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Subgroups of Patients with Distinct Health Utility Profiles after AKI

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Key Points

- Health utility profiles can be identified at 60 days after AKI.
- Patient subgroups with distinct health utility profiles have different characteristics at index hospitalization and outcomes at 1 year.
- These profiles may be useful when considering resources to improve the physical and emotional health of patients after AKI.

Abstract

Background A large amount of interindividual variability exists in health-related quality of life outcomes after AKI. This study aimed to determine whether subgroups of early AKI survivors could be identified on the basis of distinct health utility impairment profiles ascertained at 60 days after AKI and whether these subgroups differed in clinical and biomarker characteristics at index hospitalization and outcomes at 1-year follow-up.

Methods This retrospective analysis used data from the Biologic Markers of Renal Recovery for the Kidney study, an observational subcohort of the Acute Renal Failure Trial Network study. Of 402 patients who survived to 60 days after AKI, 338 completed the Health Utility Index 3 survey, which measures impairments in eight health attributes. Latent class analysis was used to identify subgroups of patients with distinct health utility profiles.

Results Three subgroups with distinct health utility impairment profiles were identified: Low (28% of participants), Moderate (58%), and High (14%) with a median of one, four, and six impairments across the eight health attributes at 60 days after AKI, respectively. Patient subgroups differed in weight, history of cerebrovascular disease, intensity of dialysis, hospital length of stay, and dialysis dependence. Serum creatinine and blood urea nitrogen at index hospitalization did not differ among the three subgroups. The High impairment subgroup had higher levels of IL-6 and soluble TNF receptor 2 at study day 1. The three subgroups had different 1-year mortality rates: 5% in the Low, 21% in the Moderate, and 52% in the High impairment subgroup.

Conclusion Patient subgroups with distinct health utility impairment profiles can be identified 60 days after AKI. These subgroups have different characteristics at index hospitalization. A higher level of impairment at 60 days was associated with decreased survival.

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Introduction

AKI occurs in approximately 50% of critically ill patients and is associated with increased morbidity and mortality.[1] Knowledge gaps exist regarding health-related quality of life (HRQOL) among survivors of AKI. While some studies reported that survivors of AKI experience decreases in HRQOL,[2–4] others found no differences.[5–8] In one systematic review,[9] AKI survivors experienced meaningful HRQOL impairments as measured by instruments, such as the Medical Outcomes Study Questionnaire Short Form 36. However, many AKI survivors have also reported a satisfactory health status.[6,10–12] These inconsistent findings in HRQOL among

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AKI survivors may be related to heterogeneity in baseline levels of impairment, severity and etiology of AKI, disease course, and/or responses to treatments.[9,13]

Latent class analysis (LCA) is an analytic approach that can be used to identify subgroups of patients with distinct profiles of a clinical outcome (*e.g.*, quality of life). While used extensively in symptom research,[14] LCA has not been used to identify subgroups of patients with distinct health utility profiles after AKI. Once these subgroups are identified, demographic, clinical, and biomarker risk factors associated with these subgroups can be evaluated. The identification of risk factors of poorer HRQOL among survivors of AKI may allow for better allocation of resources after hospital discharge.

Limited evidence exists to inform strategies for the provision of health care and rehabilitation to AKI survivors. Some clinical risk factors, including age, admission status, primary service, and longer hospital stays, were associated with poor HRQOL after AKI.[15] Biological mechanisms that underlie decrements in HRQOL after AKI are not well understood. In the past decade, new biomarkers associated with inflammation, apoptosis, necrosis, and cell-cycle regulation were used to improve the prediction and prognostication of AKI.[16,17] Similar biomarkers were associated with poorer HRQOL and a higher burden of symptoms, including pain, fatigue, sleep disturbance, and depression in patients with cancer.[18–20] This study will provide new insights into potential common biomarkers associated with poorer HRQOL in patients with AKI compared with other disease states.

Using data from the Biologic Markers of Renal Recovery for the Kidney (BioMaRK) study,[21–23] this study is the first to use LCA to identify subgroups of patients with distinct health utility profiles from surveys administered at 60 days after AKI and examine associated demographic, clinical, and biological risk factors. In addition, the relationship between subgroups with distinct health utility profiles of AKI survivors at 60 days and 1-year outcomes were evaluated.

