Interhospital Transfer and Outcomes in Patients with AKI: A Population-Based Cohort Study

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Abstract

Background Patients with AKI may require interhospital transfer to receive RRT. Interhospital transfer may lead to delays in therapy, resulting in poor patient outcomes. There is minimal data comparing outcomes among patients undergoing transfer for RRT versus those who receive RRT at the hospital to which they first present.

Methods We conducted a population-based cohort study of all adult patients (≥19 years) who received acute dialysis within 14 days of admission to an acute-care hospital between April 1, 2004 and March 31, 2015. The transferred group included all patients who presented to a hospital without a dialysis program and underwent interhospital transfer (with the start of dialysis ≤3 days of transfer and within 14 days of initial admission). All other patients were considered nontransferred. The primary outcome was time to 90-day all-cause mortality, adjusting for demographics, comorbidities, and measures of acute illness severity. We also assessed chronic dialysis dependence as a secondary outcome, using the Fine and Gray proportional hazards model to account for the competing risks of death. In a secondary post hoc analysis, we assessed these outcomes in a propensity score–matched cohort, matching on age, sex, and prior CKD status.

Results We identified 27,270 individuals initiating acute RRT within 14 days of a hospital admission, of whom 2113 underwent interhospital transfer. Interhospital transfer was associated with lower rate of mortality (adjusted hazard ratio [aHR], 0.90; 95% CI, 0.84 to 0.97). Chronic dialysis dependence was not significantly different between groups (aHR, 0.98; 95% CI, 0.91 to 1.06). In the propensity score–matched analysis, interhospital transfer remained associated with a lower risk of death (HR, 0.88; 95% CI, 0.80 to 0.96).

Conclusions Interhospital transfer for receipt of RRT does not confer higher mortality or worse kidney outcomes.

Introduction

AKI is common among patients who are hospitalized and is increasingly recognized as a major contributor to hospital length of stay, morbidity, and mortality (1–5). In patients with severe AKI, RRT may be required, but may not be available at the initial hospital to which patients present. As such, patients are subjected to interhospital transfers to facilitate RRT, and this may cause delays in therapy and potential complications resulting from the transfer itself (6,7). Several studies have sought to assess the association between interhospital transfer and outcomes among patients with critical illness (8–10), with some suggesting worse outcomes among patients requiring transfer. However, these findings may be obscured by confounding associated with illness severity and the selection of patients for transfer.

There is a paucity of data examining the effect of interhospital transfer on the outcomes of patients with AKI requiring RRT. This information may inform resource utilization and guide policy related to access to dialysis-providing centers, particularly for areas that are geographically remote or under-serviced. Because RRT may reverse uremic and metabolic complications of AKI, delays in therapy associated with interhospital transfer may result in worse patient outcomes. To date, there has only been a single study examining patients transferred for the receipt of acute dialysis, which did not demonstrate an association between transfer and death or dialysis dependence at 30 days (11). This study was limited by a relatively small sample size, the inclusion of only two centers, and limited follow-up duration.

We assessed the incidence and outcomes of AKI requiring transfer for RRT in the province of Ontario, Canada, using administrative healthcare data. We hypothesized that, among patients commencing RRT for

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AKI, those who required interhospital transfer for initiation of RRT would have a higher mortality as compared with patients who were not transferred.

**Materials and Methods**

**Study Design and Participants**

We conducted a population-wide cohort study using linked administrative datasets in the province of Ontario, Canada. Ontario has >13 million residents with universal access to physician and hospital services. We identified all patients ≥19 years of age who received acute RRT within 14 days of admission to an acute-care hospital between April 1, 2004 and March 31, 2015. The 14-day period was selected to allow for the inclusion of patients in whom AKI was a core element of the initial hospital presentation, rather than a complication of the hospital stay. Patients were excluded if they had an invalid or missing identifying information (age, sex, or identifier), were non-Ontario residents, or had a recorded death date that was on/before the recorded date of initial hospitalization (i.e., those with erroneous death or hospitalization dates). We excluded patients with preexisting ESKD on the basis of the receipt of chronic dialysis or a kidney transplant before the initial hospitalization. We also excluded patients with a history of a vascular-access creation for hemodialysis during the 5 years preceding the hospitalization, because initiation of RRT in these patients more likely represents the onset of ESKD, rather than AKI. Lastly, we excluded patients who received dialysis only on the same day as cardiac surgery without subsequent RRT, because this circumstance likely represents intraoperative RRT, which is typically performed to allow for potassium control in patients with advanced CKD.

