Chronic Dialysis and Death Among Survivors of Acute Kidney Injury Requiring Dialysis

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Context Severe acute kidney injury among hospitalized patients often necessitates initiation of short-term dialysis. Little is known about the long-term outcome of those who survive to hospital discharge.

Objective To assess the risk of chronic dialysis and all-cause mortality in individuals who experience an episode of acute kidney injury requiring dialysis.

Design, Setting, and Participants We conducted a population-based cohort study of all adult patients in Ontario, Canada, with acute kidney injury who required in-hospital dialysis and survived free of dialysis for at least 30 days after discharge between July 1, 1996, and December 31, 2006. These individuals were matched with patients without acute kidney injury or dialysis during their index hospitalization. Matching was by age plus or minus 5 years, sex, history of chronic kidney disease, receipt of mechanical ventilation during the index hospitalization, and a propensity score for developing acute kidney injury requiring dialysis. Patients were followed up until March 31, 2007.

Main Outcome Measures The primary end point was the need for chronic dialysis and the secondary outcome was all-cause mortality.

Results We identified 3769 adults with acute kidney injury requiring in-hospital dialysis and 13 598 matched controls. The mean age was 62 years and median follow-up was 3 years. The incidence rate of chronic dialysis was 2.63 per 100 person-years among individuals with acute kidney injury requiring dialysis, and 0.91 per 100 person-years among control participants (adjusted hazard ratio, 3.23; 95% confidence interval, 2.70-3.86). All-cause mortality rates were 10.10 and 10.85 per 100 person-years, respectively (adjusted hazard ratio, 0.95; 95% confidence interval, 0.89-1.02).

Conclusions Acute kidney injury necessitating in-hospital dialysis was associated with an increased risk of chronic dialysis but not all-cause mortality.

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Acute kidney injury, which leads to a sudden decline in kidney function, is a common and serious complication of hospitalization in the adult population.[1-4] Many patients with severe acute kidney injury require initiation of hemodialysis or hemofiltration (termed *dialysis* throughout), and their in-hospital mortality rate ranges from 45% to 70%.[5-12] Among those who survive, as many as 15% require dialysis at the time of discharge.[6,9]

Little is known about the long-term outcomes of patients with acute kidney injury requiring in-hospital dialysis, especially once they leave the hospital and recover enough kidney function to be free of dialysis in the short term. Prior studies were conducted in single centers or within restricted geographic regions,[5,8,10,13,14] and few studies observed patients for more than 1 year.[8,14,15] Accordingly, little is known about a common clinical scenario in which prognostic implications include resource allocation, specialist follow-up, and dialysis planning.

For editorial comment see p 1227.

The universal health care system in the Canadian province of Ontario provides a unique opportunity to study long-term outcomes and health care use across multiple study centers and among an entire population. We evaluated the long-term risk of chronic dialysis and death among hospitalized patients who sustained acute kidney injury requiring acute dialysis.

METHODS

Design and Participants

We completed a retrospective matched cohort study using linked administrative health databases for all of Ontario. We identified all adults aged 19 years and older admitted to an acute care hospital between July 1, 1996, and December 31, 2006, for whom length

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of stay was less than 180 days. To identify a cohort of survivors, we focused on those individuals who lived for at least 30 days after the index hospitalization discharge date without receipt of dialysis or rehospitalization. We excluded individuals with a diagnosis of acute kidney injury, receipt of a kidney transplant, or any form of dialysis in the 5-year period preceding the index hospitalization.

As the exposed group, we selected from the previously described cohort all individuals who had both acute kidney injury and acute dialysis during the index admission. Each exposed patient was then matched with 4 unexposed hospitalized patients (without acute kidney injury or acute dialysis) according to the following matching variables: age within 5 years, sex, history of chronic kidney disease in the 5-year period prior to the index hospitalization admission date, receipt of mechanical ventilation during the index hospitalization, and logit of a propensity score for developing acute kidney injury and dialysis ±0.2 standard deviations.