Methods

Data Source

BioMaRK[21–23] is a nested observational cohort study conducted as an ancillary study to the Veterans Affairs/National Institutes of Health Acute Renal Failure Trial Network (VA/NIH ATN) study.[24,25] This multicenter, randomized trial evaluated intensive versus less intensive RRT in critically ill patients with AKI attributed to acute tubular necrosis plus sepsis or additional organ failure conducted between November 2003 and July 2007 (clinicaltrials.gov: NCT00076219). AKI was defined by oliguria (average urine output ≤20 ml/h) for >24 hours or an increase in serum creatinine (SCr) of ≥2 mg/dl in male patients or ≥1.5 mg/dl in female patients over a period of ≤4 days with a clinical plan for RRT. Patients with baseline SCr of >2 mg/dl in male patients and >1.5 mg/dl in female patients were excluded from this trial. Further details of the trial have been published.[24,25]

BioMaRK included all participants who gave additional written consent for the collection and banking of samples. Demographic and clinical characteristics as well as samples were collected around the time of AKI diagnosis. Only patients who survived to 60 days after enrollment and provided HRQOL data were included in this study. The VA/NIH ATN and BioMaRK studies were approved by the Human Rights Committee at the West Haven VA Cooperative Studies Program Coordinating Center and by the institutional review boards at each of the participating study sites.

Health Utility Measure

Survivors at 60 days after randomization were asked to complete the Health Utility Index 3 (HUI-3), a HRQOL questionnaire, by telephone or in person. If the patient was unable to participate, the questionnaire was filled out by a surrogate (n=108). The HUI-3[26] is a 40-item questionnaire that evaluates eight health attributes (*i.e.*, vision, hearing, speech, ambulation, dexterity, emotion, cognition, pain) to determine a utility score. Respondents were asked about the type and extent of impairments experienced over the past week. A preference-based scoring function was then used to convert descriptive measures of impairments into a utility subscore for each attribute. For example, a utility subscore of 1 for ambulation indicates that the patient can walk around the neighborhood without difficulty and without walking equipment and a six indicates that the patient cannot walk at all.

The eight utility subscores for each attribute were dichotomized into having no impairments for that attribute (utility subscore=1) versus having impairments for that attribute (utility subscore >1). The subscores were dichotomized to increase the stability of the latent class solution. In addition, this dichotomization simplified the interpretation of results because the subscores ranged from both one to five and one to six depending on the attribute. Where possible, inspection and logical deduction were used to complete missing elements following the method by Naiem and colleagues (5% of the subscores).[27] HUI-3 forms with missing data for all eight attributes were excluded from the analysis (n=64). The HUI-3 is a valid and reliable measure that was used in numerous studies of patients with AKI requiring RRT.[28,29]

LCA

LCA is a person-centered analytic approach that evaluates for unobserved subgroups within a population on the basis of an observed response pattern.[30,31] LCA is considered a more statistically robust method to identify subgroups of patients with distinct profiles because fit indices are available to determine the optimal number of latent classes.[32] In this study, LCA was applied to the eight HUI-3 attributes that were dichotomized into not impaired versus impaired status for each patient. Fit indices for 1 through 4-class solutions were estimated by maximum likelihood using an expectation-maximization procedure.[33] The optimal number of latent classes or patient subgroups that fit the data best was determined using the Bayesian Information Criterion (BIC), Vuong–Lo–Mendell–Rubin maximum likelihood ratio test, and size of the smallest class. The model with the best fit had the lowest BIC.[34] LCA was conducted using Mplus8.[33] All of the other analyses were conducted using STATA.[35]

Potential Risk Factors of Subgroup Membership

Once the patient subgroups with distinct health utility profiles at 60 days after study enrollment were identified,

differences among the subgroups in demographic, clinical, and biomarker risk factors that were assessed at index hospitalization were evaluated using Pearson chi-square or Kruskal–Wallis tests. *Post hoc* contrasts were performed using Bonferroni correction. The following list of risk factors was evaluated.

Demographic Characteristics

Age, sex, self-reported ethnicity, and body mass index were analyzed.

