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Original Investigation

Early Nephrologist Involvement in Hospital-Acquired Acute Kidney Injury: A Pilot Study

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Background: The optimal timing of nephrology consultation in patients with hospital-acquired acute kidney injury (AKI) is unknown.

Study Design: Prospective controlled nonrandomized intervention study.

Setting & Participants: We screened daily serum creatinine (SCr) levels of 4,296 patients admitted to the St. Louis Veterans Affairs Medical Center between September and November 2008 (control group) and January to May 2009 (intervention group). 354 patients (8.2%) met the definition of in-hospital AKI (SCr level increase of 0.3 mg/dL over 48 hours); 176 of whom met all inclusion criteria; 85 and 91 patients were enrolled in the control (standard care) and intervention groups, respectively.

Intervention: Early renal service involvement (EARLI), defined as a 1-time nephrology consultation within 18 hours of the onset of AKI.

Outcome: Primary outcome defined as 2.5-fold increase in SCr level from admission.

Measurement: Daily SCr until discharge.

Results: The 2 groups had similar characteristics at baseline and at the time of AKI. The intervention was completed at a mean of 13.1 $\pm$ 0.8 hours from the onset of AKI. Nephrology recommendations in the EARLI group included specific diagnostic, therapeutic, and preventative components. The primary outcome occurred in 12.9% of patients in the control group compared with 3.3% of patients in the EARLI group ($P = 0.02$). Patients in the EARLI group had a lower peak SCr level of 1.8 $\pm$ 0.1 versus 2.1 $\pm$ 0.2 mg/dL in controls ($P = 0.01$).

Limitations: Single-center nonrandomized study of mostly US male veterans.

Conclusions: Early nephrologist involvement in patients with AKI may reduce the risk of a further decrease in kidney function. A larger randomized trial is needed to confirm the findings.

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INDEX WORDS: Acute kidney injury; nephrology consultation.

Acute kidney injury (AKI) in hospitalized patients is a serious disease associated with an increased risk of morbidity and mortality.[1-5] Kidney function is still determined primarily using serum creatinine (SCr) level, a suboptimal filtration marker.[6] As the quest for injury biomarkers is advancing,[7] it has become more evident during the last few years that even small changes in SCr levels are associated with short- and long-term mortality.[5,8-11] This has prompted consensus groups, such as the Acute Dialysis Quality Initiative (ADQI) and the AKI Network (AKIN), to propose newer more sensitive definitions for AKI using smaller increments in SCr levels.[8,10,12] As the efforts to recognize early injury continue to develop, the potential therapeutic benefits of such early recognition are still lacking. A complicating factor is that nephrologists frequently are not involved in the care of patients with only small SCr level increments. Mehta et al[13] previously showed in an observational study that delayed nephrology consultation in patients admitted to the intensive care unit (ICU) with kidney failure (SCr $\geq$2 mg/dL or increment $\geq$1 mg/dL with pre-existing disease) was associated with increased mortality and morbidity. In another more recent observational study, Perez-Valdivieso et al[14] reported that an increase >100% in SCr level at the time of nephrology consultation was associated with higher mortality and impaired renal recovery on discharge. Because of the observational nature of these studies, it is difficult to discern whether these findings are caused by residual confounders or can be attributed solely to

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the beneficial effects of a timely nephrology consultation. The optimal timing of nephrology consultation in hospitalized patients who develop AKI is not known. To our knowledge, there is no intervention study that investigated the effect of early nephrology involvement in the era of sensitive AKI definitions.

There are a number of mechanisms by which a nephrologist could alter the course of disease. If involved early enough, a nephrologist can give proper volume assessment, recognize systemic diseases that affect the kidney and suggest appropriate diagnostic testing, adjust medication regimens to prevent further hemodynamic or toxic injury to the kidney, and assist in shaping a therapeutic and preventative renoprotective strategy. Based on this, we hypothesized that early renal service involvement (EARLI), defined as a 1-time nephrology consultation within 18 hours of the onset of hospital-acquired AKI (increase in SCr ≥0.3 mg/dL within 48 hours; AKIN definition) would decrease the risk of subsequent severe kidney failure.

