ICUs have concomitant SARS-CoV-2 infections rather than primary diagnoses of COVID-19; these infections might be considered incidental or as exacerbating, depending on whether they contributed to the person being admitted to the ICU.

Our objective was to compare in-hospital mortality and ICU length of stay for people admitted to Australian and New Zealand ICUs during 2022–23 with COVID-19 pneumonitis, incidental or exacerbating SARS-CoV-2 infections, or without SARS-CoV-2 infections.

Methods

For our retrospective cohort study, we analysed prospectively collected registry data in the Australian and New Zealand

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Intensive Care Society (ANZICS) Adult Patient Database, a binational clinical quality registry that includes data for more than three million admission episodes to more than 200 participating ICUs (98% of ICUs in Australia, 68% of ICUs in New Zealand) since 1992 (https://www.anzics.org/adult-patient-database-apd). The data are collected for quality benchmarking by the ANZICS Centre for Outcome and Resource Evaluation (CORE). We analysed de-identified data for baseline demographic characteristics, diagnosis, acute physiology status, chronic health status, laboratory parameters, invasive treatment (eg, mechanical ventilation and renal replacement therapy), and vital status at hospital discharge.

Case definitions

The ANZICS Adult Patient Database includes one diagnosis as the primary cause of each ICU admission, allocated by treating clinicians or trained data collectors in the ICU using the ANZICS modification of the APACHE IV diagnostic coding system. For admissions prior to 2022, patients with SARS-CoV-2 infections could be identified only by a subcode for pre-existing infective and inflammatory conditions; whether people with other ICU admission diagnoses had concomitant SARS-CoV-2 infections could not be determined.

The addition of a separate SARS-CoV-2 infection variable to the Adult Patient Database in January 2022 has facilitated assessment of the effect of concomitant SARS-CoV-2 infections in people with any ICU admission diagnosis. In consultation with the Australian Department of Health and Aged Care, an attribution classification system was defined for reporting purposes:

- primary COVID-19: viral pneumonitis associated with SARS-CoV-2 infection;
- exacerbating SARS-CoV-2 infections: conditions in which SARS-CoV-2 infection was listed (by subcode) as a contributing factor to the primary cause of ICU admission (eg, asthma);
- incidental SARS-CoV-2 infections: SARS-CoV-2 infection was listed on admission or detected at any time during the ICU admission of people with diagnoses not covered by the two other classifications (eg, trauma).

A positive rapid antigen test or polymerase chain reaction test for SAR-CoV-2 was required for classification, but the method and frequency of testing in individual hospitals was not recorded (full list of diagnoses and their categorisation: Supporting Information, table 1).

Case selection

We initially included all adults (16 years or older) admitted to participating ICUs in Australia or New Zealand during 1 January 2022 – 30 June 2023. Re-admissions and cases in which information on survival was not recorded were excluded. Admissions of people with unknown SARS-CoV-2 infection status were also excluded from the primary analysis.

Outcome measures

The primary outcome was in-hospital mortality; the secondary outcome was ICU length of stay. Other outcomes were in-ICU mortality, hospital length of stay, time in ICU after being deemed ready for discharge (discharge delay), discharge delay exceeding twelve hours, after-hours discharge (ie, live discharge from ICU during the period 6 pm – 6 am), and ICU re-admission.

Statistical analysis

We summarise data as means with standard deviations (SDs), medians with interquartile ranges (IQRs), or counts and proportions, as appropriate. The statistical significance of differences in baseline characteristics was assessed in Wilcoxon rank sum, Kruskal–Wallis, Student *t*, or χ^2 tests, or by analysis of variance (ANOVA), as appropriate.

Illness severity was assessed with the Australian and New Zealand Risk of Death (ANZROD) (Supporting Information, table 2).[19] Frailty was assessed with the Clinical Frailty Scale (CFS)[20] and categorised as frailty (CFS score, 6–8), pre-frailty (4 or 5), no frailty (1–3), or frailty status unknown.

