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Original Article

ORIGINAL ARTICLE

Acute kidney injury requiring renal replacement therapy in people with COVID-19 in Ontario, Canada: a prospective analysis of risk factors and outcomes

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ABSTRACT

Background. Severely ill people with coronavirus disease 2019 (COVID-19) are at risk of acute kidney injury treated with renal replacement therapy (AKI-RRT). The understanding of the risk factors and outcomes for AKI-RRT is incomplete.
Methods. We prospectively collected data on the incidence, demographics, area of residence, time course, outcomes and associated risk factors for all COVID-19 AKI-RRT cases during the first two waves of the pandemic in Ontario, Canada.
Results. There were 271 people with AKI-RRT, representing 0.1% of all diagnosed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cases. These included 10% of SARS-CoV-2 admissions to intensive care units (ICU). Median age was 65 years, with 11% <50 years, 76% were male, 47% non-White and 48% had diabetes. Overall, 59% resided in the quintile of Ontario neighborhoods with the greatest ethnocultural composition and 51% in the two lowest income quintile neighborhoods. Mortality was 58% at 30 days after RRT initiation, and 64% at 90 days. By 90 days, 20% of survivors remained RRT-dependent and 31% were still hospitalized. On multivariable analysis, people aged >70 years had higher mortality (odds ratio 2.4, 95% confidence interval 1.3, 4.6). Cases from the second versus the first COVID-19 wave were older, had more baseline comorbidity and were more likely to initiate RRT >2 weeks after SARS-CoV-2 diagnosis (34% versus 14%; $P < 0.001$).
Conclusions. AKI-RRT is common in COVID-19 ICU admissions. Residency in areas with high ethnocultural composition and lower socioeconomic status are strong risk factors. Late-onset AKI-RRT was more common in the second wave. Mortality is high and 90-day survivors have persisting high morbidity.

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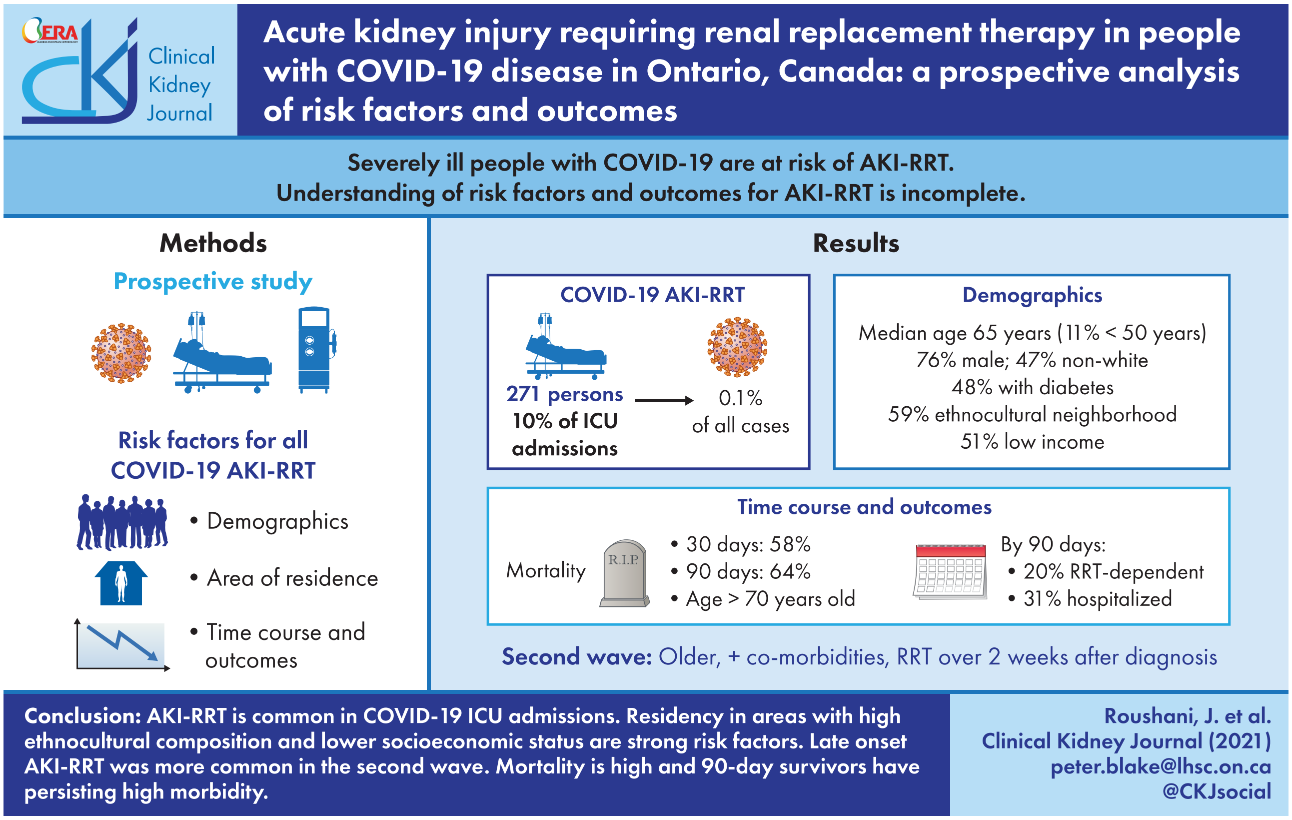
GRAPHICAL ABSTRACT



Keywords: acute dialysis, acute kidney injury, COVID-19, renal replacement therapy

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of novel coronavirus disease 2019 (COVID-19) [1]. As of 31 January 2021, in Ontario, Canada's most populous province, there had been >270 000 diagnosed infections, equivalent to 1.9% of the population, and >6000 deaths, representing a case fatality rate of 2.3% [2].

