

Late Creation of Vascular Access for Hemodialysis and Increased Risk of Sepsis

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Abstract. The creation of fistulas or grafts before starting dialysis is recommended, but whether it reduces major adverse events is largely unknown. The objective of this study was to determine if early access creation was associated with a reduced risk of hospitalization from sepsis and mortality. Fistulas or grafts created at least 4 mo before starting hemodialysis were defined as Early creations ($n = 1240$), and accesses created between 4 mo and 1 mo before starting hemodialysis were defined as Just Prior creations ($n = 997$). Accesses created within 1 mo of starting dialysis or after were defined as Late creations (reference group, $n = 3687$). Hemodialysis catheter use was defined as insertion, removal, or manipulation of a catheter before the occurrence of sepsis. Eighty percent of

accesses were fistulas. Early access creation was associated with a relative risk (RR) of sepsis of 0.57 (95% CI, 0.41 to 0.79) compared with Late access creation. Catheter use increased the risk of sepsis by 1.41 (95% CI, 1.14 to 1.81). The risk of sepsis with Early creation decreased to 0.48 (95% CI, 0.35 to 0.65) if catheter use was not adjusted. Early access creation was associated with lower mortality (RR 0.76; 95% CI 0.58 to 1.00), but this association became nonsignificant if catheter use and sepsis were adjusted. Catheter use and sepsis independently increased mortality. This study demonstrates that fistula creation at least 4 mo before starting chronic hemodialysis is associated the lowest risk of sepsis and death, primarily by reducing the use of hemodialysis catheters.

Persons with chronic kidney disease should be referred early to nephrologists for predialysis care. Persons who receive predialysis care have a slower progression of kidney disease, receive more appropriate care, and have reduced morbidity and mortality (1–6). An important aspect of predialysis care is the timely creation of vascular access, particularly fistulas. National guidelines recommend that fistulas should be created when a person's creatinine clearance is less than 25 ml/min, or when their serum creatinine is greater than 4 mg/dl (353 $\mu\text{mol/L}$), or within 1 yr of expected start of hemodialysis (7). Another target is that fistulas should be created 3 to 4 mo before use and that grafts should be created 3 to 6 wk before use (7). Despite these recommendations, approximately one third of persons starting chronic hemodialysis therapy are referred late for predialysis care, and between 30 and 60% use a catheter as their initial vascular access (8,9).

Hemodialysis patients who use a catheter for vascular access are at risk for catheter-related complications, including bacteremia and sepsis (10). Catheters are a consistent risk factor for sepsis in persons receiving hemodialysis (11,12). The rate of bacteremia in persons using tunneled, cuffed catheters for

hemodialysis vary greatly; however, they average 1 to 2 cases per 1000 catheter-days, or approximately 20% over the duration of use (10). Sepsis is associated with a very high mortality rate (13). Infection is also the second leading cause of death of persons receiving chronic hemodialysis (14).

The objective of this population-based study was to describe the timing of permanent access creation in Ontario, Canada, and to determine if early permanent vascular access creation was associated with a reduced risk of sepsis. The secondary objective was to determine if early access creation was associated with reduced mortality in the first year of hemodialysis.

Materials and Methods

Data Sources

Records from April 1, 1994, to March 31, 2001, were reviewed from several administrative databases at the Institute for Clinical Evaluative Sciences (Toronto, Ontario, Canada). The administrative databases included the Ontario Health Insurance Plan (OHIP) database, the Registered Persons Database (RPDB), the Canadian Institute for Health Information (CIHI) database, the Ontario Diabetes Database (ODD), and census data. OHIP provides universal health insurance for Canadian citizens or legal immigrants who live in Ontario for the majority of the year. In Ontario, more than 94% of physicians are reimbursed for clinical care by OHIP (one-payer system). Billing records were used to identify dialysis procedures, kidney transplants, permanent access creations, and hemodialysis catheter-related procedures. RPDB contains vital status, age, gender, and location of residence of each person with a valid OHIP health card in Ontario. The CIHI database contains demographic and clinical information regarding all hospital admissions, discharges, and same-day surgeries in Canada, including transfers and deaths. Trained hospital staff mem-

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bers transcribe the information from medical charts using standard diagnosis and procedure codes (ICD-9 and Canadian Classification of Procedures). The Ontario Diabetes Database (ODD) is a retrospective cohort of persons who have had at least two OHIP records or one CIHI record bearing a diagnostic code for diabetes. The database has been validated against the Ontario Drug Benefit Program database, where persons made claims for oral hypoglycemics or insulin. The ODD has also been validated by comparison with the National Population Health Survey and primary data collection (15). Census data were used to determine median household income by assigning the neighborhood level income quintiles to the person on the basis of their home residence postal code (16). To protect privacy, all data linkage was done via encrypted OHIP numbers. The Research Ethics Board approved the study.