The association between SARS-CoV-2 infection category and mortality was assessed using mixed effects hierarchical multivariable logistic regression (reference category: patients without SARS-CoV-2 infections), incorporating ANZROD and frailty as person-level estimates of acute and chronic illness. We report adjusted odds ratios (aORs) with 95% confidence intervals (CIs).

We assessed ICU length of stay in a mixed effects hierarchical multivariable log-linear regression model, using previously described methods;[21] we report model outputs as β coefficients with 95% CIs. To account for the non-linear relationship between illness severity and length of stay, ANZROD was categorised by 5% increments.[21] To adjust for the independent effects of death and diagnosis on length of stay, in-ICU death and diagnosis were included as variables in the regression analysis. We depict the impact of SARS-CoV-2 infection on ICU length of stay in cumulative incidence curves, using unadjusted Kaplan–Meier estimates of ICU length of stay, censored at 14 days.

In all models, geographic region,[22] month of ICU admission, and hospital type were included as covariates, and patients were clustered by site, with site a random effect. All covariates were chosen *a priori*. $P < 0.05$ (two-sided) was deemed statistically significant. No corrections were made for multiple comparisons, nor were missing data imputed. In two sensitivity analyses, we directly compared patients with incidental and exacerbating SAR-CoV-2 infections with patients without SAR-CoV-2 infections but with corresponding ICU admission diagnoses.

Ethics approval

Our study was approved, and the requirement for individual patient informed consent waived, by the human research ethics committee of the Alfred Hospital (87/22).

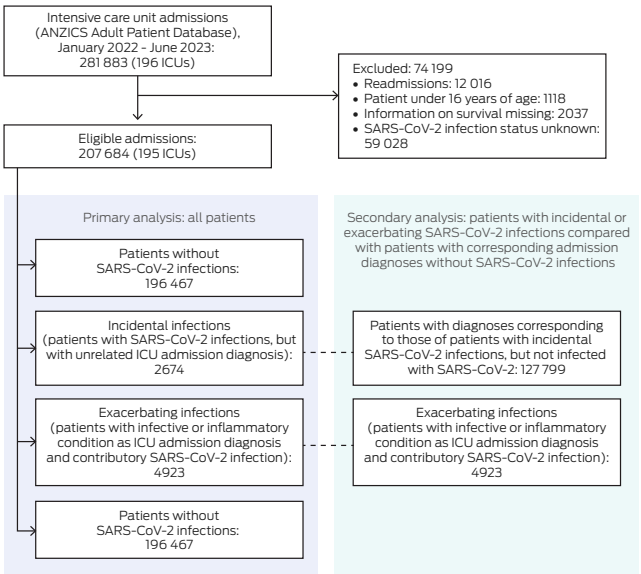
Results

We included 207 684 admissions of adults to 195 Australian and New Zealand ICUs during 2022–23 in our analysis (Box 1). Small but statistically significant differences between the characteristics of included patients and the 59 028 ICU patients with unknown SARS-CoV-2 infection status were noted, including the slightly higher mean age of included patients (62.5 [SD, 17.4] *v* 61.9 [SD, 17.6] years) and their slightly higher mean ANZROD score (8.5% [SD, 16.8] *v* 7.7% [SD, 16.4]) (Supporting Information, table 3). Data completeness was high for most variables; exceptions were blood pH, partial pressure of oxygen in arterial blood (PaO_2), and ratio of arterial oxygen partial pressure to fractional inspired oxygen (P/F ratio) (about 26% missing) and discharge delay (about 13% missing) (Supporting Information, table 4).

A total of 2674 cases (1.3%) met the criteria for incidental SARS-CoV-2 infections, 4923 (2.4%) for exacerbating infections, and 3620 (1.7%) for primary COVID-19 (Box 1). The overall prevalence of SARS-CoV-2 infections among ICU patients fell during the study period from 128 to 30 per 1000 ICU admissions; the proportions of infections classified as incidental or exacerbating infections rose, and that of primary COVID-19 declined (Box 2).