Acute kidney injury (AKI) is a well-recognized complication of COVID-19, with a significant proportion of those affected receiving renal replacement therapy (RRT) [3–14]. AKI has been associated with direct SARS-CoV-2 infection of renal tubular cells, but the principal cause is now considered to be acute tubular injury caused by volume depletion and multi-organ failure associated with COVID-19 [7].

The literature on people with COVID-19-related AKI-RRT is still quite limited. Gupta *et al.* reported a 20.6% rate of AKI-RRT in 637 people admitted to an intensive care unit (ICU) in 60 hospitals across the USA [6]. Mortality was 55% and, of those discharged from hospital, 34% still required RRT [6]. Risk factors for mortality included older age and severe oliguria [6]. Other AKI-RRT studies are small and single-center [10–12]. Multiple COVID-19 AKI studies do not focus specifically on patients with AKI-RRT but also report high mortality [3–5, 8, 9, 13].

We have used prospectively collected data since the start of the pandemic in Ontario in March 2020 to look at COVID-19 AKI-RRT both inside and outside the ICU in all the centers in the province. We specifically looked at the demographic characteristics, including neighborhood of residence, of the AKI-RRT population, the type of RRT they received and their outcomes, the risk factors for mortality and the intervals between diagnosis of SARS-CoV-2 infection, initiation of RRT and recovery or mortality. We also examined differences between the pattern of AKI-RRT in the first and second COVID-19 waves.

MATERIALS AND METHODS

Setting

Ontario has a population of ∼14.5 million [15]. The Ontario Renal Network (ORN), a part of Ontario Health, is a provincial government agency that funds and manages kidney disease services working with 27 Renal Programs [16, 17]. All dialysis in Ontario, including RRT for AKI, is funded by a single-payer—the provincial government—operating through the ORN [16, 17]. For the purpose of this study, the first wave of the pandemic in Ontario comprised the period 1 March to 1 September 2020, and the second wave from 1 September 2020 to 31 January 2021.

Data sources

Nine linked data sets were used. The ORN COVID-19 data collection tool captured information each week on people with AKI-RRT after SARS-CoV-2 infection: name, health card number, type

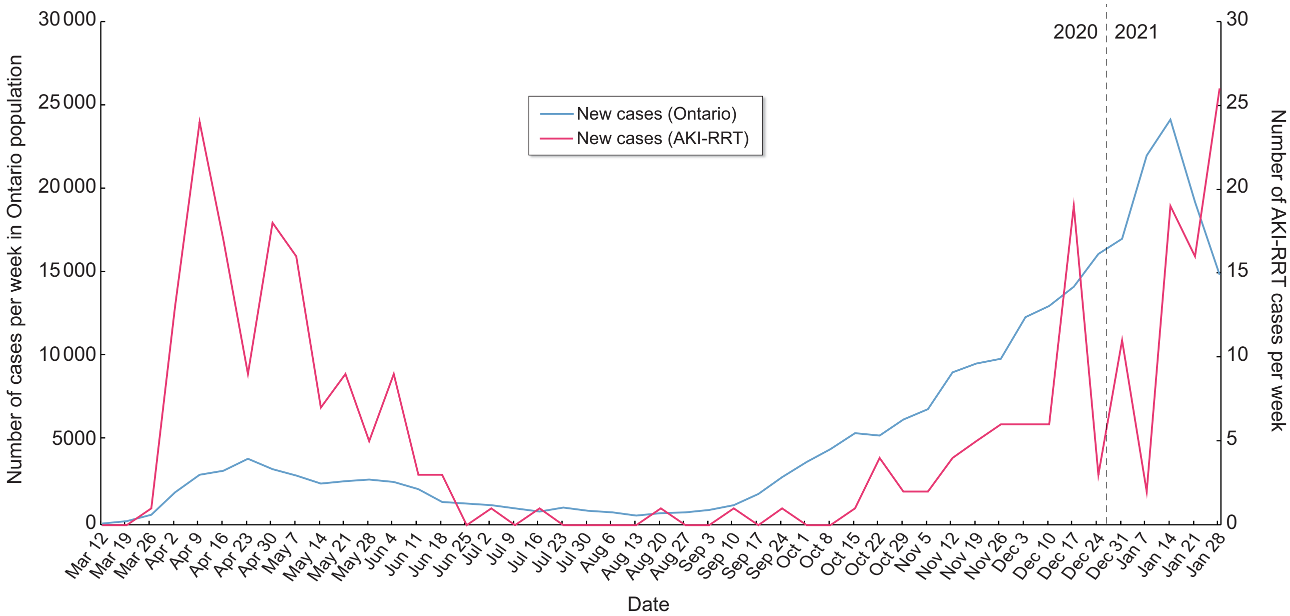


FIGURE 1: Number of diagnosed new cases of SARS-CoV-2 infection in the general population and of SARS-CoV-2-associated AKI-RRT in Ontario. The relatively lower rates of cases in the general population compared with AKI-RRT cases in the first versus the second wave likely reflects relatively lower availability of SARS-CoV-2 testing in the community during the first wave.