METHODS

Study Design and Patient Population

Approval for this pilot study was obtained from the Human Studies Committee at the Saint Louis Veterans Affairs Medical Center. This Veterans Affairs hospital is a tertiary referral academic center caring for veterans with 218 beds and a fully computerized medical records system. All patients are under the care of a primary medical or surgical team. To identify patients with early AKI, we screened SCr levels of all inpatients daily during the study period (total, 4,296 patients). Patients initially were excluded if they had chronic kidney disease stage 5 or end-stage renal disease or if they were admitted with AKI (SCr ≥0.3 mg/dL compared with baseline). Patients were considered for inclusion if they developed AKI during hospitalization using the AKIN definition (SCr level increase ≥0.3 mg/dL in any 48-hour period).[10] Further exclusion criteria were discharge the day of AKI, renal service consulted the day of AKI, hospice care, death the day of AKI, and no available baseline SCr level. Because a consultation typically is initiated by the primary teams, our study (in which a consultation is provided early in the course of AKI without solicitation) was performed in full collaboration with those teams. Because a consultation involves patients and their physicians, avoidance of contamination bias was a major consideration in the design of our study. This could be introduced when some physicians would be caring for patients in both the control and study groups. Heightened renal awareness may indirectly modify the approach of clinicians toward patients in the control arm and potentially introduce such a bias. Therefore, we used a sequential design for recruitment, but a parallel and identical prospective method for data collection. This was accomplished by identifying patients in the control group (standard care, no specific intervention, and renal consultation at the discretion of the primary service) after a lag time of 4 months from admission; that is, patients admitted in September 2008 through November 2008 were identified for recruitment in the control group in January 2009 through March 2009. The latter is the same period for the intervention (EARLI) arm of the study. Therefore, data were reviewed and collected prospectively in an identical manner for the control and EARLI groups as of January 2009 with use of the fully computerized electronic records, and this occurred in a similar fashion during the week. There also were no changes in hospital protocols in the time frame of the study. Because informed consent was required for the EARLI group (and not for the control group), we had to screen more patients in this group because of refusals (by patient or primary team) or inability to obtain consent (Fig 1). Therefore, the recruitment period was extended for 2 additional months (January 2009 to May 2009) for the EARLI group. In this group, we contacted the primary team to obtain approval before interviewing patients. After patients gave consent, a full renal consult was performed. A standardized research consult note was written in the chart (see Item S1, available as online supplementary material) and included a pertinent focused history and examination, the most likely cause of AKI, and succinct recommendations with 3 components: diagnostic, therapeutic, and preventative. This consult note then was forwarded electronically to the primary service to make them aware of the recommendations. Although we did not plan to relay our recommendations verbally, we communicated in a few instances with the treating team to answer additional inquiries that were raised about these recommendations. EARLI intervention did not preclude subsequent nephrology consultation at the discretion of the primary team.

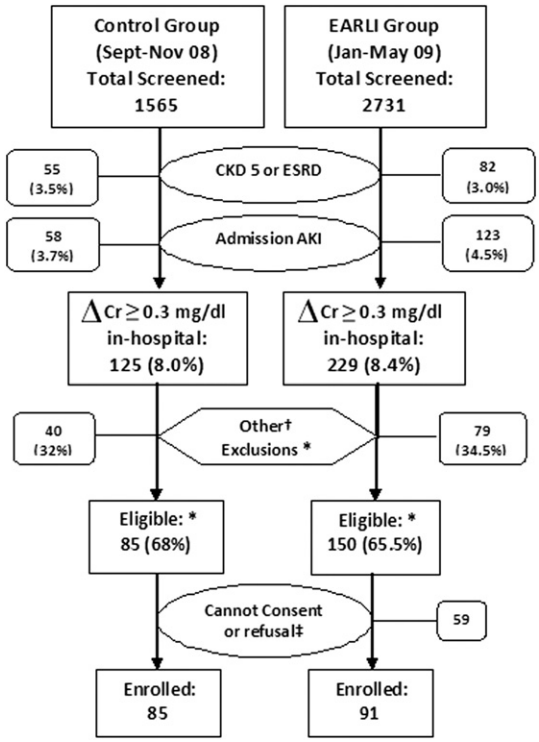

Figure 1. Early renal service involvement (EARLI) study flow chart. *Percentages of patients with in-hospital increase in creatinine (Cr) level. †Other exclusions include discharged with increasing Cr level, renal service consulted, hospice, death on the day of acute kidney injury (AKI), and no baseline Cr value. ‡Refusal by primary service or patients. Abbreviations: CKD, chronic kidney disease; ΔCr, change in Cr level; ESRD, end-stage renal disease.