Definitions of the Study Population and Outcomes

Persons starting *chronic hemodialysis* were defined as Ontario residents aged 18 years and older who received hemodialysis for a period of at least 90 d and who had no record of hemodialysis in the 2 yr before the study start. Hemodialysis billing records were reviewed for the year following the study period to capture persons starting chronic dialysis late in the study period. *First permanent access creation* was defined as a fistula or graft created within 3 yr before starting hemodialysis or within 1 yr of starting hemodialysis. We excluded persons who never had a fistula or graft created, restricting the study to those persons who had a medical indication and consented to create a permanent access. Patients having a kidney transplant before the start of hemodialysis were also excluded, as they may have had remote access creation. Catheter use (yes/no) was defined as an OHIP record of an insertion, removal, or manipulation of a hemodialysis catheter before the occurrence of sepsis during the study period. The data were not sufficiently accurate to define periods of catheter use. *Baseline comorbidity* was first defined by reviewing CIHI data 5 yr before starting hemodialysis and calculating the Charlson-Deyo Index for administrative data (17). The two diabetes components of the index were removed, and a separate variable for diabetes status was defined using the ODD. All patients were assumed to have renal disease. *Healthy starts* were defined as those persons who started hemodialysis as an outpatient with a Charlson-Deyo Index score of 0.

The timing of permanent access creation relative to the start date of hemodialysis was grouped in monthly intervals (*e.g.*, 1 mo prior, 1 mo after, 2 mo prior, 2 mo after, etc.). Monthly interval groups at similar absolute risk of sepsis were then collapsed into three groups: *Early access creation*, those with permanent access created at least 4 mo before starting hemodialysis; *Just prior access creation*, permanent access created between 4 mo and 1 mo before starting hemodialysis; *Late access creation*, permanent access created within 1 mo or after starting hemodialysis.

The primary outcome was defined as the first hospitalization for sepsis or bacteremia (hereafter both are referred to as sepsis) within the first year of hemodialysis. This outcome was based on a hospital discharge diagnosis with ICD-9 CM codes of 038.0 to 038.9 and 790.7 (see Appendix). Sepsis was excluded if it was coded as a complication of hospitalization or if it took place during the same hospitalization as the start of hemodialysis. The administrative data were not sufficiently detailed to define catheter-related sepsis. Survival of persons in the first year of hemodialysis was determined by reviewing records in the RPDB. The observation period for each person was from the start of hemodialysis to 1 year after.

Statistical Analyses

Baseline differences among access timing groups were compared using ANOVA for continuous variables and χ^2 tests for categorical variables. Permutation-style adjusted *P* values were reported while doing multiple comparisons, using the MULTTEST procedure in SAS.

The absolute risk of first hospitalization for sepsis was calculated for each monthly interval group and the collapsed groups. Cox proportional hazards models were used to analyze the time to first hospitalization for sepsis and death separately within the first year of starting hemodialysis. The following covariates, chosen a priori on the basis of clinical relevance, were entered simultaneously into the models: age, gender, type of first permanent access, timing of access (collapsed groups), catheter use, inpatient status at initiation of dialysis, diabetes status, comorbidity index (diabetes variables removed) second access creation, and an indicator of sepsis (survival model only). Second access creation and sepsis indicators were both analyzed as time-varying binary covariates such that the value of the indicator would switch from 0 to 1 at the time of the event. Persons were censored for death (sepsis model only) or kidney transplant during their 1-yr follow-up. The proportional hazards assumption was assessed for the non time-varying covariates by means of interactions with time. Interactions between timing of access and type of access, age, gender, and diabetes were also assessed and the likelihood ratio test was used to compare the models with and without interactions. The sepsis model was reviewed with and without the catheter use variable to estimate how it influenced the association between access timing and sepsis. The mortality model was reviewed with and without the catheter use and sepsis variables to estimate how they influenced the association between access timing and mortality. All analyses were done with SAS version 8.2. A two-sided *P* < 0.05 was deemed statistically significant.

Results

The Study Population

There were 8328 persons who started chronic hemodialysis between April 1, 1994, and March 30, 2001. Thirteen individuals were excluded because we could not define which type of access they received (*i.e.*, both fistula and graft procedures were coded on the same day by the surgeon). Fifty-two persons were excluded because they had a prior kidney transplant. Another 173 people were excluded because they were not eligible for OHIP coverage during the year before starting dialysis. Finally, 2166 persons were excluded because they did not have a fistula or graft created 3 yr before or within 1 yr of starting hemodialysis. The study population consisted of 5924 persons; of those, 4751 (80%) had fistulas and 1173 (20%) had grafts created. Within the 1-yr follow-up, 538 persons (9.1%) had died and 176 persons had (3.0%) received transplants.