of residence, hospitalization status, RRT modality, ICU and ventilator status, and disposition (active, recovered, deceased) [17]. This was a minimal data set but included personal health information that could be linked to other data sets. Data were collected prospectively from the second week of March 2020, when the first AKI-RRT case was diagnosed, with all renal programs submitting weekly data for all AKI-RRT cases. Hospital admissions were subsequently crosschecked with the Canadian Institute for Health Information Discharge Abstract Database, which also allowed determination of medical histories, including comorbidities, based on the International Classification of Diseases 10 diagnostic codes. Each chronic condition was defined based on 5 years of look-back data from the date of SARS-CoV-2 reporting.

The other data sets were: the Ontario Renal Reporting System, also identifying all individuals with AKI-RRT and including ethnicity, collected by data leads in each Program at registration, based on charting by clinical staff who may ask patients or relatives to self-identify ethnicity but who are not mandated to do so [17]; the Ontario Laboratories Information System, providing SARS-CoV-2 test dates and results and laboratory values generally; the Registered Persons Database, providing demographic information and date of death; the Ontario Health Insurance Plan, containing health insurance claims for physician services including dialysis; the Statistics Canada Postal Code Conversion File, linking postal codes to standard geographic areas to derive income quintile; and also the Canadian Index of Multiple Deprivation, a geographically based index used to understand inequalities through various metrics of education, health and society [18]. Ethnocultural composition is a dimension represented in this index and is defined by an area's composition of immigrant populations, including the proportions who are recent immigrants, self-identified visible minorities, born outside of Canada and have no knowledge of Canada's official languages—English and French [18].

Population

All incident AKI-RRT patients registered in the ORN COVID-19 data tool between 10 March 2020 and 31 January 2021, were included. These were people who received acute RRT in association with a diagnosis of SARS-CoV-2 infection, defined as testing positive on a nucleic acid amplification test [19]. The exclusion criteria were missing health card numbers and postal codes, non-Ontario residents, age $<$18 years, previous kidney transplantation or recent dialysis and no serum creatinine from the previous 3 years, as it was unclear whether those were truly cases of AKI. Patients with chronic kidney disease (CKD) stage 5 were excluded because the degree of insult required for these patients to need RRT is likely much smaller than those with normal renal function or lesser degrees of CKD. Clinical decision making and indications for RRT were determined by individual care givers at each of the hospital/ICU sites.

Statistical analysis

Descriptive statistics included frequency (percentages) for categorical variables and means $\pm$ standard deviations or medians and interquartile ranges (IQRs) for continuous variables. Chi-squared test was used to explore the associations of categorical variables between survivors and non-survivors and between waves 1 and 2. We analyzed age $>$70 years as a categorical variable, thinking that this would be more useful to clinical practitioners because it reflects the intersectional experience of COVID-19 and older age [6]. To explore risk factors associated with mortality, a multivariable logistic regression was used and included sex, age, geographic location, ethnicity, diabetes, type of residence, income quintile, baseline serum creatinine, time of initiation of RRT relative to SARS-CoV-2 diagnosis and the Canadian Index of Multiple Deprivation. Patients with an unknown, missing or other ethnicity were treated as one distinct

Table 1. Characteristics of all 271 people with AKI-RRT at baseline compared with Ontario's general population

Characteristic	AKI-RRT patients, $n = 271$, n (%)	Ontario population, $n \approx 14\,750\,000$ (all ages) [20, 21], $n \approx 11\,600\,000$ (adults only) [20]
Demographics		
Male	206 (76)	49% [20]
Age group		
29–49 years	29 (11)	51% [15]
50–69 years	146 (54)	33%
70+ years	96 (35)	16%
Patient location		
Toronto area	215 (79)	42% [21]
Outside Toronto area	56 (21)	58%
Residency		
Other	21 (8)	
Private residence	250 (92)	
Race		
White	111 (41)	68% [15]
Non-White	99 (37)	29%
Unknown/missing/other	61 (23)	3%
Ratio of White to non-White	1.12	2.14
Income quintile[a]		
1	72 (27)	20%
2	67 (25)	20%
3	53 (20)	20%
4	35 (13)	20%
5	44 (16)	20%
Ethnocultural composition quintile[b]		
1 and 2	29 (11)	40%
3	32 (12)	20%
4	53 (20)	20%
5	157 (58)	20%
Comorbid conditions		
Diabetes mellitus in adults (age 18+ years)	129 (48)	10% [22]
Cancer	25 (9)	
Cardiac disease	54 (20)	
CKD[c]		
eGFR <30 mL/min/1.73 m^2	10 (4)	
eGFR 30–59 mL/min/1.73 m^2	55 (20)	
eGFR 60–89 mL/min/1.73 m^2	111 (41)	
eGFR 90+ mL/min/1.73 m^2	95 (35)	
Baseline serum creatinine (mmol/L), median (IQR)	84 (71–102)	