Clinical Characteristics at Index Hospitalization

Occurrence of diabetes, cardiovascular disease, cancer, immunocompromised status, or cerebrovascular disease; cause of AKI; conventional laboratory data (*i.e.*, hemoglobin, SCr, blood urea nitrogen, serum albumin) ascertained on Day 1 of the clinical trial; intervention assignment (intensive versus less intensive RRT dosing); hospital and intensive care unit (ICU) length of stay (quantified as hospital and ICU-free days from day 60)[36]; and RRT dependence at Day 60 of the trial were analyzed.

Inflammatory and Oxidative Stress Biomarkers

GM CSF, IL-1-β, IL-6, IL-8, IL-10, IL-18, TNF-α, soluble TNF receptor (sTNFR)-1, sTNFR-2, macrophage migration inhibitory factor, and death receptor-5 were analyzed from blood sample collection on study day 1 before the initiation of protocolized RRT dosing and on study day 8.

Distal Outcomes

One-year health utility and mortality outcomes in each subgroup were examined.

Results

Of the 817 patients enrolled in the BioMaRK study, 402 patients were alive on day 60 and 338 completed the HUI-3 (Figure 1). Using LCA, three subgroups of patients with distinct health utility profiles were identified (Table 1). The three-class solution was selected because its BIC was lower than the BIC for both the two and four-class solutions.

Table 2 displays the health attribute characteristics of the three distinct patient subgroups. The three subgroups were labeled Low, Moderate, and High on the basis of the occurrence of health utility impairments observed. The largest subgroup (58%, n=197) of patients (Moderate) had a median of four impaired attributes. The probability of impairments ranged from 4% in speech to 86% in ambulation. The second largest subgroup (28%, n=94) of patients (Low) had a median of one impaired attribute. The probability of impairments ranged from 0% in speech to 64% in vision. The third subgroup (14%, n=47) of patients (High) had a median of six impaired attributes. The probability of impairments ranged from 26% in hearing to 98% in ambulation.

The Low, Moderate, and High subgroups had different rates of survey self-responses at 60 days after study enrollment (83%, 71%, and 26%, respectively). The remainder of the questionnaires was completed by surrogates. Surrogate responses reported more impairments in health utility attributes compared with self-responses. In the Low subgroup, impaired hearing was 7% among surrogate responses versus 0% among self-responses. In the Moderate subgroup, impaired dexterity was 26% versus 12% and impaired cognition was 62% versus 45%. In the High subgroup, impaired hearing was 12% versus 0% and impaired dexterity was 82% versus 50%.

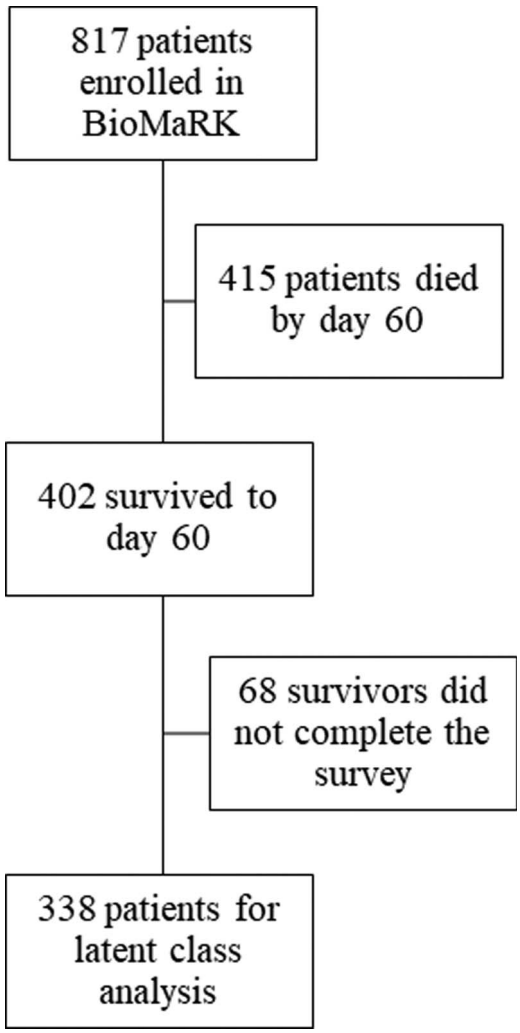

Figure 1. Flow diagram of patients in this study from the BioMaRK cohort. BioMaRK, Biologic Markers of Renal Recovery for the Kidney.