**Data Sources**

We used linked administrative healthcare datasets to identify patients, assess baseline characteristics, and ascertain outcomes. The Canadian Institute for Health Information (CIHI) Discharge Abstract Database (CIHI-DAD) was used to obtain hospitalization and transfer information. The Ontario Health Insurance Plan (OHIP) database was used to capture records for physician services, including acute dialysis. The Canadian Organ Replacement Register (CORR) was used to exclude patients with evidence of chronic dialysis or a previous kidney transplant. Baseline comorbid conditions in the 2 years before the initial hospitalization were assessed using International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and -10) codes within CIHI-DAD, and billing codes within OHIP. The Registered Persons Database was used to determine vital status. Chronic dialysis dependence was determined using CORR and OHIP. These data sources have been validated and used extensively in other analyses (12–17). All datasets were linked using unique encoded identifiers and analyzed at ICES. The use of data in this project was authorized under Section 45 of Ontario’s Personal Health Information Protection Act, which does not require review by a research ethics board. The reporting for this study followed the RECORD (REporting of studies Conducted using Observational Routinely collected health Data) guidelines for observational studies (Supplemental Tables 1–5) (18).

**Exposure**

The exposed (i.e., transferred) group consisted of all patients who underwent a transfer to a subsequent institution after being initially admitted to a hospital that did not have an on-site dialysis program. We required patients to have received dialysis within 3 days of transfer and within 14 days of the initial admission, so as to limit this group to patients in whom AKI (and specifically the need for RRT) was the likely impetus for transfer. The unexposed group (i.e., not transferred for RRT) consisted of all other patients who initiated acute dialysis within 14 days of admission (at the hospital to which they were originally admitted or >3 days after an interhospital transfer). This group also included patients who initiated acute dialysis ≤3 days after transfer if the initial hospital was associated with a dialysis program (and therefore able to provide dialysis on site). In sensitivity analyses, we assessed modified definitions of interhospital transfer, as described below.

**Outcomes**

The primary outcome was time to 90-day all-cause mortality from the initiation of acute RRT. The date of RRT initiation served as the index date or time origin for time-to-event analyses. Secondary outcomes were chronic dialysis dependence (defined as receipt of dialysis for at least 90 days, or registration within CORR as a patient on chronic dialysis) and a composite outcome of chronic dialysis dependence or receipt of a kidney transplant.

**Statistical Analyses**

Baseline characteristics were reported as frequencies (%) for categoric variables, and mean (SD) or median (interquartile range) for continuous variables. We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals for the primary and secondary outcomes. For secondary outcomes, we accounted for death using the Fine and Gray (1999) subdistribution hazards model. We evaluated the proportional hazards assumption through a time interaction with our exposure. We performed unadjusted and adjusted analyses with the following prespecified model covariates: age, sex, fiscal year, income quintile, rural status, predishminism comorbidities (ascertained using the Johns Hopkins Aggregated Diagnostic Group components [19]), previous evidence of CKD, previous nephrologist assessment, history of AKI, and admission to a teaching hospital. We also included covariates associated with illness severity during the hospitalization (before dialysis initiation), such as intensive care unit (ICU) admission, mechanical ventilation, sepsis, cardiac surgery, and abdominal aortic aneurysm repair.

All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). A two-sided P value <0.05 was considered statistically significant.

**Subgroup Analyses**

We evaluated the primary and secondary outcomes in the following subgroups: patients initiating continuous RRT (CRRT), patients initiating intermittent hemodialysis (IHD), patients who initiated dialysis within an ICU, patients with a previous CKD diagnosis, and patients with...
prior nephrologist consultation within 1 year preceding admission.

**Sensitivity and Post Hoc Analyses**

**Propensity Score–Matched Analysis**

As an alternative to the multivariable-adjusted analysis (and to address the possibility that multivariable adjustment might not sufficiently account for differences in the cohort), we constructed a propensity score–matched cohort to assess the primary and secondary outcomes. We generated a propensity score for the likelihood of transfer using all available baseline characteristics (listed in Table 1). We derived the propensity score using logistic regression. We matched transferred and nontransferred patients 1:1 using the logit of the propensity score with a specified caliper width \( \pm 0.2 \) times the SD of the logit of the propensity score, and matching on age (by year), sex, and CKD status. We used greedy, nearest-neighbor matching (without replacement) (20).

**Alternative Definitions for the Exposure**

We redefined transferred and nontransferred patients in our cohort without the requirement for transferred patients to initiate dialysis within 3 days of transfer (i.e., requiring only that patients start dialysis within 14 days of initial admission). However, we kept the requirement that the initial hospital did not have an on-site dialysis program for patients to be considered transferred for dialysis treatment. As such, in this analysis, all patients transferred from an initial hospital without a dialysis program were considered transferred for RRT if they initiated dialysis in the hospital to which they were transferred within 14 days of their initial admission. All other patients initiating dialysis within 14 days of initial admission were considered nontransferred. This analysis was done using Cox proportional hazard models with the same model covariates as the primary analysis described above.