[a]Income quintile is a measure of neighborhood socioeconomic status that divides the population into five income groups of equal size. Group 1 lives in the neighborhoods with the lowest incomes and group 5 in those with the highest incomes.
[b]Ethnocultural composition refers to the community makeup of immigrants (i.e. proportions of recent immigrants, of people born outside Canada, of those who self-identify as visible minorities and of those who cannot speak either of Canada's official languages—English and French). The population is divided into five ethnocultural quintiles of equal size. Group 1 lives in the neighborhoods with the greatest degree of ethnocultural composition, and group 5 lives in those with the least [18].
[c]Baseline eGFR within 7 days to 3 years prior to RRT initiation.
eGFR, estimated glomerular filtration rate.

group and as a factorial variable, with White ethnicity as the reference group. These variables were chosen based on the general literature on risk factors for COVID-19 incidence, morbidity and mortality and on our clinical interest as nephrologists who treat AKI. All statistical analyses were performed using SAS statistical software, with statistical significance set at two-sided $P < 0.05$.

Ethics approval

The data collection was in accordance with Ontario Health's legislative authority under the Ontario Personal Health Information Protection Act, 2004. This study followed the principles of the declaration of Helsinki.

RESULTS

As of 31 January 2021, 271 people had developed COVID-19 related AKI-RRT, representing 0.1% of the 270 180 diagnosed SARS-CoV-2 cases in Ontario, and 2% of the 13 533 hospitalized cases, as of that time (Figure 1). This represents an incidence of 20.3 cases per million population per year [2]. There were 18 people excluded because they had no serum creatinine value recorded in the previous 3 years. Of the 271 patients, 259 had an ICU admission and accounted for 10% of 2490 COVID-19 ICU admissions in Ontario. The 174 patients who died represent 2.8% of COVID-19 deaths in Ontario [2].

The median age of the 271 people was 65 years, and 11% were aged <50 years, 76% were male and 79% of them were residents of the Greater Toronto Area, where approximately 40% of Ontarians live (Table 1). Overall, 92% lived in a private residence, as

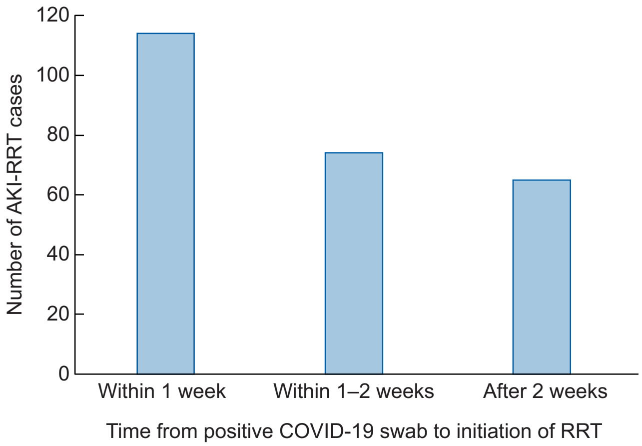


FIGURE 2: Frequency distribution of all 271 AKI-RRT cases by time between first positive COVID-19 swab and RRT initiation.

distinct from a congregate setting such as a nursing home. By ethnicity, 59% of the patients were either non-White or had an unknown ethnicity. Socioeconomically, 58% lived in the single most ethnocultural quintile of neighborhoods and 51% resided in neighborhoods in the two lowest income quintiles for Ontario (Table 1). Ontario's vaccination eligibility guidelines and the timing of the cases indicate that none of the 271 patients would have been fully or even partially vaccinated.

Baseline comorbidities included diabetes in 48%, a much higher rate than in the general Ontario population, cardiac disease in 20% and a previous cancer diagnosis in 9% [22]. The median baseline serum creatinine was 84 µmol/L, but 23% had baseline CKD 3 and 4% had CKD 4 (Table 1).

Treatment received

Of the 271 people, 96% had an ICU stay and >90% received mechanical ventilation. The median (IQR) interval between a first positive SARS-CoV-2 swab and initiating RRT was 9 (3–15) days. However, this varied greatly, with 36% starting within 48 h, 42% within 1 week while in contrast 31% started >2 weeks after their first positive swab (Figure 2). Regarding RRT modality, 42% received sustained low-efficiency dialysis (SLED) and 41% continuous renal replacement therapy (CRRT) at some stage in their course. These include 2.9% who received both. Conventional hemodialysis was used exclusively in 20% and in 51% at some stage in their course. The median time spent on dialysis was 4 days and was 2 weeks or less in 74% of patients and >2 weeks in 26% of patients. The median length of hospital stay was 18 (9–37) days (Table 2). In total, the 271 cases required 3177 patient days of AKI-RRT.