Differences in Patient Characteristics at Enrollment

Table 3 summarizes the differences in demographic and clinical characteristics at enrollment into the BioMaRK study among the three health utility impairment subgroups. The High subgroup had significantly lower weight compared with the Moderate subgroup (75 versus 87 kg), more cerebrovascular disease (7% compared with 0% in the Low subgroup and 2% in the Moderate subgroup), and a higher proportion of patients randomized to intensive RRT strategy compared with the Low subgroup (57% versus 36%).

Differences in Biomarkers on Day 1 and Day 8

Table 4 summarizes the differences in biomarkers measured during index hospitalization among the three health utility impairment subgroups. Conventional biomarkers,

Table 1. Health utility latent class solutions and fit indices for one through four classes

Model	LL	AIC	BIC	Entropy	VLMR	*P* Value
1 Class	−1489.30	2994.59	3025.18	—	—	—
2 Class	−1392.30	2818.60	2883.59	0.688	190.36	0.0088
3 Class[a]	−1359.55	2771.09	2870.49	0.726	64.28	0.0013[b]
4 Class	−1351.04	2772.08	2905.89	0.683	10.99	0.5611

[a]Baseline entropy and VLMR are not applicable for the one-class solution. LL, log-likelihood; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; VLMR, Vuong–Lo–Mendell–Rubin likelihood ratio test for the K versus K-1 model.The 3-class solution was selected because the BIC for that solution was lower than the BIC for the 2-class solution. In addition, the VLMR was significant for the 3-class solution, indicating that three classes fit the data better than two classes. The BIC increased for the 4-class solution compared with the 3-class solution, indicating that the fit of the 4-class solution was worse. Furthermore, the VLMR was not significant for the 4-class solution, indicating that too many classes had been extracted.
[b]$P < 0.005$.

such as median day 1 levels of SCr, hemoglobin, blood urea nitrogen, and serum albumin, did not differ among the three patient subgroups. However, the High health utility impairment subgroup had higher levels of IL6 (Low=135, Moderate=113, High=210 pg/ml, $P = 0.04$) and sTNFR2 (Low=5681, Moderate=5243, High=6860 pg/ml, $P < 0.01$) at study day 1. By study day 8, only levels of sTNFR2 (Low=4690, Moderate=4746, High=6094 pg/ml, $P = 0.04$) were significantly higher in the High health utility impairment subgroup.

Differences in Clinical Status at Day 60

Table 5 summarizes the differences in clinical status at 60 days among the three health utility impairment subgroups. The Low, Moderate, and High subgroups had different rates of RRT dependence (17%, 21%, and 38%, respectively) and hospital discharge (*i.e.*, 98%, 79%, and 57%, respectively) at 60 days. In addition, they had different median ICU-free days from day 60 (*i.e.*, Low=50, Moderate=46, and High=30) and hospital-free days to day 60 (*i.e.*, Low=38, Moderate=25, High=11).

Differences in 1-Year Outcomes

Of the 338 patients, 68 patients died by the 1-year follow-up. Mortality rates differed among the subgroups: 5% in the Low, 21% in the Moderate, and 52% in the High subgroup.

Supplemental Table 1 presents the occurrence of impairments among 1-year survivors in each patient subgroup. Survivors in the Low subgroup most frequently reported impairments in vision (65%), pain (41%), ambulation (20%), and cognition (20%). Survivors in the High subgroup most frequently reported impairments in ambulation (100%), vision (86%), cognition (64%), and emotion (57%).

Discussion

This study is the first to use LCA to identify three subgroups of AKI survivors with distinct health utility profiles on the basis of HUI-3 surveys administered at 60 days after study enrollment. The subgroups labeled Low, Moderate, and High had a median of 1, 4, and 6 health utility impairments, respectively. These subgroups differed in their baseline clinical characteristics (*i.e.*, weight and history of cerebrovascular disease) and intervention assignment (*i.e.*, intensive versus less intensive RRT) during index AKI hospitalization. While conventional biomarkers were not different among the three subgroups, the High subgroup had increased inflammatory biomarkers (IL6 and sTNFR2 at study day 1 and sTNFR2 at study day 8). The High health utility impairment subgroup was more likely to be RRT-dependent and had fewer ICU and hospital-free days at study day 60. Furthermore, the subgroups had strikingly different 1-year mortality rates, ranging from 5% (Low) to 52% (High).