The receipt of mechanical ventilation was used as a surrogate for admission to a critical care unit.[16] The propensity score was used to characterize known risk factors for acute kidney injury and dialysis.[17] The propensity score was derived using a multivariable logistic regression model that included the following variables: age (continuous in years), sex, and income quintile at the hospital discharge date; chronic kidney disease in the 5 years preceding the hospital admission date; number of hospitalizations or health care visits to any physician or emergency department in the 5 years preceding the hospital discharge date; receipt of coronary, carotid, or peripheral arterial revascularization, cardiac valve surgery, coronary angiography, cardiac stress testing, echocardiography, single 12-lead or ambulatory 24-hour electrocardiography, pacemaker insertion or carotid Doppler ultrasonography in the 5 years before the hospital discharge date; diagnosed liver dysfunction, heart failure, diabetes mellitus, cancer, cerebrovascular disease, cardiac dysrhythmias, myocardial infarction or angina, peripheral artery disease, major infection, alcoholism, and score on the Charlson Comorbidity Index[18] in the 5 years before the hospital discharge date; quarter and year of the index hospitalization; and sepsis, receipt of mechanical ventilation, nonruptured aortic aneurysm repair, or cardiac surgery, all within the index hospitalization. Although 4 nonexposed matches were sought for each exposed patient, those with at least 1 match were included.

Data Sources

The study was completed using linked provincial health care administrative databases at the Institute for Clinical Evaluative Sciences. These databases have been used in numerous large-scale epidemiologic studies.[19,20] Hospitalization records were obtained from the Canadian Institute for Heath Information Discharge Abstract Database (DAD), which was used to identify an acute hospitalization, the presence of acute kidney injury, and receipt of acute dialysis, as well as in-patient comorbidities and procedures (eTable, available at http://www.jama.com). The DAD contains the encrypted health care number, age and sex of the individual, date of admission and discharge, and as many as 16 diagnoses in the *International Classification of Diseases, Ninth Revision* (before the year 2002) and 25 diagnoses in the *International Classification of Diseases, Tenth Revision* (from 2002 onward) (eTable, available at http://www.jama.com). The Ontario Health Insurance Plan database contains records of all physician billing for outpatient and inpatient services, including a service date and a single diagnosis. The Registered Persons Database contains health care identifiers for all eligible individuals, as well as a date of death.

Income quintile was based on the 2001 Statistics Canada Census, which assigns income quintiles to each neighborhood community, with 1 representing the lowest income quintile and 5 representing the highest.

The health care databases were linked anonymously using encrypted individual health card numbers to safeguard patient confidentiality. The current study was approved by the research ethics board at Sunnybrook Health Sciences Centre.

Determining Exposure Status

The acute kidney injury and dialysis cohort was assembled by identifying hospitalized patients with both a diagnostic code in the DAD of acute kidney injury and either a procedure code in the DAD for dialysis or a physician claim for dialysis made through the Ontario Health Insurance Plan database during the index hospitalization (eTable, available at http://www.jama.com). To focus our interest on acute kidney injury survivors, participants were included who survived for at least 30 days postdischarge with no evidence of dialysis treatment or the need for rehospitalization during this time.

Study Outcome

Patients were tracked for outcomes beginning 30 days after discharge. The main study outcome was receipt of chronic dialysis for at least 90 days. The date of the first dialysis claim was considered to be the date of initiation of chronic dialysis. The secondary outcome was all-cause mortality occurring more than 30 days after hospital discharge.

Statistical Analyses

Continuous variables for individuals with and without acute kidney injury and dialysis were expressed as a mean (SD) or median (interquartile range [IQR]), and compared using an unpaired *t* test or Kruskal-Wallis test, respectively. Categorical variables were expressed as a percentage and compared using a χ^2 test.

Time-to-event analyses were performed until March 31, 2007. For the chronic dialysis end point, an individual was censored at death or at the end of the study period. Incidence rates of both chronic dialysis and all-cause mortality were determined for participants with and without acute kidney injury and dialysis. Crude hazard ratios (HRs) and 95% confidence intervals (CIs) were derived from Cox proportional hazards models, and matched individuals without acute kidney injury and dialysis were the reference group. We further adjusted for age (continuous in years) and the propensity score for acute kidney injury and dialysis in the multivariable models, in case there was residual confounding beyond the matching process. Survival curves for chronic dialysis and all-cause mortality were generated from unadjusted Cox models. Adjusted HRs for receipt of chronic dialysis were further stratified according to participant characteristics.