Patient outcomes

Of these 271 people, 174 (64%) died within 90 days of initiating RRT. Most deaths were soon after RRT initiation, with 31% occurring within 7 days and 45% within 14 days. However, 18 (10%) died >4 weeks after starting RRT (Figure 3). The mortality rate was 58% at 30 days after the start of dialysis and 62% at 60 days. Of the 174 people who died, just 8 (3%) recovered renal function sufficiently to not require RRT for at least 1 week before their death. At 90 days after the start of RRT, 78 of the 97 survivors (80%) were no longer on RRT but 19 (20%) remained RRT-

Table 2. Treatments received by the 271 people with AKI-RRT

	AKI-RRT patients, $n = 271$
Intensive care admission, *n* (%)	259 (96)
On ventilator, *n* (%)	246 (91)
Length of hospital stay (in days), median (IQR)	18 (9–37)
Type of RRT received, *n* (%)[a]	
Conventional acute hemodialysis	139 (51)
Sustained low efficiency dialysis	114 (42)
Continuous renal replacement therapy	111 (41)
Time to RRT initiation from a positive COVID-19 swab, *n* (%)	
Within 1 week	114 (42)
1–2 weeks	74 (27)
After 2 weeks	65 (24)
Missing	18 (7)
Median days (IQR)	9 (3–15)
Time on RRT, *n* (%)	
<1 week	158 (58)
1–2 weeks	44 (16)
>2 weeks	69 (26)
Median days on RRT (IQR)	4 (0–15)

[a]Total exceeds 100% as many received more than one RRT modality.

dependent, including 14 who had been discharged from hospital and 30 (31%) were still hospitalized. In total, 31% of AKI-RRT cases had recovered renal function and were discharged, 11% were alive in the hospital but not on RRT and 7% of patients remained on RRT in hospital (Figure 4).

Predictors of mortality

The baseline characteristics of the 174 non-survivors and 97 survivors were compared (Table 3). On multivariable analysis, a significantly larger proportion of patients aged 70 years and older died than those aged 29 to 69 years [odds ratio (OR) 2.4, 95% confidence interval (95% CI) 1.3, 4.6] (Table 4). The relationship between age and mortality was also significant when age was analyzed as a continuous variable. There was a trend towards higher mortality in those who initiated RRT >2 weeks after a positive SARS-CoV-2 test as compared with RRT start within 1 week (OR 1.9, 95% CI 1.0, 3.9, $P = 0.069$). There were no differences between non-survivors and survivors for sex, geographic location, ethnicity, diabetes or other comorbidities, income quintile or baseline serum creatinine, and none for type of RRT received or for time on dialysis. The relationship between ethnicity and mortality was unchanged when those with 'unknown/missing/other' ethnicity were omitted from the analysis (See Appendix).

Comparison of first and second wave

The incidence of AKI-RRT by time shows that there were two distinct periods for AKI-RRT incidence, corresponding to the two waves of infection seen in the general Ontario community (Figure 1). There was a relatively lower rate of AKI-RRT cases compared to the number of SARS-CoV-2 cases in the general population in the second wave versus the first. The characteristics and course of the 138 people diagnosed during the first

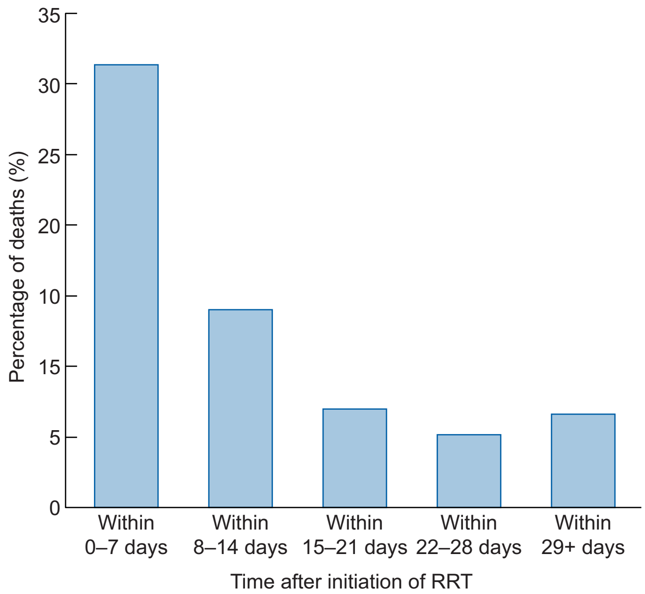


FIGURE 3: Distribution of the incidence of deaths among 174 AKI-RRT deaths by time after initiation of RRT.

wave were compared with the 133 people from the second wave (Table 5). In the second wave, there was a significantly higher proportion of people aged 70 years or older, with cardiac disease (25% versus 15%), and with baseline CKD stages 3 and 4 (29% versus 20%). There was a significantly longer interval between the first positive SARS-CoV-2 swab and RRT initiation in the second wave, with more than twice as high a proportion patients initiating RRT >2 weeks after diagnosis (34% versus 14%) (Table 5). There were no other significant differences between the baseline characteristics, treatments received and outcomes of the patients in the two waves.