Definitions

In addition to the definitions discussed, we used the following other preset definitions. Baseline SCr level was defined as the most frequent value within a year before admission, excluding inpatient readings. In case this was not available, the most recent value within a year was considered. In case there was no prior SCr value within a year, patients were excluded if they had an admission SCr

level >1.2 mg/dL. AKI on admission was defined as admission SCr level ≥0.3 mg/dL compared with baseline. AKI SCr level was the SCr value that satisfied AKIN criteria for AKI (≥0.3 mg/dL).[10] Our prespecified primary outcome was defined as 2.5-fold increase in SCr level (maximum SCr vs admission SCr) or an increase ≥2 mg/dL if SCr was ≥4 mg/dL or requiring renal replacement therapy. We chose this outcome because it combines AKIN stage 3 (>3-fold peak SCr increase) and AKIN stage 2 with more severe disease (maximal SCr increase >50th percentile of that category; ie, >2.5- to 3-fold). Preliminary observations suggested that this outcome may be the most sensitive for our pilot study. We also examined peak SCr level distribution by increments of 0.5-fold maximal increase compared with admission. CKD was defined as estimated glomerular filtration rate <60 mL/min, estimated using the 4-variable MDRD (Modification of Diet in Renal Disease) Study equation. Secondary outcomes also reported were death during hospitalization and cardiovascular events. We also examined post-AKI length of stay. Reasons for admission were reported under 3 categories: cardiovascular (congestive heart failure [CHF], chest pain, myocardial infarction, arrhythmia, syncope, and hypo-/hypertension), other medical (all other medical admissions), and surgical (elective and acute surgical diagnosis). No cardiac surgery or bypass was performed in this hospital. Most surgeries performed were general, urologic, orthopedic, and peripheral vascular.

Data Analysis

Baseline demographics of the control and intervention groups were tabulated. A χ^2 test was used to compare proportions for categorical variables, and *t* test was used to examine differences in mean values for continuous data. Crude primary and secondary (death and cardiovascular events) outcomes were compared using Fisher exact test. Univariate regression analysis was performed to determine the effect of individual variables on the risk of the primary outcome. Independent variables included in this analysis were demographics (age and race), baseline kidney function, and albuminuria; chronic illnesses (diabetes mellitus, hypertension, peripheral vascular disease, and CHF); type of admission (cardiovascular, other medical, or surgical); risk factors for AKI (ICU stay, contrast exposure within 72 hours, and infection before AKI); blood pressure before AKI; medications (angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs], and statins); and AKI SCr level. Results are reported as odds ratio (OR) and the corresponding confidence interval (CI). ORs that do not cross unit and $P < 0.05$ were considered statistically significant. We also performed linear regression analysis aimed at examining the effect of EARLI on peak serum SCr level and a subgroup analysis to study the effect of EARLI on peak SCr level based on the presumed cause of AKI (prerenal vs other). Results were reported as parameter estimate with the corresponding CI. Comparison of length of stay was performed using *t* test after logarithmic transformation because its distribution tends to be skewed.

RESULTS

Study Flow and Baseline Demographics

The study flow chart is shown in Fig 1. Daily SCr levels for 4,296 patients (1,565 for the control group and 2,731 for the EARLI group) were monitored during hospitalization. During the control and EARLI recruitment periods, 8.0% and 8.4% of patients screened met criteria for in-hospital AKI, respectively. In these AKI subgroups, 68% and 65.5% in each respective group remained eligible after applying other exclusion criteria. Approval from the primary service and informed consent from participants were required in the EARLI group. This could not be obtained for 59 patients (34 patients refused, 13 refusals by primary service, and 12 patients incompetent to give consent). In all, 85 patients were enrolled in the control group, and 91 patients, in the EARLI group.