The baseline characteristics of the Early, Just prior, and the Late access creation groups are presented in Table 1. Compared with the Late access creation group, persons in the Early creation group and the Just prior group were younger (*P* = 0.025 and *P* = 0.007), had less comorbidity (*P* < 0.001 for both), were less likely to start hemodialysis as an inpatient (*P* < 0.001 for both), were more likely to receive a fistula (*P* < 0.001 for both), and were less likely to use a catheter (*P* < 0.001 for both). Persons in the Just prior group were more likely to be male (*P* = 0.006) compared to the Late creation

Table 1. Baseline characteristics of persons starting chronic hemodialysis by timing of access creation

Variable	Early ^b Access Creation (n = 1240)	Just Prior ^c Access Creation (n = 997)	Late Access ^d Creation (n = 3687)	P-value ^e		
				Overall	Early vs Late	Just Prior vs Late
Age, mean ± SD	60 ± 15	59 ± 16	61 ± 16	0.001	0.025	0.007
Male, %	64.4	66.6	61.5	0.006	0.121	0.006
Diabetes, %	42.9	47.7	46.3	0.049	0.071	0.657
Comorbidity index, ^a %						
0	59.4	55.8	41.3	<0.001	<0.001	<0.001
1	18.0	21.9	23.2			
2	13.5	12.2	18.0			
3+	9.1	10.1	17.5			
Inpatients start, %	22.3	23.5	68.8	<0.001	<0.001	<0.001
Fistula as 1st access, %	88.1	84.3	76.5	<0.001	<0.001	<0.001
Income quintile, mean ± SD	2.8 ± 1.4	2.8 ± 1.4	2.8 ± 1.4	0.400	0.429	0.558
Catheter use, %	35.9	42.5	89.1	<0.001	<0.001	<0.001

^a Comorbidity index is the Charlson-Deyo Index modified by subtracting the renal disease and diabetes components.

^b Early access creation group is the creation of a fistula or graft at least 4 mo prior to starting hemodialysis.

^c Just prior creation is the creation of a fistula or graft between 4 and 1 mo prior to starting hemodialysis.

^d Late creation is the creation of a fistula or graft within 1 mo or after starting hemodialysis.

^e Overall P-values calculated using ANOVA for continuous variables and chi-square tests for categorical variables. Permutation-style adjusted P-values were calculated for multiple comparisons.

group. The difference in the presence of diabetes was marginally significant across the three groups but NS when performing multiple comparisons. There was no difference in the income quintiles across the three groups.

Timing of Permanent Access Creation and Absolute Risk of Sepsis

The majority of persons had a permanent access created either just before or after starting hemodialysis, creating a bell-shaped distribution when plotting persons in monthly interval groups (Figure 1, vertical bar). A total of 2729 (46%) of 5924 persons had their first permanent access created before starting hemodialysis. Catheter use increased when access was created later, relative to the start of hemodialysis. Catheter use was detected in 35.9%, 42.5%, and 89.1% of the Early, Just prior, and Late creation groups, respectively ($P < 0.001$). The median times between starting hemodialysis and access creation for persons starting hemodialysis without permanent access were 62 d for fistulas and 53 d for grafts. The times between referral to a surgeon and access creation could not be reliably determined from the databases.

A total of 483 (8.20%) persons were hospitalized for sepsis within the first year of hemodialysis. The risk of sepsis in the first year of hemodialysis decreased the earlier the first permanent access was created (Figure 1, line). In the Early access creation group, the risk of sepsis was 4.4% (55 of 1240). The risk increased to 6.6% (66 of 997) in the Just prior group and rose further to 9.0% (365 of 3687) if the access was created late. There was an unexpected drop in the risk of sepsis for persons who had access placed more than 9 mo after starting dialysis; however, the risk was still high compared with the Early and Just prior groups. The risk of sepsis of healthy starts

(n = 1716) in the Early access, Just prior, and Late access groups was 3.7%, 4.8%, 7.2% ($P = 0.019$), respectively. The risk of sepsis in healthy starts who had fistulas placed early and had no record of catheter use or second access creation was 1.2%.