Based on the actual number of participants enrolled in the current study, we had greater than 95% statistical power to detect an HR of 2.00 or more for the primary study outcome at a conventional *P* value of .05. All *P* values were 2-sided, and the significance level was set at .05. Analyses were performed using SAS 9.1 for UNIX (SAS Institute Inc, Cary, North Carolina).

RESULTS

We identified 4066 individuals with acute kidney injury requiring dialysis who survived at least 30 days after hospital discharge without receiving dialysis or further hospitalization (FIGURE 1). At least 1 match was identified for 3769 (92.7%) of the exposed patients (TABLE 1). Hence, 3769 individuals with acute kidney injury and dialysis and 13 598 matches with neither acute kidney injury nor dialysis were included in this study.

The mean age of the enrolled participants was 62 years, approximately 40% were women, and the mean Charlson Comorbidity Index score was 2.7 (Table 1). Slightly more than 25% of participants in each group had documented chronic kidney disease in the 5-year period before the index hospital admission. During their hospitalization, 47% of patients with acute kidney injury and dialysis received mechanical ventilation, compared with 42% of those without acute kidney injury and dialysis. The respective rates for cardiac surgery were 11.5% and 10.0%. Approximately 15% of participants in each group had sepsis. The rates of cardiac and noncardiac arteriography were also comparable between groups (Table 1).

Figure 1. Creation of the Acute Kidney Injury and Dialysis Study Cohort

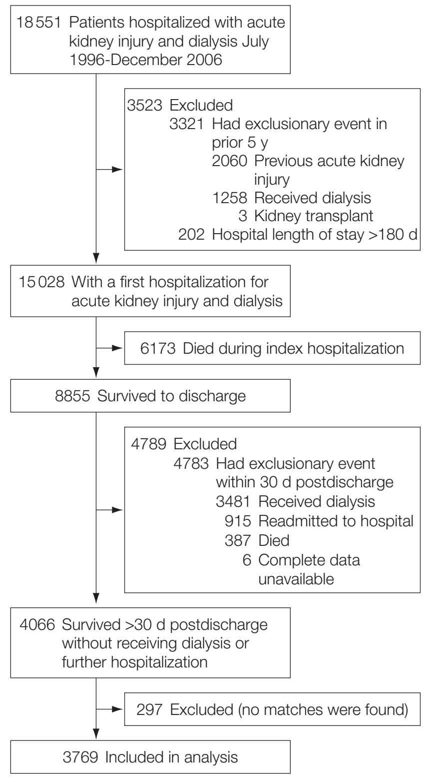


Table 1. Characteristics of Hospitalized Patients by Group

Characteristic	With Acute Kidney Injury and Dialysis at Index Hospitalization (n = 3769)[a]	Without Acute Kidney Injury or Dialysis at Index Hospitalization (n = 13 598)[a]
Age at cohort entry, mean (SD), y	61.9 (16.3)	62.2 (16.3)
Women	1504 (39.9)	5476 (40.3)
Charlson Comorbidity Index, mean (SD), score[b]	2.7 (2.3)	2.8 (2.5)
Chronic kidney disease ≤5 y before the index hospitalization admission date	1059 (28.1)	3684 (27.1)
Comorbid conditions ≤5 y before the index hospitalization discharge date		
Myocardial infarction	1692 (44.9)	5947 (43.7)
Cancer	1566 (41.5)	5775 (42.5)
Diabetes mellitus	1548 (41.1)	5741 (42.2)
Heart failure	1437 (38.1)	5168 (38.0)
Cerebrovascular disease	682 (18.1)	2515 (18.5)
Liver disease	510 (13.5)	2019 (14.8)
Peripheral vascular disease	147 (3.9)	513 (3.8)
Procedure or condition during index hospitalization		
Mechanical ventilation	1761 (46.7)	5700 (41.9)
Sepsis	579 (15.4)	2045 (15.0)
Cardiac surgery	435 (11.5)	1365 (10.0)
Noncardiac arterial angiography	312 (8.3)	1210 (8.9)
Coronary angiography with or without percutaneous coronary intervention	289 (7.7)	1153 (8.5)
Abdominal aortic aneurysm repair	153 (4.1)	458 (3.4)
Propensity score for receipt of acute dialysis for acute kidney injury, mean (SD)	3.8 (2.6)	4.2 (2.3)
Follow-up, median (interquartile range), y	3 (1-5)	3 (1-5)

[a] All dates are presented as No. (%) unless otherwise indicated.
[b] Charlson Comorbidity Index scores range from 0 to 37, with a higher value indicating greater comorbidity.