Prior studies have evaluated risk factors of poorer HRQOL in patients after AKI. In this study, the patients

Table 2. Differences among the latent classes in the occurrence of impairments in the eight health attributes at 60 days among survivors of AKI

Impaired Health Utility Attributes from the HUI-3	Low (A), *n*=94 (28%)		Moderate (B), *n*=197 (58%)		High (C), *n*=47 (14%)	
	n	%	*n*	%	*n*	%
Vision	60	64	132	67	35	74
Hearing	1	1	17	9	12	26
Speech	0	0	7	4	46	98
Ambulation	18	19	170	86	46	98
Dexterity	6	6	31	16	34	72
Emotion	5	5	137	70	35	74
Cognition	10	11	95	48	34	72
Pain	23	24	139	71	27	57

HUI-3, Health Utility Index 3.

Table 3. Differences in demographics and clinical characteristics among the three patient subgroups at enrollment

Characteristics	Low (A)		Moderate (B)		High (C)		*P* Value[a]
	N=94 (28%)		*n*=197 (58%)		*n*=47 (14%)		
Demographic characteristics							
Age (yr)	55	(45–67)	61	(51–68)	62	(51–71)	0.07
Male (versus female)	58	(62%)	134	(68%)	34	(72%)	0.39
Ethnicity							0.67
Black	13	(14%)	29	(15%)	8	(17%)	
Hispanic	6	(6%)	8	(4%)	2	(4%)	
White	73	(78%)	156	(79%)	34	(72%)	
Other	2	(2%)	4	(2%)	3	(6%)	
Weight (kg)	84	(67–92)	87	(73–100)	76	(66–91)	0.03 B>C
Clinical characteristics (yes/no)							
Risk factor							
Diabetes	22	(23%)	69	(35%)	15	(32%)	0.14
Cardiovascular disease	30	(32%)	78	(40%)	19	(40%)	0.41
Cancer	13	(14%)	38	(19%)	13	(27%)	0.14
Immunocompromised	22	(23%)	32	(16%)	10	(21%)	0.31
Cerebrovascular disease	0	(0%)	3	(2%)	3	(7%)	0.02 A<B
AKI etiology							
Sepsis	43	(46%)	94	(48%)	30	(64%)	0.10
Postsurgical	49	(52%)	99	(50%)	29	(62%)	0.37
Multifactorial	50	(53%)	105	(53%)	32	(68%)	0.17
Intervention							
Intensive (versus less intensive) RRT	34	(36%)	95	(48%)	27	(57%)	0.04 A<C

Data presented as *n* (%) if categorical and median (lower interquartile range–upper interquartile range) if skewed.
[a]*P*-value for overall comparison; significant pairwise contrasts displayed.

with the High health utility impairment profile had significantly lower weights. This result is consistent with prior studies that note weight loss and failure to regain weight after experiencing a critical illness are associated with poor HRQOL.[37,38] However, this study's results differed from prior studies in that age and baseline renal function were not associated with latent class membership. The Prolonged Outcomes Study of the Randomized Evaluation of Normal versus Augmented Level Replacement Therapy found that increased age and reduced baseline renal function were associated with worse physical quality of life.[39] In a secondary analysis of 462 critically ill patients with AKI,[40] age and preexisting frailty were independently associated with worse scores on the clinical frailty scale. These inconsistent findings may be related to the fact that this study's sample was older and patients with significant CKD were excluded.

This study's results differ from a prior analysis of the parent clinical trial that found that RRT intensity was not associated with health utility after AKI.[15] Among the three subgroups of patients with distinct health utility profiles, the patients with the High health utility impairment profile were most likely to have been assigned to the intensive RRT arm. This finding may be because of the use of the LCA to identify health utility profiles.[15] The advantage of LCA is that, rather than being confined to observed variables, a sample can be organized into subgroups of similar individuals while accounting for unobserved (*i.e.*, latent) heterogeneity within and between groups.[41] Case mix or heterogeneity in a sample is identified as a contributor to null results in clinical trials.[42] Findings from a previous LCA suggested molecularly distinct AKI subphenotypes with differential responses to vasopressin therapies and different clinical outcomes.[43]

In addition to being the most likely to be assigned to the intensive RRT arm, the High health utility impairment subgroup had the highest rates of RRT dependence at 60 days. Prior literature indicates that intensifying RRT from 3 to 6 days a week was associated with impaired renal recovery, and impaired renal recovery was associated with decrements in HRQOL.[15,42,43] Additional studies are needed to understand the relationship between RRT intensity, recovery of kidney function, and health utility.

