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BRIEF COMMUNICATION

Association between COVID-19 vaccination and 28-day all-cause mortality in SARS-CoV-2–infected older people living in residential aged care facilities

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COVID-19 vaccine, mortality, SARS-CoV-2 infection, residential facilities, morbidity.

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Abstract

This retrospective cross-sectional study reviewed the association between COVID-19 vaccination and the 28-day all-cause mortality amongst SARS-CoV-2–infected older people living in residential aged care facilities. A lower mortality rate was observed in fully vaccinated residents compared with not fully vaccinated residents. Further research is required to investigate the optimal timing of vaccination boosters and vaccine efficacy as variants evolve.

The coronavirus disease 2019 (COVID-19) pandemic has had profound effects on older people living in residential aged care facilities (RACFs).[1] By the end of 2020, Australia had recorded 908 COVID-19–related deaths, which included 678 residents living in RACFs.[2] These residents are at risk of acquiring infections through exposure to co-residents, carers and visitors. They are intrinsically vulnerable to complications from infections. The prioritisation of COVID-19 vaccination in this susceptible population via the Australian Commonwealth Government COVID-19 immunisation programme commenced in April 2021.

In 2021, the overall COVID-19 death toll in Australia increased as case numbers increased; however, there was a reduced number of COVID-19-related deaths amongst the RACF population[3] compared with 2020. Studies have suggested that COVID-19 vaccines reduce mortality and disease burden in the general population,[4–6] including older adults.[7] Overseas studies have also suggested that frail severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–infected RACF residents who were vaccinated had better outcomes than those who were not.[8] During the third wave of COVID-19 in late 2021, there were concerns about the effect of waning immunity on outcomes in this cohort of people, as it had been 4 to 6 months since the majority of residents received their second vaccination and were considered 'fully vaccinated' (FV). At that time, there were no published Australian studies comparing outcomes between RACF residents who were FV with residents who were not FV (NFV).

We hypothesised that double vaccination for COVID-19 would improve outcomes in frail multimorbid older adults living in RACFs even several months after administration of the second dose. We compared the characteristics and outcomes of SARS-CoV-2–infected RACF residents who were FV with those who were NFV during the third wave of COVID-19 in Melbourne, Victoria, driven by the Delta variant.

A retrospective audit was conducted using the Residential In-Reach (RIR) database at Northern Health during their involvement in nine RACF COVID-19 outbreaks between 9 September and 9 December 2021. This study was approved by the Northern Health Office of Research (ALR 74.2021). We included older RACF residents with a positive SARS-CoV-2 polymerase chain reaction (PCR) result and excluded residents aged <65 years and those without a positive SARS-CoV-2 PCR. Two comparison groups were identified for the same time period: FV (at that time meaning double vaccinated) and NFV residents (received one dose or no COVID-19 vaccinations).

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Data extracted from the RIR database included residents' care plans, clinical handovers, hospital records and vaccination records. Baseline characteristics collected included age, sex, vaccination status, vaccine type, date of last vaccine, SARS-CoV-2 PCR-positive date, age-adjusted Charlson Comorbidity Index (ACCI),[9] smoking status, presence of hypertension, extremes of weight, severe cognitive impairment with or without behavioural and psychological symptoms of dementia and frailty scores using the Clinical Frailty Scale (CFS).[10]

The primary outcome measure was 28-day mortality from the date of the first positive SARS-CoV-2 PCR test. Secondary outcomes measures included development of symptoms related to COVID-19 infection (respiratory symptoms, hypoxia, fever, anorexia, gastrointestinal symptoms, delirium), need for medical interventions (oxygen, supplemental fluids, systemic steroids, antibiotics, others) and complications (falls and hospitalisations).

Descriptive analysis was conducted to compare the demographic and clinical details of FV residents with those who were NFV. Chi-square or Fisher exact tests were used to compare categorical variables across groups, whilst Student *t* tests and Mann–Whitney (rank sum) tests were used to test for differences between groups for normally and nonnormally distributed continuous variables, respectively. Variables with *P* values of less than 0.2 on univariable analysis were included in multivariable logistic regression analysis, with both backwards and forwards stepwise regression techniques utilised. Statistical analysis was conducted using STATA version 15.1 (StataCorp). A *P* value of less than 0.05 was considered to indicate statistical significance.

Of the 191 residents included in this analysis, 158 (82.7%) were FV with double doses of a COVID-19 vaccine and 33 (17.3%) were NFV, which included 11 being partially vaccinated and 22 unvaccinated. Residents who were FV were older than the NFV group. The majority of the FV residents had received the Pfizer vaccine between April and June 2021. Median duration from the second vaccination until SARS-CoV-2–positive PCR was 167 days (interquartile range [IQR], 136–185 days). Of the ACCI factors listed, solid tumour, dementia and leukaemia were noted to be significantly different when comparing the two groups (Appendix).