Need for Chronic Dialysis

After a median (IQR) follow-up of 3 (1-5) years, the incidence rates of chronic dialysis were 2.63 and 0.91 per 100 person-years among those with and without acute kidney injury and dialysis in the index hospitalization, respectively, corresponding to a crude HR of 3.26 (95% CI, 2.73-3.89) (TABLE 2; FIGURE 2A). After adjusting for age and the propensity score, the HR changed little (3.23; 95% CI, 2.70-3.86; Table 2).

The increased risk of chronic dialysis following a hospitalization complicated by acute kidney injury and dialysis was consistent across patient subgroups (FIGURE 3). This was especially so among patients without a preexisting diagnosis of chronic kidney disease (adjusted HR, 15.54; 95% CI, 9.65-25.03).

All-Cause Mortality

The incidence rate for all-cause mortality was 10.10 per 100 person-years among patients with acute kidney injury and dialysis, which was slightly lower than among those without in-hospital acute kidney injury (Figure 2B). After adjusting for age and the propensity score, the future risk of death was not significantly different between groups (HR, 0.95; 95% CI, 0.89-1.02; Table 2).

Unmatched Participants

There were 297 (7.3%) participants with acute kidney injury and dialysis who could not be matched to a suitable control. Their respective incidence rates of chronic dialysis and all-cause mortality were 4.89 per 100 person-years and 14.18 per 100 person-years, which were higher than rates for the 3769 patients who were successfully matched (Table 2).

COMMENT

We analyzed all patients admitted to Ontario hospitals over a 10-year period and found that survivors of a hospitalization complicated by acute kidney injury requiring dialysis were approximately 3 times more likely to require chronic dialysis compared with those without acute kidney injury. However, no difference was observed between these groups for long-term mortality.

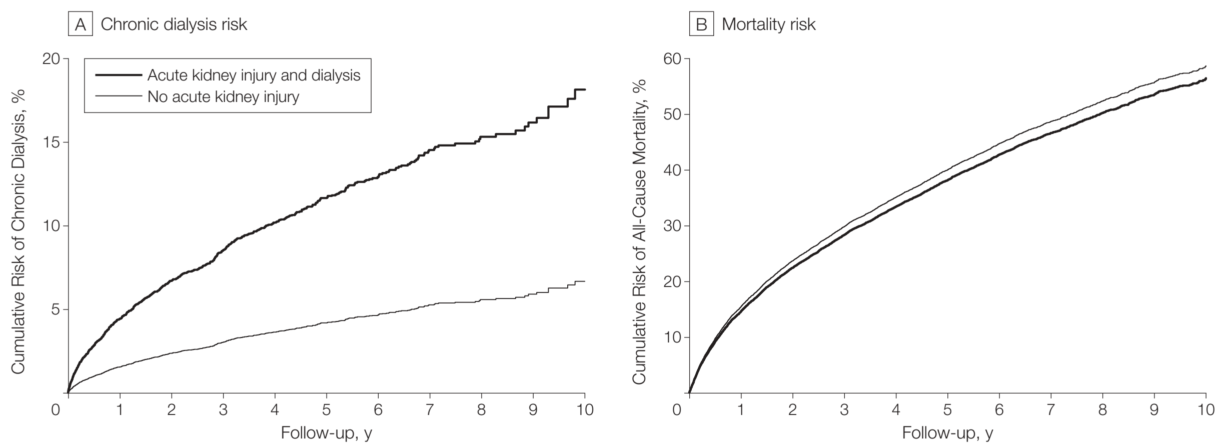
This study was designed to evaluate long-term renal health among survivors of acute kidney injury receiving dialysis in a large population with universal access to health care. Patients with acute kidney injury have a high acuity level during their hospitalization and a