In an additional analysis, we also adjusted the primary multivariable model with an added covariate for time from initial hospital admission to dialysis start (in days) to assess whether possible delays in dialysis initiation influenced outcomes.

**Results**

**Baseline Characteristics**

Between April 1, 2004 and March 31, 2015, 27,270 patients experienced a hospitalization during which dialysis was initiated within 14 days of admission and who met all eligibility criteria (Figure 1). Among these patients, 2113 underwent interhospital transfer and initiated dialysis within 3 days of transfer. There were 98 hospitals included, of which 59 had an associated dialysis program. Transferred and nontransferred patients were similar with respect to most demographic characteristics (Table 1), but transferred patients were less likely to be in a lower income quintile and were more likely to reside in rural areas. The geographic location of the initial hospital for both transferred and nontransferred patients is shown in Figure 2 (Ontario is divided into 14 health service regions termed Local Health Integration Networks).

Several characteristics of the hospitalization differed between groups (Table 1). In particular, the initial hospital for transferred patients was less likely to be a teaching hospital (1% among transferred versus 41% among nontransferred patients), and transferred patients were more likely to have spent part of their hospital stay in the ICU (73% among transferred versus 68% among nontransferred patients). Sepsis within 14 days of admission was more frequent in transferred (26%) compared with nontransferred (17%) patients. Transferred patients were also more likely to have been hospitalized in the year prior compared with nontransferred patients, including higher rates of emergency room visits and hospital admissions.

The groups were similar with respect to measures of comorbidity, as measured by the Charlson Comorbidity Index and Johns Hopkins Aggregated Diagnosis Groups score. Transferred and nontransferred patients did, however, differ in kidney history, with nontransferred patients having higher rates of both CKD (36% in nontransferred versus 31% in transferred patients) and previous AKI (29% in nontransferred versus 24% in transferred patients).

The initial RRT modality received was similar in both groups (CRRT, 27% in nontransferred versus 28% in transferred patients; IHD, 73% in nontransferred versus 72% in transferred patients). There were 29 patients (0.11%) who had evidence of any acute peritoneal dialysis during their hospitalization.

**Outcomes**

Total follow-up time was 16,894 person-years. Median follow-up was 365 days in both groups, with a lower quartile of 23 and 20 days for the transferred and nontransferred groups, respectively. All-cause mortality at 90 days was similar in transferred and nontransferred patients (35% and 33%, respectively) (Table 2). After multivariable adjustment, transferred patients had a lower rate of death compared with nontransferred patients, with an adjusted HR (aHR) of 0.90 (95% CI, 0.84 to 0.97; \( P=0.004 \)). Chronic dialysis dependence did not differ between the groups, with an aHR of 0.98 (95% CI, 0.91 to 1.06; \( P=0.63 \)). The composite outcome of dialysis dependence or kidney transplant also did not differ between the groups. Cumulative incidence curves for all-cause mortality and chronic dialysis dependence are shown in Supplemental Figures 1 and 2, respectively.

The time from hospital admission to RRT initiation was shorter in nontransferred individuals, with a median time (interquartile range) from initial hospital admission to dialysis initiation in transferred and nontransferred patients of 3 (2–6) days and 3 (1–6) days, respectively (Wilcoxon rank sum test, \( P<0.001 \)). A histogram of the distributions of time to dialysis initiation from initial hospital admission for each group is depicted in Figure 3.

**Subgroup Analyses**

There was no association between transfer status and 90-day mortality among the subgroups of patients initiating CRRT or IHD (\( P \) for interaction=0.12; Figure 4). We also performed these subgroup analyses using the alternate definition of transfer exposure (i.e., transferred patients with dialysis start within 14 days of initial presentation) and
## Table 1. Baseline characteristics of transferred and nontransferred patients