The median time in hospital prior to ICU admission was 9.4 hours (IQR, 4.8–25.9 hours); the median times by infection group were similar. The mean age of people with incidental infections (58.7 years; SD, 19.3 years) was lower than for people in the other three categories. A smaller proportion of people with incidental infections were classified as frail (10%) than of patients with exacerbating SARS-CoV-2 infections (18.3%) or primary COVID-19 (15.9%), and the proportions with diabetes or one of three chronic disease types were also smaller. The proportion of patients who were immunosuppressed was larger for those with primary COVID-19 (22.8%) than for people with exacerbating (15.6%), incidental (7.7%), or no SARS-CoV-2 infection (6.9%). The proportion of elective surgical admissions was larger for people without SARS-CoV-2 infections (38.0%) than for people with incidental (14.6%) or exacerbating SARS-CoV-2 infections (0.1%). Median PaO_2 and P/F ratio values were lower for patients with primary COVID-19 than for those with exacerbating, incidental, or no SARS-COV-2 infections (Box 3). The characteristics of ICU patients with incidental or exacerbating SARS-CoV-2 infections were similar to those of patients with corresponding ICU admission diagnoses but without SARS-CoV-2 infections (Supporting Information, tables 6 and 7).

1 Selection of intensive care unit (ICU) admissions, Australia and New Zealand, 1 January 2022 – 30 June 2023, for inclusion in our primary and secondary analyses



ANZICS = Australian and New Zealand Intensive Care Society; COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2. ◆