Timing of Access Creation, Catheter Use, and Relative Risk of Sepsis

The adjusted relative risks (RR) of hospitalization for sepsis in the first year of dialysis in the Early access creation and Just prior access creation groups were 0.48 (95% CI, 0.35 to 0.65) and 0.72 (95% CI, 0.54 to 0.95), respectively, relative to those with Late access creation. This analysis adjusted for differences among the groups in age, gender, type of permanent access, starting dialysis as an inpatient, diabetes, comorbidity, and second access creation but not catheter use. When catheter use was introduced in the model (Table 2), the RR was 1.41 (95% CI, 1.08 to 1.85), and the effect of early access creation rose to 0.57 (95% CI, 0.41 to 0.79). Other factors independently associated with hospitalization for sepsis were male gender ($P = 0.043$), diabetes ($P = 0.002$), inpatient start ($P = 0.022$), and graft use ($P = 0.038$). Second access creation was associated with a trend for increased sepsis ($P = 0.079$). Diabetes and access type had significant interactions with time, indicating that their association with sepsis increases over time. The RR for these variables in Table 2 are averages over time. Age and comorbidity index were not associated with risk of sepsis in the first year of chronic hemodialysis. There was no significant interaction between the timing of access placement and type of access, age, gender, and diabetes.

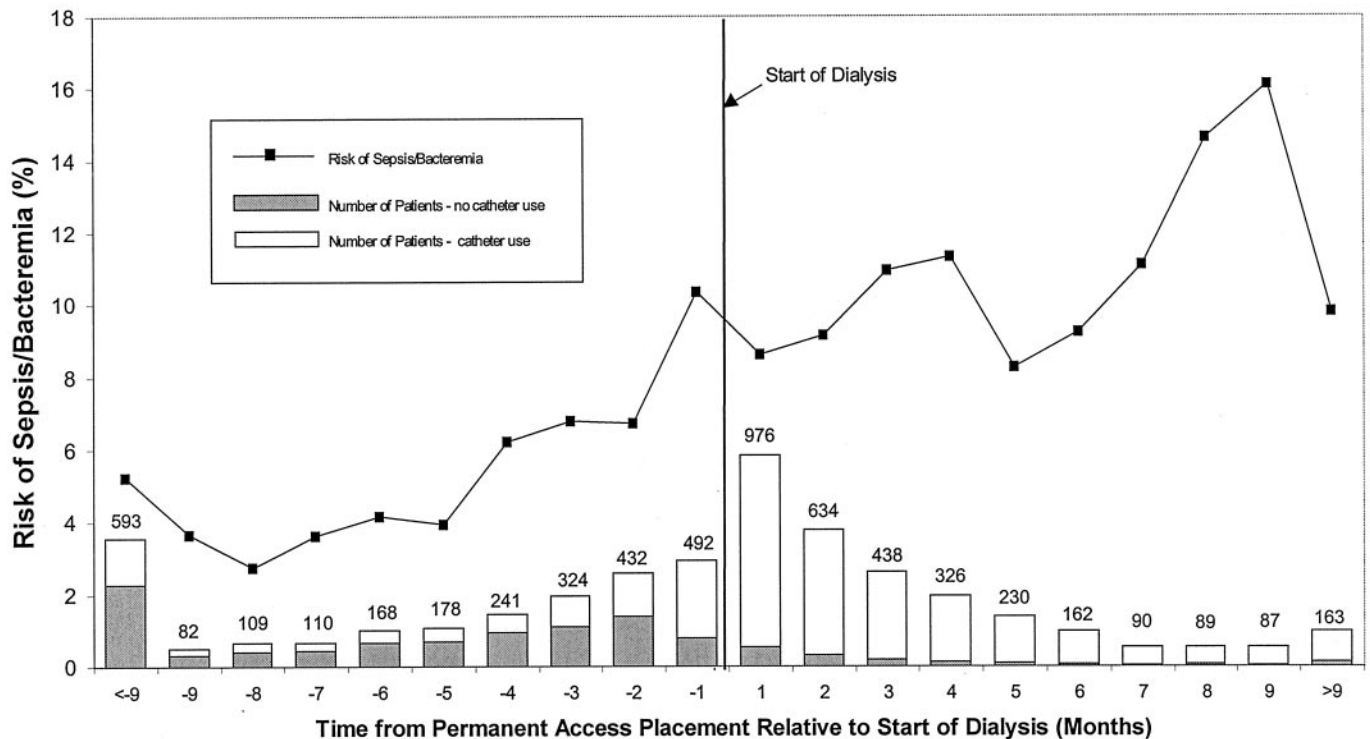


Figure 1. Risk of sepsis in persons starting chronic hemodialysis by timing of permanent access creation in monthly intervals. The vertical bars and the accompanying number are the number of people who had a permanent access created in that month relative to the start of chronic hemodialysis. The gray portion of the vertical bar is the number of persons with no detected catheter use in administrative data. The white portion of the vertical bar is the number of people with catheter used detected. Most accesses are placed just before or after the initiation of dialysis, but 593 had access created 9 mo or more before starting hemodialysis (first gray bar). The line represents the absolute risk of being hospitalized for sepsis in that monthly group in the first year of dialysis. The earlier the access is placed, the less use of catheters and the lower the risk of hospitalization from sepsis.