| Characteristics                                      | Nontransfers (N=25,157) | Transfers (N=2113) | Standardized Difference | Total Cohort (N=27,270) |
|------------------------------------------------------|--------------------------|--------------------|-------------------------|-------------------------|
| **Age at index date (yr)**                           |                          |                    |                         |                         |
| Mean±SD                                              | 65±15.46                 | 65±14.73           | 0.03                    | 64.86±15.41             |
| Median (IQR)                                         | 67 (55–77)               | 67 (56–76)         |                         | 67 (55–77)              |
| **Female sex**                                       |                          |                    |                         |                         |
| Missing                                              | 129 (1)                  | 15 (1)             | 0.03                    | 144 (1)                 |
| 1 (low)                                              | 6184 (25)                | 426 (20)           | 0.11                    | 6610 (24)               |
| 2                                                    | 3519 (22)                | 485 (23)           | 0.03                    | 6004 (22)               |
| 3 (mid)                                              | 4694 (19)                | 440 (21)           | 0.05                    | 5134 (19)               |
| 4                                                    | 4501 (18)                | 430 (20)           | 0.06                    | 4931 (18)               |
| 5 (high)                                             | 4130 (16)                | 317 (15)           | 0.04                    | 4447 (16)               |
| **Income quintile**                                  |                          |                    |                         |                         |
| Missing                                              | 129 (1)                  | 15 (1)             | 0.03                    | 144 (1)                 |
| 1 (low)                                              | 6184 (25)                | 426 (20)           | 0.11                    | 6610 (24)               |
| 2                                                    | 3519 (22)                | 485 (23)           | 0.03                    | 6004 (22)               |
| 3 (mid)                                              | 4694 (19)                | 440 (21)           | 0.05                    | 5134 (19)               |
| 4                                                    | 4501 (18)                | 430 (20)           | 0.06                    | 4931 (18)               |
| 5 (high)                                             | 4130 (16)                | 317 (15)           | 0.04                    | 4447 (16)               |
| **Distance from patient’s home to initial hospital (km)** |                          |                    |                         |                         |
| Mean±SD                                              | 28±73.93                 | 17±55.61           | 0.17                    | 27.38±72.91             |
| Median (IQR)                                         | 7 (4–23)                 | 6 (3–14)           |                         | 7 (3–21)                |
| **Distance from patient’s home to transferred hospital (km)** |                          |                    |                         |                         |
| Mean±SD                                              | 49±80.56                 | 25 (12–55)         |                         |                         |
| Median (IQR)                                         | 25 (12–47)               |                    |                         |                         |
| **Distance from first hospital to transferred hospital (km)** |                          |                    |                         |                         |
| Mean±SD                                              | 45±75.9                  | 45±75.9            |                         |                         |
| Median (IQR)                                         | 22 (12–47)               |                    |                         |                         |
| **Teaching hospital as initial admission hospital**   |                          |                    |                         |                         |
| Mean±SD                                              | 10,427 (41)              | 18 (1)             | 1.14                    | 10,445 (38)             |
| Median (IQR)                                         | 949 (45)                 |                    |                         |                         |
| **Teaching hospital as transferred hospital**         |                          |                    |                         |                         |
| **Dialysis program associated with initial hospital** |                          |                    |                         |                         |
| Mean±SD                                              | 22,353 (89)              | 0 (0)              | 4                       | 22,353 (82)             |
| Median (IQR)                                         | 22,353 (89)              |                    |                         |                         |
| **Specialty of physician billing for dialysis**       |                          |                    |                         |                         |
| Nephrology                                           | 8827 (35)                | 666 (32)           | 0.08                    | 9493 (35)               |
| Internal medicine                                    | 15,382 (61)              | 1381 (65)          | 0.09                    | 16,763 (62)             |
| Other                                                | 948 (4)                  | 66 (3)             | 0.04                    | 1014 (4)                |
| Nephrology consult in 7 d before index dialysis      | 17,863 (71)              | 1683 (80)          | 0.2                     | 19,546 (72)             |
| Nephrology consult in 1 yr before (outpatient or inpatient) | 13,790 (55)              | 1070 (51)          | 0.08                    | 14,860 (55)             |
| **Number of previous nephrology consults in 1 yr prior** |                          |                    |                         |                         |
| Mean±SD                                              | 5±11.13                  | 4±10.08            | 0.08                    | 5.04±11.05              |
| Median (IQR)                                         | 1 (0–5)                  | 0 (0–4)            |                         | 1 (0–5)                 |
| **Number of ER visits before hospital encounter in 1 yr prior** |                          |                    |                         |                         |
| Mean±SD                                              | 3±3.14                   | 3±3.2             | 0.13                    | 2.66±3.16               |
| Median (IQR)                                         | 2 (1–3)                  | 2 (1–4)            |                         | 2 (1–3)                 |
| **Number of hospitalizations before hospital encounter in 1 yr prior** |                          |                    |                         |                         |
| Mean±SD                                              | 1±1.37                   | 1±1.46            | 0.32                    | 0.95±1.39              |
| Median (IQR)                                         | 0 (0–1)                  | 1 (0–2)            |                         | 1 (0–1)                 |
| **Charlson Comorbidity Index**                       |                          |                    |                         |                         |
| Mean±SD                                              | 2±2.19                   | 2±2.27            | 0.02                    | 2.47±2.20              |
| Median (IQR)                                         | 2 (0–4)                  | 2 (0–4)            |                         | 2 (0–4)                |
| **Johns Hopkins Aggregated Diagnosis Groups score**  |                          |                    |                         |                         |
| Mean±SD                                              | 10±4.41                  | 10±4.38           | 0.01                    | 9.80±4.40              |
| Median (IQR)                                         | 10 (7–13)                | 10 (6–13)         |                         | 10 (7–13)              |