Baseline demographics and clinical and laboratory characteristics of the 2 groups are listed in Table 1. Overall, the 2 groups had similar baseline characteristics. Average age was 67.7 ± 4 years in the control group and 67.6 ± 2.1 years in the EARLI group. A total of 89.4% of patients in the control group and 90.1% of patients in the EARLI group had hypertension, whereas diabetes mellitus occurred in 42.3% and 51.6% ($P = 0.2$) of the control and EARLI groups, respectively. Average admission SCr level was 1.3 ± 0.1 mg/dL in both groups. Chronic kidney disease (estimated glomerular filtration rate <60 mL/min) was equally prevalent in both groups (40.0% and 40.7% in the control and EARLI groups, respectively). The control group had more patients with a diagnosis of CHF. However, CHF did not have a significant independent effect on the risk of developing severe kidney failure using univariate regression analysis. Other baseline characteristics, such as type of admission, albuminuria, and other chronic medical conditions, are listed in Table 1. The 2 groups also had similar characteristics on the days preceding AKI: similar numbers of ICU patients, frequencies of contrast exposure, and infections. The control and EARLI groups also had similar mean arterial pressures the day before and the day of AKI. ACE-inhibitor and ARB use before AKI (surveyed the day before) were similar in the control and EARLI groups (61.5% vs 56.2%, respectively; $P = 0.5$). Similarly, statin use was not different between groups. As expected by design, there was no difference between groups in average SCr level at the time of AKI (1.8 ± 0.1 vs 1.7 ± 0.1 mg/dL in the control and EARLI groups, respectively; $P = 0.3$).

EARLI: Diagnosis and Recommendations

Our intervention (EARLI) consisted of a 1-time nephrology consult at the onset of hospital-acquired AKI. EARLI was completed at a mean of 13.1 ± 0.8 hours from the onset of AKI (time 0 corresponded to the time the blood sample for AKI SCr measurement was drawn). To ensure consistency, a standardized research consult template was used and is provided in Item S1. The most likely cause of AKI was provided based on history, chart review, examination (EARLI group), and available laboratory data (Table 2). Prerenal cause (which included true volume depletion, but

Table 1. Baseline Demographic, Clinical, and Laboratory Characteristics of Patients by Study Group

	EARLI (n = 91)	Control (n = 85)	*P*
Baseline			
Age (y)	67.6 ± 2.1	67.7 ± 4	0.9
White (%)	68.1	55.3	0.08
African American (%)	31.9	44.7	—
Men (%)	100	97.6	0.2
DM (%)	51.6	42.3	0.2
COPD (%)	29.7	30.6	0.9
PVD (%)	16.5	23.5	0.2
CKD[a] (%)	40.7	40.0	0.9
HTN (%)	90.1	89.4	0.9
CHF (%)	38.5	54.1	0.04
Baseline SCr (mg/dL)	1.3 ± 0.1	1.4 ± 0.1	0.6
Albuminuria (%)	63.2	53.8	0.2
eGFR (mL/min/1.73 m^2)	69.7 ± 5.4	67.5 ± 5.2	0.6
Admission SCr (mg/dL)	1.3 ± 0.1	1.3 ± 0.1	0.7
Admission cardiovascular (%)	41.8	47.1	0.5
Admission other medical (%)	48.4	41.2	0.3
Admission surgical (%)	13.2	17.7	0.4
Pre-AKI			
ICU within 24 h (%)	27.5	25.9	0.8
Surgery within 72 h (%)	16.5	23.5	0.2
Infection (%)	28.6	35.3	0.3
Contrast within 72 h (%)	19.8	21.2	0.8
MAP 24 h prior (mm Hg)	94.0 ± 3.3	94.3 ± 2.8	0.9
ACEi/ARB (%)	56.2	61.5	0.5
Diuretic (%)	57.1	51.8	0.5
Statin (%)	50.0	55.4	0.5
NSAID (%)	3.6	2.2	0.7
AKI day			
SCr (mg/dL)	1.7 ± 0.1	1.8 ± 0.1	0.3
MAP (mm Hg)	88.7 ± 3.0	87.7 ± 2.9	0.6
Hb (g/dL)	11.6 ± 1.0	11.1 ± 0.9	0.2
Subsequent renal consult[b] (%)	4.4	10.6	0.2