Timing of Access Creation, Catheter Use, Sepsis, and Mortality

Persons with and without sepsis had a crude 1-yr mortality rate of 18.3% compared with 8.3% ($P < 0.001$), respectively. Early access creation had a RR of mortality of 0.76 (95% CI, 0.58 to 1.00) compared with Late access creation not adjusting for catheter use or sepsis. When catheter use alone was introduced in the model, its RR for death was 1.56 (95% CI, 1.21 to 2.01) and the benefit of early access creation was eliminated (RR, 0.94; $P = 0.67$). When sepsis was introduced in the model, its RR was 3.13 (95% CI, 2.48 to 3.94); however, early access creation still showed a trend toward increased survival (RR, 0.80; $P = 0.11$). When both catheter use and sepsis were introduced into the mortality model, the RR of early access creation, catheter use, and sepsis were 0.95 (95% CI, 0.71 to 1.27), 1.49 (95% CI, 1.16 to 1.91), and 3.06 (95% CI, 2.43 to 3.87), respectively. Other significant risk factors for mortality were age ($P < 0.001$), comorbidity index ($P < 0.001$), and using a graft for access ($P = 0.003$).

Discussion

The primary objective of this study was to determine if early access creation reduced hospitalization for sepsis in the first year of hemodialysis. Almost half of the persons had perma-

nent access created before starting hemodialysis, with 80% being fistulas. Early access creation was associated with a 43% reduction in the risk of sepsis and a 24% reduction in the risk of death. The greatest reduction in sepsis and death was seen when fistulas were created at least 4 mo before starting hemodialysis, which supports the opinion-based K/DOQI guidelines. This lead-time was associated with 36% catheter use, which was the lowest use in the study but was still substantial. Persons who had access created within 1 mo of starting hemodialysis had a slightly reduced risk of catheter use but did not have a reduced risk of sepsis. Avoidance of catheters explained only a portion of the reduced risk of sepsis associated with early access creation. In contrast, avoidance of catheter use appeared to explain the majority of mortality benefit associated with early access creation, although sepsis was still strongly associated with death.

These findings link observations of other studies examining access, sepsis, and mortality. The risk of sepsis in dialysis patients averages approximately 10% per year, and those patients who experience sepsis have twice the mortality of those who do not (11,12,18,19). Case fatality rates are as high as 26% in some centers (13). In cross-sectional studies, catheter use is associated with increased mortality from infection (20). Catheter use has also been associated with death from cardiac

Table 2. Risk factors for being hospitalized for sepsis in the first year of chronic hemodialysis, including timing of permanent access creation

Risk Factor	Group	% (n = 5924)	Hazard Ratio	P-value	95% CI
Access timing	Within 1 month prior/after	62.2	1.00		
	1 to 4 mo prior	16.8	0.82	0.197	(0.61 to 1.11)
	>4 mo prior	20.9	0.57	<.001	(0.41 to 0.79)
Catheter use		70.1	1.41	0.012	(1.08 to 1.84)
Age at start of dialysis (yr)	<50	24.4	1.00		
	50 to 64	28.5	0.85	0.196	(0.66 to 1.09)
	65 to 74	28.9	0.87	0.284	(0.68 to 1.12)
	75+	18.3	0.86	0.287	(0.64 to 1.14)
Gender	Male	63.0	1.22	0.043	(1.01 to 1.48)
Access type	Fistula	80.2	1.00		
	Graft	19.8	1.26	0.038	(1.01 to 1.55)
Started dialysis as inpatient		51.5	1.28	0.022	(1.04 to 1.57)
Diabetes		45.8	1.34	0.002	(1.12 to 1.61)
Comorbidity score ^a	0	47.5			
	1	21.9	0.99	0.902	(0.77 to 1.26)
	2	16.1	1.16	0.265	(0.90 to 1.50)
	3+	14.5	1.14	0.361	(0.87 to 1.49)
2nd access creation ^b		34.1	1.23	0.079	(0.98 to 1.55)

The number of hospitalizations for sepsis was 483 (8.20%).

^a Comorbidity score is the Charlson-Deyo index modified by subtracting the renal disease and diabetes components.

^b 2nd Access creation is defined as a time-dependent covariate.

The relative risks of sepsis in the Early access creation and the Just prior access creation groups were 0.48 (95% CI, 0.35 to 0.65) and 0.72 (95% CI, 0.54 to 0.95), respectively, if catheter use was not included in the model.