FV was associated with a lower mortality rate of 15.2% (24 of 158) compared with 39.4% (13 of 33) for NFV residents (odds ratio [OR], 0.27 [95% CI, 0.12–0.63], $P = 0.002$). This result was observed at the point when our FV group was approximately 4.5 to 6.2 months (IQR, 136–185 days) since receiving their second doses of COVID-19 vaccines. The likelihood of death was also lower in residents who had at least one dose of COVID-19 vaccination compared with completely unvaccinated (OR, 0.34 [95% CI, 0.13–0.85], $P = 0.020$). When considering the vaccine type, observed ORs difference (OR, 0.24 and 0.50) between AstraZeneca and Pfizer was not statistically significant ($P = 0.165$ and $P = 0.102$, respectively) (Table 1).

Upon multivariable analysis, with adjustment for potential confounding effects, it was found that the effect of double vaccination on mortality was relatively unchanged (odds ratio [OR], 0.30 [95% CI, 0.10–0.92]) when compared with univariable analysis shown in Table 1 (OR, 0.27 [95% CI, 0.12–0.63]). The OR for the fully vaccinated (FV) status variable remained in the range of 0.25–0.30, irrespective of which combination of factors were considered in the multivariable model.

The fully vaccinated (FV) group had a longer mean lag time (2.5 vs 1.0 days, $P = 0.037$) between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR) positivity and symptom development compared with the not FV (NFV) group. They also had lower incidences of respiratory symptoms (75.8% vs 93.9%, $P = 0.020$) and less hypoxia (38.8% vs 57.6%, $P = 0.048$). There was no significant

Table 1 Comparison of vaccination status for the primary outcome death

Factor	Odds ratio	95% CI	*P* value
Fully vs not fully vaccinated			
No vaccination or single dose (NFV)	1	-	-
First and second dose (FV)	0.27	0.12–0.63	0.002
Unvaccinated vs partially vaccinated/FV			
Not vaccinated	1	-	-
Minimum of first dose	0.34	0.13–0.85	0.020
Vaccination status			
No vaccination	1	-	-
One dose	1.71	0.35–7.46	0.508
Two doses	0.42	0.15–1.12	0.083
Vaccine type			
No vaccine	1	-	-
Pfizer	0.50	0.18–1.33	0.165
AstraZeneca	0.24	0.04–1.33	0.102

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Table 2 Symptoms, interventions and complications

Factor	NFV	FV	*P* value
Symptoms			
Days from positive PCR to symptom, mean (SD)	1.0 (3.0)	2.5 (3.8) ($n = 149$)	0.037
Respiratory	31 (93.9%)	119 (75.8%)	0.020
Hypoxia (oxygen saturation <92%)	19 (57.6%)	61 (38.9%)	0.048
Fever	6 (18.2%)	18 (11.5%)	0.30
Gastrointestinal	6 (18.2%)	28 (17.9%)	0.97
Anorexia	21 (63.6%)	87 (55.4%)	0.39
Delirium	9 (27.3%)	33 (21.0%)	0.43
Interventions			
Oxygen	19 (57.6%)	65 (41.1%)	0.084
Dexamethasone	12 (36.4%)	51 (32.3%)	0.65
Supplemental fluids	17 (51.5%)	62 (39.2%)	0.19
Antibiotics	11 (33.3%)	44 (27.8%)	0.53
Any other treatment	11 (33.3%)	38 (24.1%)	0.27
Days from positive PCR to intervention, mean (SD)	3.1 (2.8) ($n = 27$)	4.3 (3.5) ($n = 101$)	0.100
Complications			
Hospitalisation	10 (30.3%)	53 (33.5%)	0.72
Days from positive PCR to hospitalisation, mean (SD)	3.5 (4.1) ($n = 10$)	5.6 (5.4) ($n = 53$)	0.25
Fall	7 (21.2%)	39 (25.0%)	0.65

difference for development of fever, anorexia, gastrointestinal symptoms and delirium between FV and NFV patients. There were also no significant differences for symptomatic coronavirus 2019 (COVID-19) requiring interventions such as oxygen, dexamethasone, fluids, antibiotics and other treatments when comparing the two groups. Whilst approximately a quarter of SARS-CoV-2–infected residents had falls (25.0% vs 21.2%, $P = 0.65$) and one-third required hospital admission (30.3% vs 33.5%, $P = 0.71$), there were no significant differences between NFV and FV (Table 2). Values are presented as number (percentage) unless otherwise indicated.

Discussion

Consistent with overseas studies of older people living in the community and in nursing homes who contracted SARS-CoV-2,[4,7,8] we found in this cross-sectional study that vaccination for frail multimorbid older people in RACFs in our local area appears to have a protective effect on mortality, even at a point where waning immunity was a real concern.[11]

Whilst some studies have suggested that chronic disease burden is associated with mortality in patients with COVID-19,[12] this was not found to be significant in our multimorbid cohort. After accounting for ACCI, we found that being FV was still associated with a lower mortality rate. Similarly, age is a well-established risk factor for mortality in SARS-CoV-2–infected individuals.[13,14] In our study cohort, although the median age was higher in the FV (87 vs 82 years) group, their mortality rate was observed to be lower than that in the NFV group.