Of all of the biomarkers evaluated, the subgroup with High health utility impairment had higher IL6 and sTNFR2 at study day 1 and higher sTNFR2 at study day 8. In studies of oncology patients, elevations of cytokines, including IL6, were associated with increases in pain, depression, and sleep disturbance, and elevated sTNFR2 levels were associated with increased severity of fatigue.[20] These same biomarkers were associated with neuropsychiatric symptoms in coronavirus disease 2019 and heart failure.[44,45] A potential hypothesis is that dysregulation of these inflammatory pathways may be associated with poorer HRQOL (*i.e.*, fatigue, depression) independent of disease.[20] On the other hand, increases in IL6 and sTNFR2 were associated with increased mortality and rapid loss of kidney function after AKI.[23,46] Additional studies are needed to determine whether

Table 4. Differences in laboratory markers among the three patient subgroups

Biomarkers	Low (A), n=94 (28%)		Moderate (B), n=197 (58%)		High (C), n=47 (14%)		P Value[a]
	Median	IQR	Median	IQR	Median	IQR	
Day 1							
SCr (mg/dl)	1.3	1–2.4	1.5	1.1–2.2	1.3	0.9–1.8	0.09
Hemoglobin (g/dl)	9.7	8.7–10.9	9.9	9.1–10.8	9.7	8.4–10.4	0.30
Blood urea nitrogen (mg/dl)	23	16–42	28	17–50	25	17–43	0.44
Serum albumin (g/dl)	2.5	1.9–3	2.4	2.0–3.0	2.4	1.8–3.0	0.79
Day 1							
GM CSF (pg/ml)	9	3–21	7	3–19	8	3–12	0.84
IL1 β (pg/ml)	23	23–46	23	23–27	23	23–40	0.18
IL6 (pg/ml)	134	54–280	113	56–245	210	98–1096	0.04 A and B<C
IL8 (pg/ml)	68	38–160	70	34–128	102	53–435	0.05
IL10 (pg/ml)	13	6–32	13	6–28	23	8–52	0.15
IL18 (pg/ml)	89	39–167	85	38–145	97	48–170	0.39
TNF-α (pg/ml)	2	2–4	2	2–4	2	2–3	0.67
sTNFR1 (pg/ml)	12,122	8626–15,967	12,064	8700–16,228	14,009	9700–19,448	0.22
sTNFR2 (pg/ml)	5681	4204–8084	5243	3907–6948	6860	4719–8928	<0.01 A and B<C
MIF (pg/ml)	251	62–743	193	80–555	180	70–483	0.81
DR5 (pg/ml)	183	118–333	195	121–369	237	142–392	0.50
Day 8							
GM CSF (pg/ml)	13	3–31	9	3–22	8	3–19	0.37
IL1 β (pg/ml)	23	23–56	23	23–25	23	23–53	0.15
IL6 (pg/ml)	69	33–119	66	41–143	96	54–137	0.24
IL8 (pg/ml)	47	28–71	55	33–102	69	29–179	0.08
IL10 (pg/ml)	10	5–23	8	4–16	11	6–20	0.20
IL18 (pg/ml)	66	34–138	68	34–132	79	40–143	0.69
TNF-α (pg/ml)	2	2–6	2	2–5	2	2–3	0.35
sTNFR1 (pg/ml)	10,494	7665–15,573	11,629	8354–14,914	14,169	9997–17,184	0.07
sTNFR2 (pg/ml)	4690	3072–6699	4746	3360–6872	6094	4290–8604	0.04 A<B<C
MIF (pg/ml)	116	35–285	109	43–250	94	39–143	0.63
DR5 (pg/ml)	178	104–319	177	95–341	224	135–325	0.43

IQR, interquartile range; SCr, serum creatinine; sTNFR, soluble TNF receptor; MIF, macrophage migration inhibitory factor; DR-5, death receptor 5; mg, milligrams; dl, deciliters; g, gram; pg, picogram; ml, milliliter.
[a]P-value for overall comparison; significant pairwise contrasts displayed.

changes in levels of IL6 and sTNFR2 are early markers of poorer health utility at 60 days after AKI and the role of renal clearance of these biomarkers in HRQOL.