Table 3. Risk factors for mortality in the first year of hemodialysis including timing of access

Risk Factor	Group	% (n = 5924)	Hazard Ratio	P-value	95% CI
Timing of access creation	Late	62.2	1.00		
	Just prior	16.8	1.09	0.509	(0.85 to 1.40)
	Early	20.9	0.76	0.050	(0.58 to 1.00)
Age at start date	<50	24.4	1.00		
	50 to 64	28.5	1.50	0.022	(1.06 to 2.13)
	65 to 74	28.9	2.48	<.001	(1.79 to 3.43)
	75+	18.3	3.61	<.001	(2.60 to 5.01)
Male	Yes	63.0	1.06	0.504	(0.89 to 1.27)
Access type	Fistula	80.2	1.00		
	Graft	19.8	1.34	0.003	(1.10 to 1.62)
In hospital start	Yes	51.5	1.10	0.361	(0.90 to 1.33)
Diabetes	Yes	45.8	1.07	0.453	(0.90 to 1.27)
Comorbidity score ^a	0	47.5	1.00		
	1	21.9	1.77	<.001	(1.37 to 2.30)
	2	16.1	2.64	<.001	(2.04 to 3.40)
	3+	14.5	3.27	<.001	(2.54 to 4.20)
Second access creation ^b		34.1	0.88	0.196	(0.73 to 1.07)

The number of death was 538 (9.08%).

^a Comorbidity score is the Charlson-Deyo index, modified by subtracting the renal disease and diabetes components.

^b 2nd Access creation is defined as a time-dependent covariate.

If catheter use alone was entered into the model, the relative risk is 1.56 (95% CI, 1.21 to 2.01) and the association between the timing of permanent access creation and mortality again becomes nonsignificant. If catheter use and sepsis are simultaneously entered into this model, the relative risks are 1.49 (95% CI, 1.16 to 1.91) and 3.06 (95% CI, 2.43 to 3.87), respectively, and the association between the timing of permanent access creation and mortality becomes nonsignificant.

causes, suggesting it is a marker of comorbidity (20). In contrast, fistulas have been associated with the lowest risks of infection, sepsis, and death (21,22). Additional factors found to increase the risk of sepsis in this study and by other investigators were diabetes, creation of a graft rather than a fistula, and starting dialysis as an inpatient (12,22,23). Second access creation was also associated with an increased risk of sepsis in this study. This evidence strengthens the association between vascular access events, infection, and mortality in persons receiving chronic hemodialysis.

A potential criticism of this study is that the benefit of early access creation is confounded by less comorbidity in those groups. Patients in the Early and Just prior creation groups were younger, had a lower Charlson-Deyo Index score, had more fistulas created, and were more likely to start hemodialysis as an outpatient. Previous studies have found these factors, along with obesity, diabetes, peripheral vascular disease, cardiac disease, lower hemoglobin, and lower albumin, to be less prevalent in persons referred early for predialysis care (1,24,25). Patients receiving predialysis care are also more likely to receive erythropoietin, vitamin D supplements, phosphate binders, and antihypertensive therapy (24). Some of these factors, such as older age, diabetes, low albumin, low hemoglobin, and hospitalization, also increase the risk of infection (12,22,23,26). We attempted to minimize this confounding by first excluding persons who had never received permanent access. This was done to eliminate the possibility that severe comorbidity may have contraindicated access creation (e.g., severe heart failure). Second, we adjusted for diabetes and other comorbidity using the validated Ontario Diabetes Database (ODD) and the Charlson-Deyo Index. This index has been found to accurately predict survival in persons receiving dialysis (27–30). The association between access timing and infection was also maintained in the healthy start subgroup who had little comorbidity and started hemodialysis as outpatients. Despite these methods, the administrative data did not contain detailed clinical information, so we acknowledge that adjustment for comorbidity is incomplete and the association between access timing and sepsis and mortality is likely still confounded.

Given the lack of detailed clinical information, another limitation is that we were unable to determine the proportion of infections or deaths that were related to access. In Ontario, catheter insertion and removal is associated with small monetary reimbursement, and it is often performed by trainees; therefore, it is difficult to track from billing records. The binary variable of catheter use in this study was crude; although catheter use was still associated with outcomes, future studies with more detailed catheter data should reexamine the associations. We were also unable to determine if the cause of hospitalization was related to access, although vascular access is a common source of hospitalization in hemodialysis patients, particularly catheters (11,12). Bias may also have been introduced if persons with catheters were more likely to be admitted for suspected sepsis.

We were also unable to study the effect of race, which has been associated with late referral and access outcomes in the

United States, as this variable is not contained in administrative databases in Ontario (4). The Canadian Organ Replacement Registry reports 63% of incident dialysis patients in Ontario are white (31). These limitations of administrative data may be partly counterbalanced by the generalizability of a study conducted at a provincial level.