DISCUSSION

In Ontario, 271 patients, representing 2% of hospitalizations, including 259 patients, comprising 10% of ICU admissions due to COVID-19, developed AKI-RRT in the first 11 months of the pandemic. At the 90-day follow-up, 31% of these patients recovered renal function and were discharged, 7% were still on RRT, but 64% had died, demonstrating what a devastating illness this is. Patients aged 70 years and older had an even higher mortality.

These 271 people required 3177 patient-days of acute RRT and so provided an enormous workload for already stressed ICU and nephrology services. This is especially so since the activity was concentrated into two 6-week periods, particularly in the Toronto area, and this put enormous strain on the required human resources, especially because maintenance dialysis units were simultaneously affected by the pandemic [5, 6, 17]. Available CRRT equipment alone would not have been sufficient to provide RRT to all these people, as well as to on-going non-COVID-19 AKI-RRT cases, but many Ontario centers use SLED and conventional acute hemodialysis, and supply of machines for these modalities is relatively abundant.

A number of features stand out from the baseline demographics of the AKI-RRT population. There is a remarkable 76% male preponderance, which is not seen in the general Ontario population infected with SARS-CoV-2 [2]. A similar male preponderance was seen in other COVID-19 AKI-RRT studies and to a lesser degree in other COVID-19 AKI populations [5, 6, 9, 12]. A male preponderance in AKI-RRT of other causes has recently been reported [23]. Almost 50% of the AKI-RRT cohort had baseline diabetes, similar to the 53% noted in the US study but far in excess of the 10% prevalence of diabetes in the Ontario adult population [6, 22]. With regard to ethnicity, 41% of the AKI-RRT population were identified as White, as compared with 68% in the general population of Ontario [11]. However, ethnicity data were missing in 22% of the cohort. The ratio of those identified as White compared with non-White was 1.12 in the AKI-RRT cohort compared with 2.14 in the general population [13]. More strikingly, almost 60% of people with AKI-RRT came from the quintile of neighborhoods with the greatest degree of ethnocultural composition in Ontario and approximately 80% from the two most socioeconomically deprived quintiles [14]. These neighborhoods often have high rates of multigenerational households and of high-density workplaces. All this is consistent with risk factors for SARS-CoV-2 infection and its complications reported elsewhere and

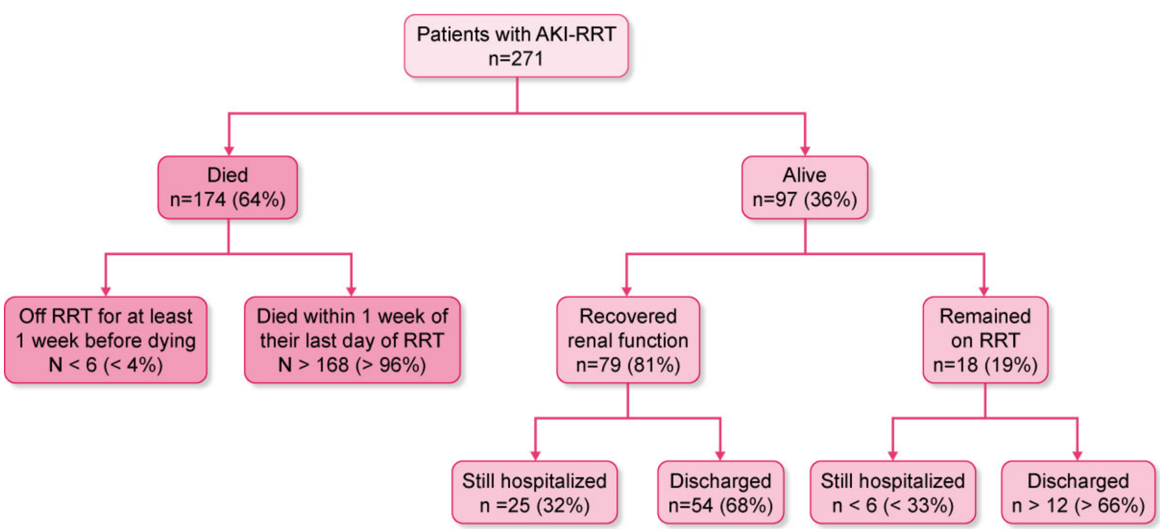


FIGURE 4: The 90-day outcomes of 271 COVID-19 patients with AKI-RRT. When number of cases is <6, the exact number cannot be stated for Ontario Health privacy reasons.