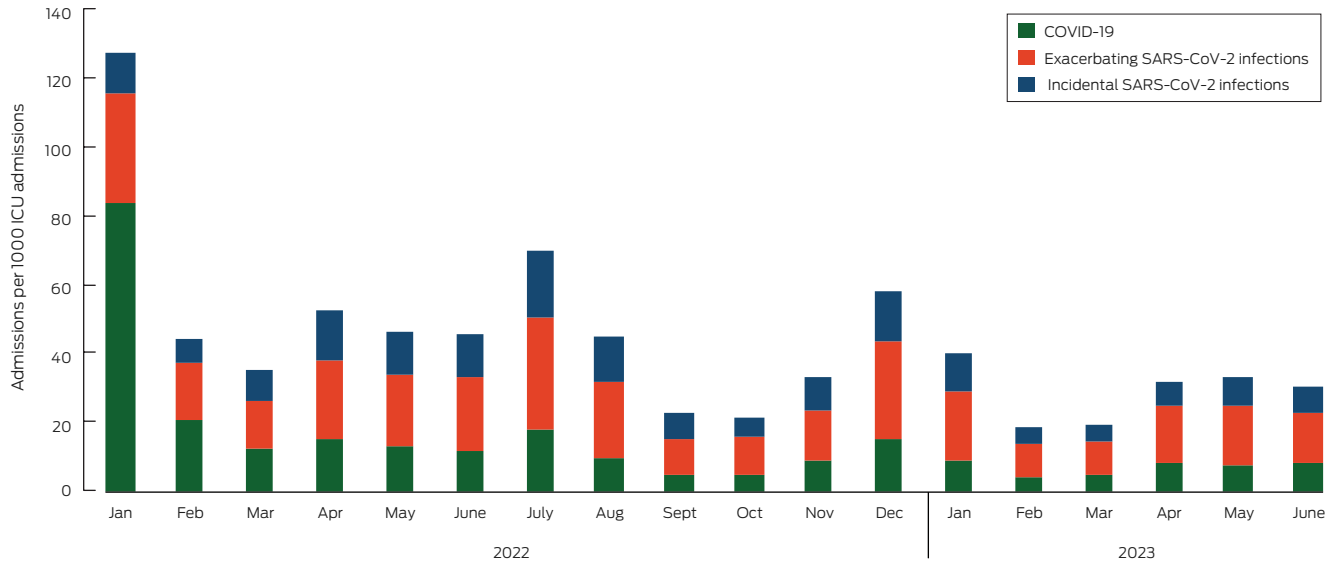
Primary outcome

Unadjusted in-hospital mortality for people with incidental SARS-CoV-2 infections (288 deaths, 10.8%) was lower than for those with exacerbating infections (928 deaths, 18.8%) or primary COVID-19 (830 deaths, 22.9%) and higher than for patients without SARS-CoV-2 infections (15 486 deaths, 7.9%) (Box 4). After adjustment for illness severity, frailty, geographic region, and type of hospital, mortality was higher for patients with incidental SARS-CoV-2 infections (aOR, 1.28; 95% CI, 1.10–1.50), exacerbating infections (aOR, 1.35; 95% CI, 1.22–1.48), or primary COVID-19 (aOR, 2.54; 95% CI, 2.30–2.81) than for patients without SARS-CoV-2 infections (Box 5).

Secondary outcome

Median length of ICU stay was longer for patients with incidental or exacerbating SARS-CoV-2 infections or primary COVID-19 than for people without SARS-CoV-2 infections (Box 4, Box 6).

2 Admissions to Australian and New Zealand intensive care units of people with SARS-CoV-2 infections, 1 January 2022 – 30 June 2023, by infection classification*



COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2. * The data underlying this graph are included in the Supporting Information, table 5. ◆

3 Baseline characteristics for people admitted to Australian and New Zealand intensive care units (ICUs), 1 January 2022 – 30 June 2023, by SARS-CoV-2 infection classification

Characteristic	SARS-CoV-2 infection type			
	None	Incidental	Exacerbating	Primary COVID-19
Number of patients	196 467	2674	4923	3620
Age (years), mean (SD)	62.4 (17.5)	58.7 (19.3)	64.0 (16.6)	66.1 (15.3)
Sex (men)	110 525 (56.3%)	1573 (58.9%)	2713 (55.2%)	2284 (63.2%)
Other medical conditions				
Diabetes	44 880 (22.8%)	565 (21.1%)	1613 (32.8%)	1182 (32.7%)
Chronic: cardiovascular	17 275 (8.8%)	159 (5.9%)	516 (10.5%)	301 (8.3%)
Chronic: respiratory	15 008 (7.6%)	120 (4.5%)	793 (16.1%)	443 (12.2%)
Chronic: dialysis	6512 (3.3%)	84 (3.1%)	294 (6.0%)	234 (6.5%)
Immunosuppressed	13 574 (6.9%)	205 (7.7%)	769 (15.6%)	824 (22.8%)
Cancer	12 021 (6.1%)	145 (5.4%)	396 (8.0%)	320 (8.8%)
Clinical Frailty Scale score[20]				
Not frail (1–3)	102 540 (52.2%)	1511 (56.5%)	2005 (40.7%)	1468 (40.6%)
Pre-frail (4 or 5)	54 660 (27.8%)	711 (26.6%)	1625 (33.0%)	1161 (32.1%)
Frail (6–9)	19 007 (9.7%)	268 (10.0%)	903 (18.3%)	576 (15.9%)
Frailty status unknown	20 260 (10.3%)	184 (6.9%)	390 (7.9%)	415 (11.5%)
Illness severity				
ANZROD, mean (SD)	8.1% (16.5)	9.7% (16.8)	18.1% (22.8)	15.8% (17.2)
ANZROD, median (IQR)	1.4% (0.4–6.5%)	2.5% (0.7–9.4%)	8.3% (2.5–24.6%)	9.3% (4.1–20.8%)
APACHE III score, mean (SD)	51.2 (23.9)	54.3 (24.1)	64.4 (28.0)	60.4 (21.8)
Mechanical ventilation	64 662 (32.9%)	1349 (50.4%)	1,230 (25.0%)	997 (27.5%)
Blood values				
pH, mean (SD)*	7.36 (0.09)	7.37 (0.09)	7.35 (0.12)	7.40 (0.10)
PaO_2 (mmHg), median (IQR)†	87 (70–124)	85 (69–123)	72 (63–91)	66 (59–76)
P/F ratio, median (IQR)‡	295 (207–375)	285 (200–370)	228 (149–329)	138 (100–198)
Time in hospital prior to ICU admission (hours), median (IQR)	9.5 (4.9–25.9)	8.8 (4.0–26.2)	7.2 (3.3-18.2)	9.6 (4.0-39.1)
Admission source				
Operating theatre	105 043 (53.5%)	1187 (44.4%)	4 (0.1%)	1 (< 0.1%)
Emergency department	55 031 (28%)	955 (35.7%)	3146 (63.9%)	1844 (50.9%)
Hospital ward	24 412 (12.4%)	329 (12.3%)	1190 (24.2%)	1344 (37.1%)
Other hospital	11 322 (5.8%)	197 (7.4%)	566 (11.5%)	410 (11.3%)
Other/unknown admission source	659 (0.3%)	6 (0.2%)	17 (0.3%)	21 (0.6%)
Admission category				
Elective surgical	74 633 (38.0%)	390 (14.6%)	3 (0.1%)	0
Emergency surgical	31 522 (16.0%)	819 (30.6%)	0	0
Medical	90 312 (46.0%)	1465 (54.8%)	4920 (99.9%)	3620 (100%)