This study was conducted in the Ontario Health Care System, in which insurance barriers to health care are minimized. Adequate predialysis care has been previously associated with having health insurance in the United States; therefore, this confounding factor is not present in this study (2). The lack of baseline differences in socioeconomic status among groups indicates relatively equal access to predialysis care. However, universal health care systems may have longer waiting times (32). The average time to fistula creation in the late creation group was 62 d. The associations between timing of access creation and adverse events may be less dramatic in health care systems with shorter waiting times.

In summary, sepsis is a critical event in the first year of hemodialysis. Early access creation is associated with a significantly reduced risk of catheter use, sepsis, and mortality. The risk was minimized when accesses were created at least 4 mo before starting hemodialysis. Creating permanent access up to 1 mo before starting dialysis was still associated with measurable benefit. Early referral of persons with chronic renal failure does increase early access creation and the use of fistulas (2,25,33). Future research should confirm these findings and help determine methods for increasing early referral and timely fistula creation to avoid catheter use. Developing tools to accurately predict when hemodialysis will be required would also be beneficial. Interventions that promote early access creation likely represent a significant opportunity to reduce the high mortality in the hemodialysis population.

Appendix: Diagnostic Codes Uses to Define Bacteremia or Sepsis

ICD-9 Codes: 038.0, streptococcal septicemia; 038.1, staphylococcal septicemia; 038.2, pneumococcal septicemia; 038.3, Anaerobic septicemia; 038.40, Gram-negative septicemia—not otherwise specified; 038.41, *H. influenza* septicemia; 038.42, *E. coli* septicemia; 038.43, pseudomonas septicemia; 038.44, serratia septicemia; 038.49, Gram-negative septicemia—other specified septicemia (excludes anthrax, gonococcal, herpetic, meningococcal, and septic plague); 038.8, septicemia—other specified septicemia; 038.9, septicemia—not otherwise specified; 038.4, Gram-negative septicemia—not otherwise specified. CCP Code: 790.7, bacteremia.