Our study observed a positive association between FV status and lower mortality rates in SARS-CoV-2–infected residents 4.5 to 6.2 months since the FV group received a dose of vaccine. It had been suggested that humoral immunity considerably wanes 6 months after COVID-19 vaccine.[15] Overseas studies have since found that boosters improve detectable neutralising activity[16] and vaccine efficacy[17] against the Omicron variant; however, it is not known whether this translates to mortality rate reduction in the RACF population. Currently in Australia, an additional two booster doses (a third and fourth dose) 3 months after the first two COVID-19 vaccinations is recommended for people aged 50 years and older.[18] Future studies are needed to look at the optimal timing of further vaccination doses and the associated mortality and morbidity benefits.

Although we have observed lower incidences of respiratory symptoms and hypoxia in our FV residents, there were no significant differences in the other secondary outcomes. This may suggest that morbidity outcomes and healthcare needs of these RACF residents are not fully mitigated by vaccines alone and ongoing measures are needed to support RACFs as COVID-19 outbreaks continue to occur.

One limitation of this study was the small sample size relative to the number of variables to be explored in multivariable analysis. Whilst forwards and backwards stepwise regression modelling techniques were utilised to counter this, it is likely that the analysis was underpowered and several clinically relevant variables were not able to be detected as statistically significant on multivariable analysis. The association between vaccination status and mortality remained consistent in the range of an OR of 0.25 to 0.30, regardless of which variables were included

in the multivariable model, although it must also be acknowledged that residual confounding may still exist.

The retrospective nature of the study also means interpretation of records could be subjective amongst investigators (e.g., scoring of CFS) and dependent on availability of information. Not included in this study were the goals of patient care or advanced care plans, which can significantly influence clinical decisions such as provision of intervention and hospital transfer.

In conclusion, we found FV SARS-CoV-2–infected frail older residents living in RACFs during the third wave of COVID-19 in Melbourne had a lower mortality rate compared with partially and unvaccinated individuals. Our study highlights that vaccination continues to play a vital role in protecting our vulnerable multimorbid older RACF population, with a persisting mortality benefit several months after a second dose of the COVID-19 vaccination. Further studies are needed to guide future vaccination schedule and investigate efficacy of current vaccines as new variants evolve.

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APPENDIX 1

Baseline characteristics of residents

Factor	NFV	FV	*P* value
N	33	158	
Age, median (IQR)	82 (76–87)	87 (82–90)	0.002
Sex			0.48
Female	23 (69.7%)	100 (63.3%)	
Male	10 (30.3%)	58 (36.7%)	
Vaccine type			<0.001
No vaccine	22 (66.7%)	0 (0.0%)	
Pfizer	9 (27.3%)	140 (88.6%)	
AstraZeneca	2 (6.1%)	18 (11.4%)	
Total ACCI score, median (IQR)	6.0 (5.0–8.0)	7.0 (6.0–9.0)	0.070
Diabetes			0.37
No diabetes	23 (69.7%)	89 (56.3%)	
Diabetes – no end-organ damage	7 (21.2%)	48 (30.4%)	
Diabetes – end-organ damage	3 (9.1%)	21 (13.3%)	
Liver disease	1 (3.0%)	4 (2.5%)	0.87
Solid tumour			0.036
None	29 (87.9%)	134 (84.8%)	
Localised	2 (6.1%)	23 (14.6%)	
Metastatic	2 (6.1%)	1 (0.6%)	
Congestive cardiac failure	12 (36.4%)	59 (37.3%)	0.92
Myocardial infarction	6 (18.2%)	39 (24.7%)	0.42
Pulmonary disease	12 (36.4%)	42 (26.6%)	0.26
Peripheral vascular disease	4 (12.1%)	18 (11.4%)	0.91
Cerebrovascular accident/transient ischaemic attack	11 (33.3%)	35 (22.2%)	0.17
Dementia	22 (66.7%)	128 (81.0%)	0.068
Hemiplegia	3 (9.1%)	12 (7.6%)	0.77
Connective tissue disease	2 (6.1%)	8 (5.1%)	0.82
Leukaemia	1 (3.0%)	0 (0.0%)	0.028
Malignant lymphoma	0 (0.0%)	4 (2.5%)	0.36
Peptic ulcer disease	1 (3.0%)	10 (6.3%)	0.46
Moderate/severe chronic kidney disease	4 (12.1%)	31 (19.6%)	0.31
Smoker	2 (6.1%)	4 (2.5%)	0.29
Hypertension	21 (63.6%)	104 (65.8%)	0.81
Extremes of weight, mean (SD)	63.2 (18.8) ($n = 24$)	68.7 (15.7) ($n = 124$)	0.14
Severe cognitive impairment	15 (45.5%)	72 (45.6%)	0.99
Behavioural and psychological symptoms of dementia	8 (24.2%)	59 (37.3%)	0.15
Clinical Frailty Scale			0.23
6	2 (6.1%)	6 (3.8%)	
7	21 (63.6%)	123 (77.8%)	
8	10 (30.3%)	29 (18.4%)	

ACCI, age-adjusted Charlson Comorbidity Index; FV, fully vaccinated; IQR, interquartile range; NFV, not fully vaccinated; SD, standard deviation.