Note: Values shown as percentage or mean ± 95% confidence limit. Conversion factors for units: SCr in mg/dL to μmol/L, ×88.4; Hb in g/dL to g/L, ×10.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotension receptor blocker; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; EARLI, early renal service involvement; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; HTN, hypertension; ICU, intensive care unit; MAP, mean arterial pressure; NSAID, nonsteroidal anti-inflammatory drug; PVD, peripheral vascular disease; SCr, serum creatinine.

[a]Defined as eGFR <60 mL/min.

[b]Indicates patients who eventually received an official renal consult during their hospital stay (excluding the EARLI consult in the intervention group).

also decreased effective perfusion, such as congestive failure, and liver disease) was the most common AKI type in both the EARLI and control groups (61.5% and 58.5%, respectively). Laboratory data ordinarily used for differentiating types of AKI frequently were unavailable. Therefore, it was difficult to distinguish prerenal from early intrinsic disease in 18.7% and 17.6% of patients in the EARLI and control groups, respectively. Intrinsic renal causes of AKI were called with certainty when there was a clear cause (such as contrast or hypotensive shock) in addition to the overall clinical context. A summary of recommendations by category (diagnostic, therapeutic, and preventative) is listed in Table 3. When a test was recommended, an interpretation also was clearly outlined. To measure the effect of EARLI on the therapeutic approach of primary teams, we also list in Table 3 the differences in withholding ACE-inhibitor/ARB therapy and adjusting diuretic dosages between the 2 groups 24 hours after AKI. ACE-inhibitor/ARB and diuretic therapy were withheld (or adjusted) more frequently in the EARLI group as a result of the intervention. Because of different practices in various wards, it was difficult to ascertain exactly the amount of fluid delivered in the 2 groups during that same period.

Table 2. AKI Causes in the EARLI and Control Groups

	EARLI	Control
Prerenal	56 (61.5)	50 (58.5)
Prerenal and/or early renal	17 (18.7)	15 (17.6)
Early renal	16 (17.6)	18 (21.2)
Postrenal	2 (2.2)	2 (2.4)

Note: Values shown as number (percentage).

Abbreviations: AKI, acute kidney injury; EARLI, early renal service involvement.

In the control group, a nephrology consultation was called for 9 patients (10.6%). Average time from the onset of AKI to completion of the consult was 56.7 ± 18.1 hours. There were several instances in the control group when patients' SCr levels increased significantly and nephrology consult was not called.

Incidence of the Primary Outcome

The effect of EARLI in the form of a 1-time consultation on the primary outcome is listed in Table 4. EARLI decreased the incidence of this outcome from 12.9% in the control group to 3.3% in the intervention group ($P = 0.02$). Peak SCr level also was decreased in the EARLI compared with control group (1.8 vs 2.1 mg/dL, respectively; $P = 0.01$).

Figure 2 shows the maximal SCr level increase (relative to admission SCr level) for both groups, presented in 4 categories as fold increases compared with admission: <1.5-, 1.5- to 1.9-, 2.0- to 2.4-, and ≥2.5-fold. In addition to having a lower proportion of patients reaching the primary outcome (≥2.5-fold SCr increase), the EARLI group also had a higher proportion of patients with mild peak SCr level increases (<1.5-fold increase) compared with controls. There was no difference between the 2 groups in the middle 2 categories. This suggests that EARLI causes a left shift to the peak SCr level distribution (apparent at the 2 tails), which results in more patients with milder peak increases and fewer patients with severe SCr level peaks.