Table 2. Risk of Chronic Dialysis and All-Cause Mortality by Group

	Acute Kidney Injury and Dialysis at Index Hospitalization (n = 3769)		Without Acute Kidney Injury or Dialysis at Index Hospitalization (n = 13 598)		Hazard Ratio (95% Confidence Interval)	
Outcome	No. of Events (%)	Incidence Rate Per 100 Person-Years	No. of Events (%)	Incidence Rate Per 100 Person-Years	Crude[a]	Adjusted[b]
Chronic dialysis	322 (8.5)	2.63	403 (3.0)	0.91	3.26 (2.73-3.89)	3.23 (2.70-3.86)
All-cause mortality	1311 (34.8)	10.10	4884 (35.9)	10.83	0.95 (0.88-1.02)	0.95 (0.89-1.02)

[a] Reflects the effect of acute kidney injury and dialysis vs matched individuals without acute kidney injury.
[b] Further adjusted for age (continuous in years) and the propensity score for acute kidney injury and dialysis.

Figure 2. Risk of Chronic Dialysis in Association With Acute Kidney Injury and Dialysis During Index Hospitalization



No. at risk (A)

Year	0	1	2	3	4	5	6	7	8	9	10
Acute kidney injury and dialysis	3769	2761	2116	1683	1305	964	676	462	294	158	58
No acute kidney injury	13 598	10 224	7850	6080	4639	3383	2342	1555	905	473	169

No. at risk (B)

Year	0	1	2	3	4	5	6	7	8	9	10
Acute kidney injury and dialysis	3769	2906	2262	1805	1404	1038	732	495	311	167	59
No acute kidney injury	13 598	10 368	8011	6245	4780	3496	2429	1619	952	498	175

wide array of preexisting illness.[11] Accordingly, we identified matched controls based on a series of key characteristics including the propensity to experience an episode of acute kidney injury requiring dialysis. Because we sought to evaluate long-term outcomes among survivors of severe acute kidney injury, and to reduce the possibility of survivor-treatment bias, we required a 30-day period following hospital discharge in which a participant survived and was free of dialysis.

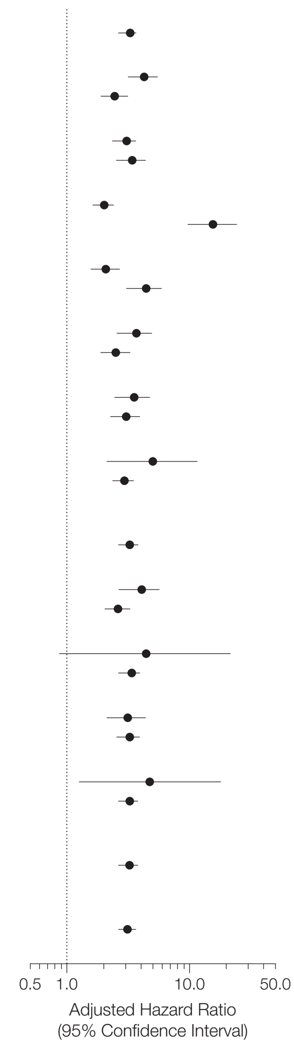
We completed our study using administrative data, so there may have been a misclassification of the study exposure (acute kidney injury and dialysis) or other adjustment variables. In a recent validation study, the combination of a diagnostic code for acute kidney injury and a procedure code for dialysis had both sensitivity and specificity of more than 90% for capturing the combination of acute kidney injury and dialysis.[21] However, given the low sensitivity of an acute kidney injury diagnosis code in isolation (28%-35%), it is possible that some participants classified as not having acute kidney injury actually did, leading to an underestimation of outcome differences between groups. In addition, we could not match approximately 7% of study patients with acute kidney injury and dialysis to unaffected controls. Since unmatched individuals had higher rates of chronic dialysis and mortality than those with at least 1 match, their exclusion attenuated the reported effect sizes. Finally, we cannot exclude the possibility of residual confounding despite our rigorous matching and adjustment on important variables.