ANZROD = Australian and New Zealand Risk of Death mortality prediction model;[19] COVID-19 = coronavirus disease 2019; IQR = interquartile range; PaO_2 = partial pressure of oxygen in arterial blood; P/F ratio = ratio of arterial oxygen partial pressure to fractional inspired oxygen (= PaO_2/FiO_2); SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SD = standard deviation. * Missing data, by infection type: none, 51 858 (35.9%); incidental, 1020 (35.6%); exacerbating, 1395 (39.5%); primary COVID-19, 702 (39.2%). † Missing data, by infection type: none, 51 908 (35.9%); incidental, 1018 (35.8%); exacerbating, 1393 (39.5%); primary COVID-19, 700 (39.1%). ‡ Missing data, by infection type: none, 51 935 (35.9%); incidental, 1018 (35.5%); exacerbating, 1397 (39.6%); primary COVID-19, 701 (39.1%). ◆

After adjusting for diagnosis and illness severity, incidental and exacerbating infections were each associated with longer ICU stays than having no SARS-CoV-2 infection (Box 7). The mean difference was 3.3 hours (95% CI, 2.4–4.2 hours) for patients with incidental infections and 0.8 hours (95% CI, 0.2–1.5 hours) for those with exacerbating SARS-CoV-2 infections. After adjustment for covariates, the association between ICU length of stay and COVID-19 pneumonitis was not statistically significant, suggesting that the longer ICU stays were primarily attributable to baseline illness severity (Box 7).

4 Outcomes for people admitted to Australian and New Zealand intensive care units (ICUs), 1 January 2022 – 30 June 2023, by SARS-CoV-2 infection classification

Characteristic	SARS-CoV-2 infection type			
	None	Incidental	Exacerbating	Primary COVID-19
Number of patients	196 467	2674	4923	3620
Primary outcome: in-hospital deaths	15 486 (7.9%)	288 (10.8%)	928 (18.8%)	830 (22.9%)
Secondary outcome: ICU length of stay (days), median (IQR)	1.8 (0.9–3.5)	2.3 (1.1–4.9)	2.8 (1.5–5.3)	4.0 (1.9–8.3)
Discharged from ICU alive	1.8 (0.9–3.4)	2.3 (1.1–4.8)	2.8 (1.6–5.1)	3.7 (1.8–7.1)
Died in ICU	2.3 (0.8–5.5)	3.0 (1.0–7.7)	3.1 (0.9–7.0)	9.3 (3.9–16.2)
Other outcomes: general				
In-ICU deaths	10 149 (5.2%)	182 (6.8%)	641 (13.0%)	572 (15.8%)
Hospital length of stay (days), median (IQR)	7.7 (4.0–14.2)	9.5 (4.3–19.2)	8.3 (4.5–16.2)	11.5 (6.8–21.3)
Other outcomes: people discharged from ICU alive				
ICU re-admission	7394 [4.0%]	126 [5.1%]	177 [4.1%]	194 [6.4%]
Discharge delay (hours), median (IQR)*	5.0 (2.8–9.5)	5.9 (3.0–14.2)	6.7 (3.3–23.3)	6.1 (3.3–14.2)
Discharge delay greater than 12 hours	34 090 [18.3%]	589 [23.7%]	1253 [29.3%]	763 [25.0%]
After-hours discharge	27 189 [14.6%]	508 [20.4%]	978 [22.9%]	660 [21.7%]