In univariate regression analysis, EARLI was associated with significant risk reduction of the primary outcome (OR, 0.25; CI, 0.66-0.95; $P = 0.03$). Of the

Table 3. Nephrology Recommendations and Therapeutic Implementation

	EARLI Group	Control Group	*P*
Diagnostic recommendations			
Urine studies[a]	79.1	—	—
Other laboratory tests	28.6	—	—
Other[b]	14.3	—	—
Therapeutic recommendations			
Holding ACEi/ARB therapy	48.4	—	—
IV fluids	45.1	—	—
Adjusting diuretic dosages	35.2	—	—
Adjusting other medications[c]	19.8	—	—
Other[d]	7.7	—	—
Preventative recommendations			
Pharmacovigilance related	17.6	—	—
Contrast precautions	8.8	—	—
Therapeutic implementation within 24 h of AKI			
Holding ACEis/ARBs	32.0[e]	10.0[e]	0.01
Adjusting diuretic dosages	25.5[f]	7.1[f]	0.03

Note: Values shown as frequencies.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin receptor blocker; EARLI, early renal service involvement; IV, intravenous.

[a]Urinalysis or fractional excretion of sodium/urea.

[b]Includes imaging and procedures.

[c]Medications, including antihypertensives and antibiotics.

[d]Includes procedures, transfusion, and new medication.

[e]Percentage of those on ACEi/ARB therapy.

[f]Percentage of those on diuretic therapy.

Table 4. Primary and Secondary Outcomes of Patients in the EARLI and Control Groups

	EARLI	Control	*P*
Renal outcomes			
Primary outcome[a]	3 (3.3)	11 (12.9)	0.02
Peak SCr (mg/dL)	1.8 ± 0.1	2.1 ± 0.2	0.01
Dialysis	1 (1.1)	1 (1.2)	—
Secondary outcomes			
Death	4 (4.4)	7 (8.2)	0.4
Cardiovascular events	1 (1.1)	1 (1.2)	—

Note: Values shown as number (percentage) or mean ± confidence limit.

Abbreviations: EARLI, early renal service involvement; SCr, serum creatinine.

[a]Primary outcome defined as 2.5-fold increase in SCr level from admission or an increase of ≥2 mg/dL if SCr was ≥4 mg/dL.

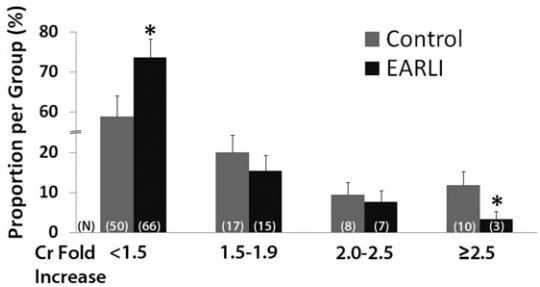

Figure 2. Maximal increase in serum creatinine (Cr) level. Bar graphs represent the proportion of patients in each group classified by fold increase in maximal Cr level compared with admission value. *Statistical significance ($P < 0.05$) between the early renal service involvement (EARLI) and control groups. One patient in the control group included in 2.0- to 2.4-fold increase met the primary outcome with a Cr level >4 mg/dL and absolute increase >2 mg/dL.

relevant demographic and risk variables, only contrast exposure was associated with increased risk of the primary outcome (OR, 3.37; CI, 1.06-10.74; $P = 0.04$), whereas statin use was associated with decreased risk of the primary outcome (OR, 0.13; CI, 0.03-0.60; $P < 0.01$). In linear regression analysis, EARLI also was associated with a significant risk reduction of higher peak SCr level (parameter estimate, −0.30; CI, −0.54 to −0.06; $P = 0.01$). When we performed the same analysis on the subgroup of participants with prerenal AKI compared with other causes, EARLI was associated with risk reduction of a higher peak SCr level in only the prerenal group (parameter estimate, −0.30; CI, −0.59 to −0.01; $P = 0.04$) compared with the other group (parameter estimate, −0.29; CI, −0.70 to 0.13; $P = 0.2$). Secondary outcomes of in-hospital death and cardiovascular events (myocardial infarct or stroke) also are listed in Table 4. Death occurred in 4.4% of the EARLI group compared with 8.2% of the control group ($P = 0.4$). Post-AKI length of stay was 5.1 ± 0.9 days in EARLI group compared with 6.7 ± 1.8 days in the control group ($P = 0.7$).