We could not obtain measures of kidney function, such as serum creatinine or urinary protein excretion, neither at discharge nor during post-discharge follow-up, and were limited to measuring the outcome of chronic dialysis, for which reliable claims-based data exist. Indeed, many patients who survived acute kidney injury and dialysis may have had persistent or worsening renal dysfunction after hospital discharge, but not so severe as to warrant dialysis. We also used a widely accepted definition for chronic dialysis—the receipt of dialysis for at least 90 days. A shortcoming of this approach is that it misclassifies individuals who truly developed end-stage renal disease, but who died in the first 90 days after commencing chronic dialysis. However, since the risk of death was not significantly higher in individuals with acute kidney injury and dialysis than matched patients with no acute kidney injury, it is unlikely that this potential misclassification had an effect on the risk of chronic dialysis.

Small studies have previously evaluated the outcomes of survivors of acute kidney injury requiring dialysis. Schiffl studied 425 patients with acute tubular necrosis who required acute dialy-

Figure 3. Risk of Chronic Dialysis Associated With Acute Kidney Injury and Dialysis at Index Hospitalization by Participant Characteristics

	No. of Events/No. at Risk[a]	
	Acute Kidney Injury and Dialysis	No Acute Kidney Injury
All participants	322/3769	403/13598
Age		
≥65 y	186/1941	198/7146
<65 y	136/1828	205/6452
Sex		
Men	192/2265	250/8122
Women	130/1504	153/5476
Chronic kidney disease		
Yes	195/1059	362/3684
No	127/2710	41/9914
Diabetes mellitus		
Yes	159/1548	278/5741
No	163/2221	125/7857
Myocardial infarction		
Yes	167/1692	208/5947
No	155/2077	195/7651
Heart failure		
Yes	166/1437	223/5168
No	156/2332	180/8430
Cerebrovascular disease		
Yes	53/682	60/2515
No	269/3087	343/11083
Peripheral arterial disease		
Yes	21/147	33/513
No	301/3622	370/13085
Cancer		
Yes	137/1566	145/5775
No	185/2203	258/7823
Liver disease		
Yes	24/510	50/2019
No	298/3259	353/11579
Mechanical ventilation		
Yes	98/1761	84/5700
No	224/2008	319/7898
Sepsis		
Yes	29/579	24/2045
No	293/3190	379/11553
Cardiac surgery		
Yes	35/435	20/1365
No	287/3334	383/12233
Aortic aneurysm repair		
Yes	9/153	8/458
No	313/3616	395/13140



[a]The numerator denotes the number of events (requirement for chronic dialysis) and the denominator denotes the number of patients at risk within that subgroup.
Hazard ratios are adjusted for the propensity score for acute kidney injury and dialysis and participant age. Effect estimates are not shown; models did not converge.

sis at a single institution.[10,14] Among the 225 participants alive at discharge, survival was 66% and 53% at 1 and 5 years, respectively. Morgera et al used follow-up data for 89% of the 301 patients discharged from their institution following acute kidney injury and receipt of continuous dialysis.[8] Survival at 6 and 12 months was 77% and 69%, respectively. Information about renal function, available for about one-third of survivors, revealed that 10% required chronic dialysis and 40% had some degree of persistent renal insufficiency. Bagshaw et al observed a 1-year survival rate of 90% and a chronic dialysis rate of 22% among 97 Albertans discharged alive following dialysis for acute kidney injury.[13] While these studies clearly shed some light on the health outcomes of acute kidney injury survivors, most data were derived from single centers or local health regions and were based on small cohorts. The absence of a comparator group in these studies also prevents one from determining the degree to which acute kidney injury and dialysis is a prognosticator for long-term health status in excess of global patient comorbidity before and during the index hospitalization. Finally, since survivorship was assessed starting from the hospital discharge date, patients who died shortly following discharge, and who may not have been candidates for future dialysis, may have been inappropriately included.