### Table Notes
- All values are presented as mean ± standard deviation (SD) or median (interquartile range [IQR]) as appropriate.
- Standardized differences are calculated using the formula: \( \frac{X_2 - X_1}{SD_{total}} \), where \( X_1 \) and \( X_2 \) are the means of the two groups, and \( SD_{total} \) is the pooled standard deviation.
- Table entries include missing values noted as 'Missing' with corresponding counts and percentages.
- The number of patients varies due to missing data in some characteristics.
found no association between transfer status and 90-day mortality (in patients on CRRT, aHR, 0.95 [95% CI, 0.86 to 1.06]; in patients on IHD, aHR, 0.98 [95% CI, 0.90 to 1.06]; P for interaction = 0.09). Transferred patients whose hospitalization included a stay in ICU were found to have a lower hazard of mortality, with an aHR of 0.88 (95% CI, 0.82 to 0.96), whereas this was not the case for transferred patients whose hospitalization did not include an ICU stay (aHR, 0.96; 95% CI, 0.82 to 1.12; P for interaction = 0.004). Transferred patients without a previous CKD diagnosis and without a nephrologist consultation in the preceding year had a lower risk of mortality (aHRs of 0.85 [95% CI, 0.78 to 0.92] and 0.85 [95% CI, 0.76 to 0.94], respectively) versus nontransferred patients, whereas those with known CKD or prior nephrologist consult had no difference in mortality associated with transfer status.

Table 1. (Continued)

| Characteristics | Nontransfers (N=25,157) | Transfers (N=2113) | Standardized Difference | Total Cohort (N=27,270) |
|-----------------|------------------------|--------------------|-------------------------|------------------------|
| Acute myocardial infarction | 2286 (9) | 189 (9) | 0.01 | 2475 (9) |
| Congestive heart failure | 7208 (29) | 606 (29) | 0 | 7814 (29) |
| Cerebrovascular disease | 2465 (10) | 221 (11) | 0.02 | 2686 (10) |
| Diabetes mellitus (type 1 and 2) | 11,483 (46) | 1046 (50) | 0.08 | 12,529 (46) |
| All malignancies | 6755 (27) | 519 (25) | 0.05 | 7274 (27) |
| Chronic liver disease | 1614 (6) | 104 (5) | 0.07 | 1718 (6) |
| Peripheral vascular disease | 2143 (9) | 185 (9) | 0.01 | 2328 (9) |
| CKD | 9026 (36) | 652 (31) | 0.11 | 9678 (36) |
| Previous AKI | 7215 (29) | 503 (24) | 0.11 | 7718 (28) |
| Cardiac arrhythmia | 5632 (22) | 493 (23) | 0.02 | 6125 (23) |
| Ischemic heart disease | 8402 (33) | 679 (32) | 0.02 | 9081 (33) |
| COPD | 3813 (15) | 328 (16) | 0.01 | 4141 (15) |
| HIV/AIDS | 132 (1) | 8 (0) | 0.01 | 140 (1) |
| Hypertension | 14,574 (58) | 1248 (59) | 0.02 | 15,822 (58) |

Characteristics of hospital admission

| Characteristics | Nontransfers (N=25,157) | Transfers (N=2113) | Standardized Difference | Total Cohort (N=27,270) |
|-----------------|------------------------|--------------------|-------------------------|------------------------|
| ICU admission during hospitalization | 17,039 (68) | 1542 (73) | 0.12 | 18,581 (68) |
| Mechanical ventilation within 14 d of admission | 12,661 (50) | 1089 (52) | 0.02 | 13,750 (50) |
| Sepsis within 14 d of admission | 4399 (17) | 544 (26) | 0.20 | 4943 (18) |
| Nonruptured aortic aneurysm within 14 d of admission | 674 (3) | 24 (1) | 0.12 | 698 (3) |
| Cardiac surgery with 14 d of admission | 1659 (7) | 62 (3) | 0.17 | 1721 (6) |
| Initial dialysis modality received | Continuous RRT | 6778 (27) | 585 (28) | 0.02 | 7363 (27) |
| Intermittent hemodialysis | 18,379 (73) | 1528 (72) | 0.02 | 19,907 (73) |

All values are given as n (%) unless otherwise specified. IQR, interquartile range; ER, emergency room; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit.