COVID-19 = coronavirus disease 2019; IQR = interquartile range; SD = standard deviation; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2. * Missing data, by infection type: none, 23 962 (14.8%); incidental, 302 (14.3%); exacerbating, 465 (12.2%); primary COVID-19, 19 311 (11%). ◆

5 In-hospital mortality among people admitted to Australian and New Zealand intensive care units (ICUs), 1 January 2022 – 30 June 2023, by SARS-CoV-2 infection classification (primary outcome): mixed effects hierarchical multivariable logistic regression analyses*

Analysis	Adjusted odds ratio (95% CI)
Primary outcome: in-hospital mortality	
Primary analysis: all patients	
No SARS-CoV-2 infection	1
Incidental SARS-CoV-2 infection	1.28 (1.10–1.50)
Exacerbating SARS-CoV-2 infection	1.35 (1.22–1.48)
Primary COVID-19	2.54 (2.30–2.81)
Sensitivity analyses (corresponding diagnoses)†	
No SARS-CoV-2 infection	1
Incidental SARS-CoV-2 infection	1.41 (1.20–1.66)
Exacerbating SARS-CoV-2 infection	1.19 (1.08–1.31)

CI = confidence interval; COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2. * Adjusted for Australia and New Zealand Risk of Death, frailty, month of ICU admission, hospital, hospital type, and state/territory. Primary analysis results for other factors (ANZROD, frailty, state/territory, hospital type, month of ICU admission) are reported in the Supporting Information, table 8. † Outcome for patients with incidental SARS-CoV-2 infections compared with outcome for 127 799 patients with corresponding ICU admission diagnoses but without SARS-CoV-2 infections; outcome for patients with exacerbating SARS-CoV-2 infections compared with outcome for 54 679 patients with corresponding ICU admission diagnoses but without SARS-CoV-2 infections. ◆

Other outcomes

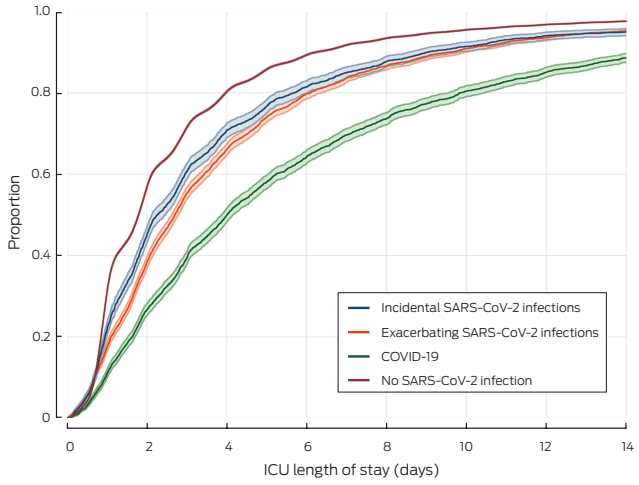
The median delay in discharge from the ICU was longer for people with SARS-CoV-2 infections than for patients without SARS-CoV-2 infections, and larger proportions were discharged overnight (20.4–22.9% *v* 14.6%). Median hospital stay was longer than for people without SARS-CoV-2 infections for patients with primary COVID-19 (11.5 days; IQR, 6.8–21.3 days), or exacerbating (8.3 days; IQR, 4.5–16.2 days) or incidental SARS-CoV-2 infections (9.5 days; IQR, 4.3–19.2 days) than for people without SARS-CoV-2 infections (7.7 days; IQR, 4.0–14.2 days) (Box 4).