Ishani et al previously used American Medicare administrative data to identify approximately 7000 patients older than 67 years with hospital-associated acute kidney injury who survived to discharge.[22] Postdischarge mortality was doubled and the risk of chronic dialysis was increased by nearly 7 times among survivors of acute kidney injury. These risks were accentuated in patients with preexisting chronic kidney disease. However, their cohort study[22] was limited to individuals older than 67 years, and they did not distinguish between patients with acute kidney injury who required dialysis and those who did not. This study used a fairly limited set of covariates, and thus, increased the likelihood of confounding within their risk estimates. Among individuals in our study with preexisting chronic kidney disease, an episode of acute kidney injury and dialysis was associated with an approximate 2-fold higher risk of a chronic dialysis, which rose to about 15 times higher among patients without previous chronic kidney disease (Figure 3). Comparing our findings with those of Ishani et al[22] is challenging, since the Ishani study included controls with neither acute kidney injury nor prior chronic kidney disease. In contrast, more than one quarter of our control cohort had a history of preexisting chronic kidney disease.

Injury to the kidney, especially that necessitating acute dialysis, seems to independently predispose a patient to long-term dialysis, even among those who are free of dialysis at hospital discharge. This parallels basic science data that demonstrate the long-term effects of ischemia-reperfusion injury on the loss of the renal vasculature and progressive renal fibrosis.[23,24] Acute kidney injury may induce irreversible chronic kidney damage in patients with previously healthy kidneys, and accelerate kidney disease progression among patients with preexisting chronic kidney disease.

In contrast to other studies,[22] we found that a prior history of acute kidney injury and dialysis was not independently associated with long-term mortality (HR, 0.95; 95% CI, 0.89-1.02). Indeed, there was a surprising trend that suggested a lower associated risk of death in patients with prior acute kidney injury and dialysis. There are 2 likely explanations for this finding. First, although our comparator group comprised individuals without acute kidney injury (in whom acute dialysis was not indicated), those with acute kidney injury who received dialysis may have been a selected group of individuals who were more likely to survive. The tendency to administer lifesaving therapies to those most likely to have a favorable prognosis has been demonstrated in other settings. For example, patients at lowest risk for cardiovascular disease and the highest likelihood of survival were prescribed efficacious drug therapies more commonly than those at higher risk.[25] Second, as mentioned previously, approximately 7% of the 4066 survivors with acute kidney injury and dialysis were excluded from the data analyses due to a lack of at least 1 appropriate match. These individuals exhibited a higher mortality rate over time. Had these individuals been included in the final analyses, the small nonsignificant trend toward reduced mortality would likely have been further diminished.

Our findings expand on prior knowledge to provide clinicians with new information about the long-term effect of acute kidney injury that arises during a hospitalization. First, if affected patients survive to hospital discharge, then they remain at high risk of needing dialysis over the next 3 to 5 years. Patients who survive a hospitalization complicated by acute kidney injury requiring dialysis may benefit from specialized care to address complications of chronic kidney disease, and also from concerted efforts to prevent progression to chronic dialysis. At the same time, their high mortality rate is similar to hospitalized patients without acute kidney injury or need for dialysis. Hence, an episode of acute kidney injury requiring in-hospital dialysis may not be an independent contributing factor to long-term survival.

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Study concept and design: Wald, Quinn, Scales, Mamdani, Ray.
Analysis and interpretation of data: Wald, Luo, Li.
Drafting of the manuscript: Wald, Ray.
Critical revision of the manuscript for important intellectual content: Wald, Quinn, Luo, Li, Scales, Mamdani.
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Additional Information: eTable is available at http://www.jama.com.

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REFERENCES

1. Brivet FG, Kleinknecht DJ, Loirat P, Landais PJ; French Study Group on Acute Renal Failure. Acute renal failure in intensive care units–causes, outcome, and prognostic factors of hospital mortality; a prospective, multicenter study: French Study Group on Acute Renal Failure. *Crit Care Med*. 1996;24(2):192-198.

2. de Mendonça A, Vincent JL, Suter PM, et al. Acute renal failure in the ICU: risk factors and outcome evaluated by the SOFA score. *Intensive Care Med*. 2000; 26(7):915-921.

3. Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol*. 2005;16(11):3365-3370.

4. Liangos O, Wald R, O'Bell J, Price L, Pereira B, Jaber B. Epidemiology and outcomes of acute renal failure in hospitalized patients: a national survey. *Clin J Am Soc Nephrol*. 2006;1(1):43-51.