Table 3. Baseline characteristics and treatments received for the 271 people with AKI-RRT by outcome

Characteristic	Survivors, $n = 97$, n (%)	Non-survivors, $n = 174$, n (%)	P-value
Demographics			
Male	73 (75)	133 (76)	0.828
Age group			0.006
29–69 years	73 (75)	102 (59)	
70+ years	24 (25)	72 (41)	
Race			0.853
White	41 (42)	70 (40)	
Non-White	36 (37)	63 (36)	
Unknown/missing	20 (21)	41 (24)	
Income quintile[a]			0.95
1	25 (26)	47 (27)	
2	25 (26)	42 (24)	
3	21 (22)	32 (18)	
4	15 (16)	20 (12)	
5	11 (11)	33 (19)	
Ethnocultural composition quintile[b]			0.799
1 and 2	11 (11)	18 (10)	
3	10 (10)	22 (13)	
4	19 (20)	34 (20)	
5	57 (59)	100 (58)	
Comorbid conditions			
Diabetes mellitus	44 (45)	85 (49)	0.581
Cancer	7 (7)	18 (10)	0.394
Cardiac disease	16 (16)	38 (22)	0.291
CKD[c]			0.996
eGFR <59 mL/min/1.73 m^2	23 (24)	42 (24)	
eGFR 60–89 mL/min/1.73 m^2	38 (39)	73 (42)	
eGFR 90+ mL/min/1.73 m^2	36 (37)	59 (34)	
Treatment received			
Intensive care admission	87 (90)	172 (99)	<0.001
On ventilator	82 (85)	170 (98)	<0.001
Time to RRT start from a positive COVID-19 Swab (days)			0.083
Within 1 week	44 (45)	70 (40)	
1–2 weeks	28 (29)	46 (26)	
After 2 weeks	15 (16)	50 (29)	
Missing	10 (10)	8 (5)	
Median (IQR)	7 (3–13)	10 (4–16)	

[a]Income quintile is a measure of neighborhood socioeconomic status that divides the population into five income groups of equal size. Group 1 lives in the neighborhoods with the lowest incomes and group 5 in those with the highest incomes.
[b]Ethnocultural composition refers to the community makeup of immigrants (i.e. proportions of recent immigrants, of people born outside Canada, of those who self-identify as visible minorities and of those who cannot speak either of Canada's official languages—English and French). The population is divided into five ethnocultural quintiles of equal size. Group 1 lives in the neighborhoods with the greatest degree of ethnocultural composition, and group 5 lives in those with the least [18].
[c]Baseline eGFR within 7 days to 3 years prior to dialysis start.
P-values were calculated using the Chi-Squared test for analysis of categorical variables. eGFR, estimated glomerular filtration rate.

emphasizes the socioeconomic and ethnocultural factors underlying so much of the COVID-19 pandemic's worst effects in many countries [17, 24–28]. The need for strategies to protect these vulnerable populations is apparent and, in addition to vaccination, might also include focused workplace and community interventions [17, 26–28].

The mortality rate of 64% and the renal function recovery rate of 31% in this study were both higher than those reported in the US multicenter study, but this may just reflect longer follow-up [6]. The association of older age with mortality was expected [6]. The combination of a 31% rate of persisting hospitalization and a 19% rate of continuing RRT-dependence in 90-day survivors emphasizes the lasting morbidity associated with this condition. The high mortality with COVID-19 AKI-RRT is not much different from that in other types of sepsis-associated AKI-RRT [6, 7, 9]. The absence of any correlation between baseline comorbidities and mortality likely indicates the overwhelming influence of the severity of the infection on outcome in this population and was also seen in the US AKI-RRT study [6].

When comparing AKI-RRT in the two waves of COVID-19, we found a lower rate of AKI-RRT cases than the number of infections in the general population in the second wave versus the first. The decreasing incidence of AKI-RRT and of AKI in general throughout the pandemic has been reported from the USA and Switzerland [29, 30]. The relatively lower rate of AKI-RRT in the second wave may also reflect the lower availability of SARS-CoV-2 testing in the community during the first wave. This suggests that AKI-RRT may be preventable through better initial management of COVID-19. We found in the second wave a higher proportion of people with AKI-RRT aged 70 years or older, with

Table 4. Multivariable logistic regression predicting risk of mortality

		95% confidence limits	
	Odds ratio	Lower limit	Upper limit
Sex			
Female	1.125	0.59	2.144
Type of residence			
Other	0.421	0.156	1.14
Age			
70+ years	2.406	1.27	4.559
Geographic location			
Non-GTA	1.061	0.518	2.175
Ethnicity			
Other non-White	1.13	0.596	2.144
Unknown/missing	1.15	0.546	2.421
Diabetes			
Yes	1.102	0.63	1.926
Income quintiles			
1 to 2	1.128	0.544	2.339
Baseline serum creatinine			
Severe–moderate (eGFR <60)	0.674	0.34	1.336
RRT initiation			
After 2 weeks	1.926	0.951	3.901
Within 2 weeks	1.014	0.543	1.896
Deprivation index			
4 to 5	0.864	0.419	1.782

Reference categories: sex male, private residency, age younger than 70 years, geographic location within the Greater Toronto Area (GTA), ethnicity White, no diabetes, highest three income quintiles, mild–normal (eGFR 60+) baseline serum creatinine, renal replacement therapy within 1 week and the lower 3 deprived quintiles. eGFR, estimated glomerular filtration rate.

cardiac disease, and with baseline CKD 3 and 4. We found no other studies comparing AKI-RRT cases between successive COVID-19 waves, although a single-center ICU study in France found no differences between their first two waves in age or comorbidity [31]. One hypothesis is that improvements in COVID-19 management after the first wave helped reduce AKI-RRT in patients with fewer risk factors, giving greater predominance to those who were more vulnerable with older age, and more comorbidity. The difference in time course to development of AKI-RRT with more than twice as high a proportion of cases occurring >2 weeks after diagnosis of COVID-19 in the second wave is important. It may be that better initial management of COVID-19 is avoiding some of the early AKI-RRT related to fulminant infection, allowing patients to survive longer, but some then develop late onset AKI-RRT due to the cumulative renal insults that occur during a prolonged ICU stay.