Patients initiating acute dialysis within 14 days of hospital admission between April 1, 2004 - March 31, 2014:

42,386

Exclusions:

1) Dialysis code in preceding 1 year or registered as a chronic dialysis patient: 9,503
2) Previous kidney transplant (after 1981): 44
3) Vascular access creation in the preceding 1 year: 1,197
4) Evidence of dialysis on same day of cardiac surgery with no subsequent dialysis code during index episode of care: 4,372

Final Cohort: 27,270

Figure 1. | Study flow diagram depicting the identification of 27,270 patients meeting eligibility criteria for cohort inclusion.
Sensitivity Analyses

We were able to match >96% of the transferred patients in the propensity score–matched analysis. The resulting 2040 individuals in each of the transferred and nontransferred groups were similar with respect to most measured baseline characteristics (Supplemental Table 6). In this analysis, the aHR for all-cause mortality at 90 days was 0.88 (95% CI, 0.80 to 0.96) (Table 3). Chronic dialysis dependence was not different among transferred and nontransferred patients, with an aHR of 0.95 (95% CI, 0.86 to 1.05).

When the groups were redefined without the requirement for RRT initiation within 3 days of transfer, there were 2495 individuals in the transferred group and 24,775 in the nontransferred group. There was no difference in the hazard for mortality in this analysis, with an aHR of 0.95 (95% CI, 0.89 to 1.02) (Table 4).

In our final sensitivity analysis, we included time from initial hospital transfer to dialysis start (in days) as a covariate in the multivariable model. In this analysis, the transferred group again had a decreased hazard of mortality (aHR, 0.89; 95% CI, 0.83 to 0.96), and there was no significant difference in the rate of dialysis dependence between the groups.

Discussion

Patients with AKI undergoing interhospital transfer for the receipt of RRT do not have a higher mortality rate than patients with AKI who commence RRT at the hospital at which they first presented. In fact, the rate of death seemed to be lower among transferred patients. Chronic dialysis dependence, and the composite outcome of chronic dialysis or transplant, did not differ between transferred and nontransferred patients. These findings were consistent in a propensity score–matched sensitivity analysis. Our findings are congruent with the only other study examining patients transferred for AKI requiring dialysis, which suggested that patients requiring transfer fared no worse (at 30 days) than those presenting to a dialysis-providing hospital (11). Although interhospital transfers may have attendant risks of patient instability or adverse events during transport (21,22), our data suggest this

| Outcome | Outcomes at 90 d, n (%) | Outcomes at 1 yr, n (%) | Unadjusted Hazard Ratio (95% CI) | P Value | Adjusted Hazard Ratio (95% CI)* | P Value |
|---------|------------------------|------------------------|-------------------------------|---------|-------------------------------|---------|
|         | Nontransfers Transfers | Nontransfers Transfers |                               |         |                               |         |
| All-cause death | 9003 (36) 733 (35) | 11,312 (45) 936 (44) | 0.97 (0.91 to 1.04) | 0.42 | 0.90 (0.84 to 0.97) | 0.004 |
| Dialysis dependence | 7623 (30) 568 (27) | 7796 (31) 582 (28) | 0.87 (0.80 to 0.94) | 0.0006 | 0.98 (0.91 to 1.06) | 0.63 |
| Dialysis dependence or kidney transplant | 7630 (30) 568 (27) | 7805 (31) 582 (28) | 0.87 (0.80 to 0.94) | 0.0006 | 0.98 (0.91 to 1.06) | 0.63 |

Proportions are provided for 90-d and 1-yr events. ICU, intensive care unit.

*Adjusted models include age, sex, fiscal year, income quintile, rural status, history of AKI, history of CKD, Johns Hopkins Aggregated Diagnosis Groups score, prior nephrologist visit, admission to a teaching hospital, ICU admission during hospital stay, mechanical ventilation, sepsis, cardiac surgery, and abdominal aortic aneurysm repair.
may not adversely affect patient survival or persistent dialysis dependence.

Our findings have important implications for healthcare systems that serve geographically large regions where the following two different approaches to RRT delivery exist: providing widespread local access to acute dialysis versus adopting a “hub” approach, whereby patients are transferred for advanced care to a smaller number of large centers. Our data suggest the latter approach does not lead to worse clinical outcomes and may justify the current use of this strategy in our jurisdiction and other healthcare systems that serve vast territories.