Discussion

Our retrospective, multicentre observational study included data for 207 684 people admitted to 195 ICUs in Australia and New Zealand during 2022–23, including 11 217 with SARS-CoV-2 infections. The proportion of infections classified as primary COVID-19 fell, while those classified as incidental or exacerbating SARS-CoV-2 infections increased. Whether classified as incidental, exacerbating, or primary, SARS-CoV-2 infections were associated with higher adjusted in-hospital mortality. Risk-adjusted median ICU length of stay was also longer for patients with incidental or exacerbating SARS-CoV-2 infections.

Information regarding the prevalence of incidental SARS-CoV-2 infections in hospital patients is scant. An analysis of data for 250 United States hospitals that had treated large numbers of patients with COVID-19 estimated that SARS-CoV-2 infections were incidental in 10.6% of cases.[23] In a single centre Dutch study of patients infected with the BA.1 or BA.2 Omicron subvariants, 31% of SARS-CoV-2 infections were incidental; they were the primary cause of hospital admission in 45% and a contributing cause in 21% of hospital admissions.[24] We similarly found that for 24% of SARS-CoV-2 infections in people admitted to intensive care in Australia and New Zealand during 2022–23 were incidental, and the proportion grew over 18 months from less than 10% to about 25% of patients with SARS-CoV-2 infections. A combination of high levels of COVID-19 vaccination and the

6 Intensive care unit (ICU) length of stay, by SARS-CoV-2 infection type: cumulative incidence Kaplan–Meier curves*



COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2. * With 95% confidence intervals and censored at 14 days.

7 Intensive care unit (ICU) length of stay for people admitted to Australian and New Zealand ICUs, 1 January 2022 – 30 June 2023, by SARS-CoV-2 infection classification (secondary outcome): mixed effects hierarchical multivariable log-linear regression analyses*

Analysis	β coefficient (95% CI)
Secondary outcome: ICU length of stay	
Primary analysis: all patients	
No SARS-CoV-2 infection	Reference
Incidental SARS-CoV-2 infection	0.130 (0.097–0.162)
Exacerbating SARS-CoV-2 infection	0.034 (0.010–0.059)
Primary COVID-19	0.039 (–0.013 to 0.092)
Sensitivity analyses (corresponding diagnoses)†	
No SARS-CoV-2 infection	Reference
Incidental SARS-CoV-2 infection	0.127 (0.096–0.158)
Exacerbating SARS-CoV-2 infection	0.054 (0.027–0.082)

CI = confidence interval; COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2. * Adjusted for severity of illness category, diagnosis, frailty, month of admission, hospital, hospital type, and state/territory. Primary analysis results for other factors (ANZROD, frailty, ICU admission diagnostic code, state/territory, hospital type, death in ICU) are reported in the Supporting Information, table 9. † Outcome for patients with incidental SARS-CoV-2 infections compared with outcome for 127 799 patients with corresponding ICU admission diagnoses but without SARS-CoV-2 infections; outcome for patients with exacerbating SARS-CoV-2 infections compared with outcome for 54 679 patients with corresponding ICU admission diagnoses but without SARS-CoV-2 infections. ◆

predominance of the Omicron SARS-CoV-2 variant in Australia and New Zealand may have resulted in a larger proportion of patients with asymptomatic or mild disease. Together with the increasing community prevalence of SARS-CoV-2 infections, this may have led to the higher proportion of incidental disease among ICU patients.

Our findings are consistent with those of previous analyses of the influence of concomitant SARS-CoV-2 infection on outcomes for people admitted to hospital. A large observational study in the United States (more than 80 000 patients) found that mortality was 4.1 percentage points higher among people who presented with out-of-hospital ST-elevation myocardial infarction who also had COVID-19 (15.2% *v* 11.2%).[5] Similarly, the risks of in-hospital death and pulmonary complications were higher for patients with active or recent peri-operative SARS-CoV-2 infections.[6] These studies were undertaken prior to widespread COVID-19 vaccination and the predominance of the Omicron SARS-CoV-2 variant. Our study reflects the impact of SARS-CoV-2 infections during the later stages of the pandemic in a highly vaccinated population with access to a well resourced health care system. Although the now prevalent Omicron variant is less pathogenic,[13] our findings suggest that incidental, exacerbating, and primary SARS-CoV-2 infections all increase the risk of in-hospital death.