Our study has a number of strengths. Our data come from an entire province of >14 million people. The single-payer public funding and delivery of dialysis and acute hospitalization in Ontario makes it possible to report reliably and in detail on the entire population of patients who received AKI-RRT due to COVID-19, in contrast to hospital-based studies, which may not account for all cases in a region [6, 9–12]. This included the small proportion of cases who received AKI-RRT outside the ICU who were not included in other studies [6]. Prospective weekly reporting of cases from the start of the pandemic allowed for more accurate capture of incidence and outcomes over time, including follow-up data on survivors to accurately determine dialysis dependence after 90-day follow-up.

Table 5. Comparison of characteristics of people with AKI-RRT from waves 1 and 2 of the COVID-19 pandemic

Characteristic	Wave 1, $n = 138$, n (%)	Wave 2, $n = 133$, n (%)	P value
Demographics			
Male	105 (76)	101 (76)	0.977
Age group			0.024
29–69 years	98 (71)	77 (58)	
70+ years	40 (29)	56 (42)	
Comorbid conditions			
Diabetes mellitus	71 (51)	58 (44)	0.196
Cancer	13 (9)	12 (9)	0.910
Cardiac disease	21 (15)	33 (25)	0.048
CKD[a]			0.045
eGFR <59 mL/min/1.73 m^2	27 (20)	38 (29)	
eGFR 60–89 mL/min/1.73 m^2	58 (42)	53 (40)	
eGFR 90+ mL/min/1.73 m^2	53 (38)	42 (32)	
Treatment received			
ICU admission	133 (96)	126 (95)	0.578
On ventilator	133 (96)	119 (90)	0.047
Time to RRT initiation from positive COVID-19 swab			<0.001
Within 1 week	71 (51)	43 (32)	
1–2 weeks	37 (27)	37 (28)	
After 2 weeks	20 (14)	45 (34)	
Missing	10 (7)	8 (6)	
Median (IQR), days	7 (3–12)	12 (4–16)	
Recovery of renal function	39 (28)	45 (34)	0.321
Incidence of deaths by time after initiation of RRT			0.225
Within 0–7 days	39 (28)	46 (35)	
Within 8–14 days	18 (13)	20 (15)	
Within 15–28 days	19 (14)	14 (11)	
After 28 days	11 (8)	7 (5)	
Total mortality	87 (63)	87 (66)	

[a]Baseline eGFR within 7 days to 3 years prior to dialysis start.

The first wave (wave 1) of the pandemic in Ontario comprised the period 1 March to 1 September 2020, and the second wave (wave 2) from 1 September 2020 to 31 January 2021.

P-values were calculated using the Chi-squared test for analysis of categorical variables. eGFR, estimated glomerular filtration rate.

There are several limitations to this study. First, the absence of a detailed database with the characteristics of the general population infected with SARS-CoV-2 precludes detailed comparisons with the AKI-RRT population. Second, the results of this study may not be generalizable to other jurisdictions due to differences in population characteristics, healthcare resources and variant strains of SARS-CoV-2. Third, only studying AKI-RRT patients excludes cases where RRT was theoretically indicated but not received due to decisions by stakeholders in the patient's health.

CONCLUSION

In conclusion, this prospective cohort study comprises all patients with AKI-RRT associated with COVID-19 in Ontario, Canada. We describe a high incidence among critically ill COVID-19 patients and an associated high mortality, especially in older patients, and a high rate of non-recovery of renal function and persisting hospitalization in survivors. The AKI-RRT population is more likely to be male, to have diabetes, to be of non-White ethnicity, and to live in areas with higher rates of ethnocultural and economic deprivation. This study emphasizes socioeconomic and ethnic predisposition to severe COVID-19 and consequent AKI-RRT.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

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CONFLICT OF INTEREST STATEMENT

D.T., J.I., Y.T., A.Y., L.T. and R.C. are salaried employees of Ontario Renal Network, Ontario Health. M.J.O., P.O.M., A.X.G. and P.G.B. are contracted Medical Leads at Ontario Renal Network, Ontario Health. M.J.O. is the owner of Oliver Medical Management Inc., which licenses Dialysis Management Analysis and Reporting System software. He has received an honorarium for speaking at Baxter Healthcare and participated in Advisory Boards for Janssen and Amgen. P.G.B. has received an occasional honorarium from Baxter Global for speaking engagements.

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