Our results also mirror the noninferior outcomes associated with interhospital transfer in other medical and surgical settings, including traumatic brain injuries (23,24), acute surgical conditions (25), and percutaneous coronary intervention for ST-segment elevation myocardial infarctions (26–28). However, in the case of the latter, there is some evidence to suggest improved outcomes for patients who undergo direct admission to a facility providing definitive care, perhaps related to the importance of a short door-to-balloon time (29,30). As in other settings, the findings we observed may be dependent on timely and efficient patient transfer and prompt initiation of RRT thereafter. The effect of timing of RRT on outcomes in AKI remains controversial, with conflicting data from randomized trials (31–33). Notably, transferred patients and nontransferred patients differed only modestly in time from hospital admission to dialysis start: 3 (1, 6) versus 3 (2, 6) days, with a p-value of 0.0001.

Figure 3. Histogram of days from initial hospital admission to RRT initiation demonstrating shorter time to RRT initiation in non-transferred versus transferred patients. IQR, interquartile range.

Figure 4. Adjusted hazard ratios for death among predefined subgroups. CRRT, continuous RRT; ICU, intensive care unit; IHD, intermittent hemodialysis.
### Table 3. Propensity score–matched analysis providing hazard ratios for death and dialysis dependence among transferred and nontransferred patients initiating acute RRT

| Outcome               | Outcomes at 90 d, n (%) | Outcomes at 1 yr, n (%) | Unadjusted Hazard Ratio (95% CI) | P Value | Adjusted Hazard Ratio (95% CI) | P Value |
|-----------------------|-------------------------|-------------------------|---------------------------------|---------|-------------------------------|---------|
|                       | Nontransfers  | Transfers                | Nontransfers  | Transfers                |                     |         |                                |         |
| All-cause death       | 779 (38)       | 704 (35)                | 978 (48)       | 899 (44)                | 0.89 (0.81 to 0.97) | 0.008   | 0.88 (0.80 to 0.97) | 0.007   |
| Dialysis dependence   | 573 (28)       | 551 (27)                | 586 (29)       | 564 (28)                | 0.95 (0.85 to 1.05) | 0.31    | 0.95 (0.85 to 1.05) | 0.28    |

The propensity score for likelihood of transfer was derived using logistic regression with all available baseline characteristics (listed in Table 1). We matched transferred and nontransferred patients 1:1 using the logit of the propensity score with a specified caliper width approximately 0.2 times the SD of the logit of the propensity score, and matching on age (by yr), sex, and CKD status.
admission to RRT initiation, which may have mitigated potential adverse effects of being subject to an interhospital transfer and the associated delay in RRT initiation. This may suggest there is adequate recognition of patients in whom RRT may be imminently required, and appropriate prompt referral to centers with the capability of providing RRT. Since 1996, the province of Ontario has used a government-administered network to facilitate the transfer of patients who are critically ill from admitting hospitals to those able to provide specialized care, and this may have played a role in ensuring timely access to RRT.

Our results indicate a modest survival advantage for patients who have undergone transfer for the receipt of RRT. Notwithstanding efforts to adjust for key confounders, this may reflect the selection of patients for interhospital transfer who were destined to have a more favorable outcome. As such, the transferred group may systematically exclude patients who were deemed too sick to transfer and were thus more likely to have unfavorable outcomes. On the other hand, it is possible that the threshold to provide acute dialysis at hospitals with on-site dialysis capability may have been lower, with the delivery of dialysis to sicker patients who would never have been transferred for dialysis had they been admitted to a nondialysis center. Similarly, because most dialysis-providing centers in the province of Ontario are academic tertiary-care centers, the patient population presenting to these centers may have an unmeasured degree of increased complexity, including patients with highly specialized needs (e.g., advanced cancer, previous organ transplantation) or complex surgical issues.

In the subgroups of patients without a preexisting CKD diagnosis, without previous outpatient nephrologist assessment, and those requiring ICU admission, the association between transfer status and improved outcomes appeared to be accentuated. These groups, particularly the latter, may represent patients who may not be easily managed at smaller or rural hospitals with limited resources, but otherwise do not have the same degree of medical complexity as many patients who are critically ill and admitted to centers with on-site dialysis capability. It is also possible that those who had not previously had nephrologist assessment would receive this upon transfer. We did not observe any association between transfer status and mortality in subgroups of patients initiating CRRT or IHD. The proportions of patients ultimately initiating these two RRT modalities was similar among the transferred and nontransferred groups, and this may suggest that those patients who were more severely ill, in whom CRRT was indicated, were able to receive this without deleterious effect on mortality as a result of transfer.