Our findings regarding longer ICU length of stay and discharge delay for patients with SARS-CoV-2 infections are plausible. Infection control procedures can contribute to discharge delay, as it may take time to find appropriate isolation areas to which patients can be discharged from the ICU. Similarly, SARS-CoV-2 infection has been associated with reduced use of percutaneous coronary interventions and changes in surgical triage practice, at least in part because of these challenges.[5,25]

Implications

We found that a substantial majority of people admitted to intensive care with SARS-CoV-2 infections were admitted to the ICU for reasons other than primary COVID-19. Given their generally short stay in hospital before ICU admission, most were probably infected prior to coming to the hospital. Higher age and having other medical conditions is associated with lower COVID-19 vaccine efficacy and immune response, and could result in a greater risk of SARS-CoV-2 infection.[26]

The smaller proportion of elective surgery-related ICU admissions among people with incidental SARS-CoV-2 infections than among people not infected is probably the result of pre-surgical screening and the postponement of procedures. However, that some people admitted to ICU after elective surgery were found to have incidental SARS-CoV-2 infections indicates the importance of ongoing peri-operative screening at the time of hospital admission.

The influence of incidental and exacerbating infection on risk-adjusted in-hospital mortality may validate the attribution classification system for SARS-CoV-2 infections. It also indicates the significance of concomitant SARS-CoV-2 infections, even when incidental, and consequently the need for ongoing vigilance and appropriate infection control and treatment for optimising outcomes for these patients.

Median ICU and hospital stays were longer for patients with concomitant SARS-CoV-2 infections. This implies that they require more care and resources, possibly including enhanced infection control processes. It is also possible that some of the impact of SARS-CoV-2 infection on mortality is attributable to these indirect effects on processes of care rather than the pathogenicity of the virus, with public health implications with respect to resource allocation in the post-pandemic era and for future respiratory disease outbreaks.

Limitations

For our systematic evaluation of outcomes for critically ill people diagnosed with SARS-CoV-2 infections during the latter stage

of the pandemic, we analysed data for a large number of ICU admissions, a group at particular risk of poor outcomes and greater care needs. As the analysed data, collected for a high quality clinical registry by trained staff, covered most ICU admissions in Australia and New Zealand, our findings can probably be generalised to other ICUs with similar resources. We adjusted our analyses for clinically important patient and organisational factors, and sensitivity analyses yielded similar results to our main analyses.

However, the classification of incidental and exacerbating infections was an attribution method selected for its clinical plausibility, without consensus regarding its suitability. Second, we could not identify incidental infections prior to 2022. Third, we do not know the pathophysiological mechanisms underlying increased mortality, nor whether it is related to the direct effects of SARS-CoV-2 infection or to its indirect effects on processes of care, such as isolation requirements. Fourth, data on vaccination status and SARS-CoV-2-specific treatments were not available; however, our findings are probably generalisable to areas with vaccination levels as high as in Australia and New Zealand. Fifth, we had no information on specific SARS-CoV-2 subvariants, but by including the month of admission as a factor in our multivariable analyses we hope to have controlled for changes in their prevalence. Finally, we had no information about where SARS-CoV-2 infections were acquired, but the short median time in hospital prior to ICU admission suggests that most would have been acquired in the community.

Conclusion

As we enter the post-COVID-19 pandemic era, clinicians should be aware that patients with SARS-CoV-2 infections at ICU admission have a higher risk of death, irrespective of whether it is the primary cause of admission or an incidental finding.

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Supporting Information

Additional Supporting Information is included with the online version of this article.