5. McCarthy JT. Prognosis of patients with acute renal failure in the intensive-care unit: a tale of two eras. *Mayo Clin Proc*. 1996;71(2):117-126.

6. Silvester W, Bellomo R, Cole L. Epidemiology, management, and outcome of severe acute renal failure of critical illness in Australia. *Crit Care Med*. 2001; 29(10):1910-1915.

7. Metnitz PG, Krenn CG, Steltzer H, et al. Effect of acute renal failure requiring renal replacement therapy on outcome in critically ill patients. *Crit Care Med*. 2002; 30(9):2051-2058.

8. Morgera S, Kraft AK, Siebert G, Luft FC, Neumayer HH. Long-term outcomes in acute renal failure patients treated with continuous renal replacement therapies. *Am J Kidney Dis*. 2002;40(2): 275-279.

9. Uchino S, Kellum JA, Bellomo R, et al; Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) Investigators. Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA*. 2005;294(7):813-818.

10. Schiffl H. Renal recovery from acute tubular necrosis requiring renal replacement therapy: a prospective study in critically ill patients. *Nephrol Dial Transplant*. 2006;21(5):1248-1252.

11. Mehta RL, Pascual MT, Soroko S, et al; Program to Improve Care in Acute Renal Disease. Spectrum of acute renal failure in the intensive care unit: the PICARD experience. *Kidney Int*. 2004;66(4):1613-1621.

12. Palevsky PM, Zhang JH, O'Connor TZ, et al; VA/NIH Acute Renal Failure Trial Network. Intensity of renal support in critically ill patients with acute kidney injury. *N Engl J Med*. 2008;359(1):7-20.

13. Bagshaw SM, Laupland KB, Doig CJ, et al. Prognosis for long-term survival and renal recovery in critically ill patients with severe acute renal failure: a population-based study. *Crit Care*. 2005;9(6):R700-R709.

14. Schiffl H, Fischer R. Five-year outcomes of severe acute kidney injury requiring renal replacement therapy. *Nephrol Dial Transplant*. 2008;23(7): 2235-2241.

15. Ahlström A, Tallgren M, Peltonen S, Rasanen P, Pettila V. Survival and quality of life of patients requiring acute renal replacement therapy. *Intensive Care Med*. 2005;31(9):1222-1228.

16. Scales DC, Guan J, Martin CM, Redelmeier DA. Administrative data accurately identified intensive care unit admissions in Ontario. *J Clin Epidemiol*. 2006; 59(8):802-807.

17. Rubin DB. Estimating causal effects from large data sets using propensity scores. *Ann Intern Med*. 1997; 127(8 pt 2):757-763.

18. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.

19. Juurlink DN, Mamdani MM, Lee DS, et al. Rates of hyperkalemia after publication of the Randomized Aldactone Evaluation Study. *N Engl J Med*. 2004; 351(6):543-551.

20. Redelmeier D, Scales D, Kopp A. Beta blockers for elective surgery in elderly patients: population based, retrospective cohort study. *BMJ*. 2005;331(7522): 932.

21. Waikar SS, Wald R, Chertow GM, et al. Validity of International Classification of Diseases, Ninth Revision, Clinical Modification Codes for Acute Renal Failure. *J Am Soc Nephrol*. 2006;17(6):1688-1694.

22. Ishani A, Xue JL, Himmelfarb J, et al. Acute kidney injury increases risk of ESRD among elderly. *J Am Soc Nephrol*. 2009;20(1):223-228.

23. Basile DP, Donohoe D, Roethe K, Osborn JL. Renal ischemic injury results in permanent damage to peritubular capillaries and influences long-term function. *Am J Physiol Renal Physiol*. 2001;281(5):F887-F899.

24. Spurgeon KR, Donohoe DL, Basile DP. Transforming growth factor-beta in acute renal failure: receptor expression, effects on proliferation, cellularity, and vascularization after recovery from injury. *Am J Physiol Renal Physiol*. 2005;288(3):F568-F577.

25. Ko DT, Mamdani M, Alter DA. Lipid-lowering therapy with statins in high-risk elderly patients: the treatment-risk paradox. *JAMA*. 2004;291(15): 1864-1870.