Strengths and Limitations

Our study has several strengths. To our knowledge, this is the largest study examining the effect of transfer on the risk of mortality in patients with AKI requiring dialysis. We made use of clinically relevant and validated outcomes and were able to adjust for numerous potential confounders of the association between interhospital transfer and the end points of interest. Our population-level study was set in a large province comprising a vast geographic expanse containing remote hospitals and clinics, and hubs of larger hospitals in urban centers (and this allowed for the inclusion of 98 hospital sites in our study). Thus, our findings may be relevant to any healthcare system serving a large geographic area with disparate RRT access. We were also able to assess our outcomes using both multivariable-adjusted analysis and a propensity score–matched analysis with consistent results.

There are important limitations to consider. Bias may have influenced our results in two important ways. Our study design may have been subject to selection bias, because we only captured patients who ultimately initiated RRT, and could not directly assess the severity of AKI. As such, we are unable to include all patients who might have ever been considered for RRT. The patients who were sickest, who may have been deemed too ill for transfer, or had died after a transfer but before RRT, were likely excluded from our analysis and this may have influenced our results in favor of those who were transferred. Similarly, if the patients who initially presented to RRT-providing centers (which are often tertiary-care or academic facilities) indeed had an unmeasured degree of high medical complexity, this also would bias our results in favor of patients who were transferred. Also, although we were able to assess multiple measures of illness severity, we are not able to ascertain receipt of vasopressors in our healthcare administrative datasets.
We were also limited by our inability to definitively ascertain the rationale for interhospital transfer. In requiring that the initial hospital did not have the capacity to provide dialysis, and that those who had undergone transfer initiate RRT within 3 days of transfer, we attempted to identify patients in whom dialysis was the predominant reason for transfer. However, there may have been other potential indications for transfer (e.g., the need for specialized supportive techniques for patients’ cardiorespiratory status, such as extracorporeal membrane oxygenation). These other indications for transfer may have confounded the association between transfer status and the outcomes of interest. Moreover, although we used both the 3-day and 14-day definitions of transfer exposure in our analyses, these time-frames are somewhat arbitrary, and this remains a limitation of the transfer definition. Although these potential biases must be acknowledged, on the basis of our results (both the primary and sensitivity analyses), a large clinically important difference in outcomes between the transferred and nontransferred patients is unlikely.

Interhospital transfer of patients for specialized medical care remains an important public health issue, particularly in the setting of resource-intensive treatments such as RRT. Contrary to our initial hypothesis, we found that patients with AKI who underwent transfer to initiate RRT did not have inferior clinical outcomes. Our findings may suggest that hospitals that do not have RRT capabilities may not need to invest in the considerable costs required to deliver on-site RRT, provided that timely interhospital transfer of patients can be facilitated.

Disclosures
All authors have nothing to disclose.

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Author Contributions
K. Brimble, S. Dixon, A. Garg, Z. Harel, A. Harvey, N. Jeyakumar, K. Kim, A. Kitchlu, J. Shapiro, S. Silver, and R. Wald reviewed and edited the manuscript; K. Brimble, J. Dirk, N. Jeyakumar, A. Kitchlu, and R. Wald were responsible for project administration; K. Brimble, S. Dixon, S. Kim, A. Kitchlu, and R. Wald were responsible for methodology; K. Brimble and R. Wald conceptualized the study; J. Dirk, S. Dixon, A. Kitchlu, and J. Shapiro were responsible for data curation; S. Dixon, A. Kitchlu, and J. Slater were responsible for formal analysis; S. Dixon and J. Slater were responsible for validation; A. Garg, Z. Harel, A. Kitchlu, S. Silver, and R. Wald were responsible for funding acquisition; S. Kim and R. Wald provided supervision; A. Kitchlu and R. Wald wrote the original draft; J. Shapiro was responsible for visualization; and each author contributed important intellectual content during manuscript drafting or revision, accepts personal accountability for the author's own contributions, and agrees to ensure that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

Supplemental Material
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Supplemental Table 1. Checklist of recommendations for reporting of observational studies using the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement.

Supplemental Table 2. Administrative data codes used to identify cohort of individuals receiving acute dialysis during their hospital episode of care.

Supplemental Table 3. Administrative data codes used to define hospital discharge.

Supplemental Table 4. Administrative data codes used to define baseline characteristics.

Supplemental Table 5. Administrative data codes used to define outcome measures.

Supplemental Table 6. Baseline characteristics of propensity score matched cohort.

Supplemental Figure 1. Cumulative incidence function curves for all-cause mortality amongst non-transferred and transferred patients (adjusted for primary model covariates).

Supplemental Figure 2. Cumulative incidence function curves for dialysis dependence amongst non-transferred and transferred patients (adjusted for primary model covariates).

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