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References

- Kinchen KS, Sadler J, Fink N, Brookmeyer R, Klag MJ, Levey AS, Powe NR: The timing of specialist evaluation in chronic kidney disease and mortality. *Ann Intern Med* 137: 479–486, 2002
- Arora P, Obrador GT, Ruthazer R, Kausz AT, Meyer KB, Jenuleson CS, Pereira BJ: Prevalence, predictors, and consequences of late nephrology referral at a tertiary care center. *J Am Soc Nephrol* 10: 1281–1286, 1999
- Schmidt RJ, Domico JR, Sorkin MI, Hobbs G: Early referral and its impact on emergent first dialyses, health care costs, and outcome. *Am J Kidney Dis* 32: 278–283, 1998
- Ifudu O, Dawood M, Iofel Y, Valcourt JS, Friedman EA: Delayed referral of black, Hispanic, and older patients with chronic renal failure. *Am J Kidney Dis* 33: 728–733, 1999
- Jungers P, Massy ZA, Nguyen-Khoa T, Choukroun G, Robino C, Fakhouri F, Touam M, Nguyen AT, Grunfeld JP: Longer duration of predialysis nephrological care is associated with improved long-term survival of dialysis patients. *Nephrol Dial Transplant* 16: 2357–2364, 2001
- Stack AG: Impact of timing of nephrology referral and pre-ESRD care on mortality risk among new ESRD patients in the United States. *Am J Kidney Dis* 41: 310–318, 2003
- NKF-K/DOQI Clinical Practice Guidelines for Vascular Access: Update 2000. *Am J Kidney Dis* 37: S137–S181, 2001
- Reddan D, Klassen P, Frankenfield DL, Szczech L, Schwab S, Coladonato J, Rocco M, Lowrie EG, Owen WF, Jr.: National profile of practice patterns for hemodialysis vascular access in the United States. *J Am Soc Nephrol* 13: 2117–2124, 2002
- Pisoni RL, Young EW, Dykstra DM, Greenwood RN, Hecking E, Gillespie B, Wolfe RA, Goodkin DA, Held PJ: Vascular access use in Europe and the United States: Results from the DOPPS. *Kidney Int* 61: 305–316, 2002
- Schwab SJ, Beathard G: The hemodialysis catheter conundrum: hate living with them, but can't live without them. *Kidney Int* 56: 1–17, 1999
- Hoen B, Paul-Dauphin A, Hestin D, Kessler M: EPIBACDIAL: a multicenter prospective study of risk factors for bacteremia in chronic hemodialysis patients. *J Am Soc Nephrol* 9: 869–876, 1998
- Powe NR, Jaar B, Furth SL, Hermann J, Briggs W: Septicemia in dialysis patients: incidence, risk factors, and prognosis. *Kidney Int* 55: 1081–1090, 1999
- Liu JW, Su YK, Liu CF, Chen JB: Nosocomial blood-stream infection in patients with end-stage renal disease: excess length of hospital stay, extra cost and attributable mortality. *J Hosp Infect* 50: 224–227, 2002
- USRDS: Causes of death. *Am J Kidney Dis* 30: S107–S117, 1997
- Hux JE, Ivis F, Flintoft V, Bica A: Diabetes in Ontario: determination of prevalence and incidence using a validated administrative data algorithm. *Diabetes Care* 25: 512–516, 2002
- Wilkins R: Automated Geographic Coding Based on the Statistics Canada Postal Code Conversion Files, Including Postal Codes to June 2001. In: *PCCF+ Version 3G User's Guide (Geocodes/PCCF)*, Ottawa, Statistics Canada, 2001
- Deyo RA, Cherkin DC, Ciol MA: Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 45: 613–619, 1992
- Taylor G, Gravel D, Johnston L, Embil J, Holton D, Paton S: Prospective surveillance for primary bloodstream infections occurring in Canadian hemodialysis units. *Infect Control Hosp Epidemiol* 23: 716–720, 2002
- Dopirak M, Hill C, Oleksiw M, Dumigan D, Arvai J, English E, Carusillo E, Malo-Schlegel S, Richo J, Traficanti K, Welch B, Cooper B: Surveillance of hemodialysis-associated primary bloodstream infections: the experience of ten hospital-based centers. *Infect Control Hosp Epidemiol* 23: 721–724, 2002
- Dhingra RK, Young EW, Hulbert-Shearon TE, Leavey SF, Port FK: Type of vascular access and mortality in U. S. hemodialysis patients. *Kidney Int* 60: 1443–1451, 2001
- Dobkin JF, Miller MH, Steigbigel NH: Septicemia in patients on chronic hemodialysis. *Ann Intern Med* 88: 28–33, 1978
- Churchill DN, Taylor DW, Cook RJ, LaPlante P, Barre P, Cartier P, Fay WP, Goldstein MB, Jindal K, Mandin H: Canadian Hemodialysis Morbidity Study. *Am J Kidney Dis* 19: 214–234, 1992
- Tokars JI, Light P, Anderson J, Miller ER, Parrish J, Armistead N, Jarvis WR, Gehr T: A prospective study of vascular access infections at seven outpatient hemodialysis centers. *Am J Kidney Dis* 37: 1232–1240, 2001
- Powe NR: Early referral in chronic kidney disease: an enormous opportunity for prevention. *Am J Kidney Dis* 41: 505–507, 2003
- Astor BC, Eustace JA, Powe NR, Klag MJ, Sadler JH, Fink NE, Coresh J: Timing of nephrologist referral and arteriovenous access use: the CHOICE Study. *Am J Kidney Dis* 38: 494–501, 2001
- Kairairtis LK, Gottlieb T: Outcome and complications of temporary haemodialysis catheters. *Nephrol Dial Transplant* 14: 1710–1714, 1999
- Fried L, Bernardini J, Piraino B: Charlson comorbidity index as a predictor of outcomes in incident peritoneal dialysis patients. *Am J Kidney Dis* 37: 337–342, 2001
- Van Manen JG, Korevaar JC, Dekker FW, Boeschoten EW, Bossuyt PM, Krediet RT: Adjustment for comorbidity in studies on health status in ESRD patients: which comorbidity index to use? *J Am Soc Nephrol* 14: 478–485, 2003
- Collins AJ, Weinhandl E, Snyder JJ, Chen SC, Gilbertson D: Comparison and survival of hemodialysis and peritoneal dialysis in the elderly. *Semin Dial* 15: 98–102, 2002
- Hemmelgarn BR, Manns BJ, Quan H, Ghali WA: Adapting the Charlson comorbidity index for use in patients with ESRD. *Am J Kidney Dis* 42: 125–132, 2003
- The Canadian Institute for Health Information: 2000 Report, Volume 1: Dialysis and Renal Transplantation, Canadian Organ Replacement Register. Ottawa, Ontario, The Canadian Institute for Health Information, 2000
- Rayner HC, Pisoni RL, Gillespie BW, Goodkin DA, Akiba T, Akizawa T, Saito A, Young EW, Port FK: Creation, cannulation and survival of arteriovenous fistulae: Data from the Dialysis Outcomes and Practice Patterns Study. *Kidney Int* 63: 323–330, 2003
- Avorn J, Winkelmayer WC, Bohn RL, Levin R, Glynn RJ, Levy E, Owen W Jr: Delayed nephrologist referral and inadequate vascular access in patients with advanced chronic kidney failure. *J Clin Epidemiol* 55: 711–716, 2002