DISCUSSION

In this pilot study, we examined the effect of EARLI, defined as a 1-time renal consult early in the course of AKI, on the outcome of 2.5-fold increase in SCr level. We showed that EARLI considerably decreases the risk of this outcome and shifted maximal kidney injury toward the mildest form. To our knowledge, this is the first prospective intervention study investigating the timing of nephrology consultation for AKI. In addition, our results provide an intervention/outcome-based rationale for using newer definitions of AKI (such as RIFLE and AKIN). The utility of these definitions in intervention studies will complement their usefulness in disease stratification and prognosis.[15,16] A renal outcome defined by percentage of increase in SCr level is in line with recent research recommendations by the AKIN panel.[10]

Our findings carry implications pertaining to the management of hospitalized patients who develop AKI. Nephrologists frequently are called late in the course of this illness, when management becomes geared toward controlling complications rather than reversing the course of disease. This occurs despite previous observational data by Mehta et al,[13] who showed that delayed nephrology consultation in the ICU was associated with higher mortality and morbidity. The definition of kidney failure used in that study was before the era of the more recently advocated definitions that rely on minor changes in SCr levels. The investigators also could not rule out potential confounders to explain their data. However, the great merit of that study was pointing out that timing of nephrology consult may be an important factor in affecting outcomes. More recently, other investigators also showed in an observational study that a nephrology consultation for SCr level increase >100% is associated with worse renal outcomes and mortality.[14] From these observational studies, it appears that delayed renal consultation is detrimental. However, the optimal timing of renal consultation was unknown before our study. Our results assist in filling this knowledge gap by showing that nephrology involvement as early as after a 0.3-mg/dL increase in SCr level may improve kidney outcomes. Early consultation decreased the risk of worsening kidney failure and shifted the distribution of maximal kidney injury toward the mildest category.

The biomarker field will be crucial to improve renal care by detecting very early injury with high sensitivity and specificity.[7] Although such sensitive biomarkers currently are not in clinical practice, our data suggest that relying on small changes in SCr levels for timing of nephrology involvement may still fall in a therapeutic window for AKI. A nephrologist can assist in tailoring diagnostic, therapeutic, and preventative strategies that could reverse the disease process, rather than dealing with its complications. Our study was not designed to test the effect of a single intervention, such as fluid administration or adjustment of ACE inhibitors/ARBs or other medications. Rather, our approach was customized to every patient because of the heterogeneity of AKI. However, because of the high prevalence of prerenal causes in early AKI, our data suggest that appropriately reacting to prerenal AKI may have a major role in preventing progression to more severe forms of injury. This is supported by the subgroup analysis showing a significant effect of EARLI in the prerenal group. This also is in line with the paradigm proposed by Sutton and Molitoris[17] to explain the pathophysiologic process of AKI.

Our study has limitations. It is a single-center nonrandomized study of a US male veteran population, and as such, this may limit the generalizability of our results. However, our findings emphasize the need for further investigations in a broader more diverse population to further test their validity. Although small changes in SCr levels are associated with increased mortality and hospital costs,[1,4,5,11] it is unknown whether reducing an increase in SCr level also is beneficial for such well-defined outcomes. Our study was not designed to investigate these end points, but provides a solid rationale for a large study investigating the effect of early nephrologist involvement on outcomes, such as death, complications, and length of stay. It is not surprising that only a few patients required dialysis therapy because kidney failure requir-

ing dialysis is not a very common occurrence in hospitalized patients.[11] However, because we excluded hospitalized patients admitted with community-acquired AKI, the outcome of renal replacement therapy may be different in that population compared with those with hospital-acquired AKI. Although this was not supported by univariate analysis, the higher baseline prevalence of CHF in the standard-care control group might have confounded results, especially if CHF was associated with the primary outcome. Another potential bias may have been introduced in the EARLI group by patient or physician refusal to enroll in the study.

In conclusion, early nephrologist involvement in AKI may decrease the risk of severe subsequent renal failure. Our study is unique in providing an intervention-based clinical rationale for using sensitive definitions for AKI. The significance of preventing changes in SCr levels warrants further investigation in larger studies.

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SUPPLEMENTARY MATERIAL

Item S1. EARLI Consult Template.

Note: The supplementary material accompanying this article (doi:10.1053/j.ajkd.2010.08.026) is available at www.ajkd.org.

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