This study's findings underscore the effect of longer hospital stays on HRQOL. In the parent trial, longer hospital and/or ICU lengths of stay were associated with lower

Table 5. Differences in clinical status among the three patient subgroups at day 60

Clinical Status at 60 Days	Low (A)		Moderate (B)		High (C)		P Value[a]
	n=94 (28%)		n=197 (58%)		n=47 (14%)		
Dependent on RRT (yes/no)	16	(17%)	42	(21%)	18	(38%)	0.01 A=B<C
Discharged from hospital (yes/no)	92	(98%)	155	(79%)	27	(57%)	<0.01 A>B>C
ICU-free days from day 60	50	(41–55)	46	(36–53)	30	(8–41)	<0.01 A>B>C
Hospital-free days from day 60	38	(25–44)	25	(5–39)	11	(0–25)	<0.01 A>B>C

Data presented as n (%) if categorical and median (lower interquartile range–upper interquartile range) if skewed. ICU, intensive care unit.
[a]P-value for overall comparison; significant pairwise contrasts displayed.

health utility at 60 days after AKI.[15] In the Finnish Acute Kidney Injury cohort,[5] longer hospital length of stay was associated with lower EQ-5D scores, indicating worse quality of life at 6 months after AKI. Using LCA, the High health utility impairment subgroup had lower ICU and hospital-free days at study day 60.

Finally, the subgroups of patients with distinct health utility profiles at day 60 after AKI had very different mortality rates 1 year after hospital discharge. This finding suggests that the use of HUI-3 scores and LCA can identify subgroups of patients with different prognoses. These results lend support to prior literature that indicates that poorer HRQOL is an independent predictor of mortality among AKI survivors.[47]

This study has several important strengths and limitations. Strengths include the use of LCA, which accounts for heterogeneity within a sample and accommodates for missing data. The presence of distinct HUI profiles demonstrates that significant heterogeneity exists among patients after AKI and poorer HRQOL is not evenly distributed among patients. This study further leveraged biomarkers of AKI and evaluated their potential role in HRQOL. The identified clinical risk factors and biomarkers could eventually be used to risk-stratify patients who need additional support after hospital discharge and to inform goals-of-care discussions when significantly poor health utility is expected after AKI.

Limitations include a retrospective study design, lack of a validation cohort, and a relatively small sample size of 338 AKI survivors who completed the HUI-3 surveys. Since the completion of the VA/NIH ATN study in 2007, AKI outcomes may have changed with increased emphasis on improvements in posthospitalization care and modification of cardiovascular risk factors.[48,49] As such, health utility profiles of AKI-D survivors may have changed.

Survivor bias may have been introduced given that patients with clinical characteristics and biomarkers associated with poorer outcomes may not have survived to 60 days after enrollment to fill out the survey. In addition, while caregiver HUI-3 responses were validated in patients who have had a stroke,[50] surrogates completed a sizeable portion of the questionnaires. In this study, surrogates reported more health utility impairments, which may or may not truly reflect the patients' responses.

This study demonstrated that significant heterogeneity exists in the health utility domains among AKI survivors at 60 days after hospitalization. Future studies with larger sample sizes may allow for a more robust identification of risk factors of poorer health utility after AKI. Early identification of subgroups of patients with poorer health utility may allow for targeted, appropriate allocation of rehabilitation efforts to improve HRQOL among patients after AKI.

Disclosures

C.-Y. Hsu reports the following: Consultancy: I have consulted for legal cases involving acute or chronic kidney disease (Allen, King and Spalding, Lewis Brisbois, McMasters Keith Butler, Shepherd & Lewis); I also consult on an *ad hoc* basis for companies regarding kidney disease (Aria Pharma, Triangle Insights Group); I have been paid to Steering Committee member on an industry funded trial (LG Chem); Research Funding: Satellite Healthcare; and Honoraria: Royalties from UpToDate. P.M. Palevsky reports the following: Consultancy: Janssen Research & Development, LLC; and Advisory or Leadership Role: National Kidney Foundation: Immediate Past President, Member, Scientific Advisory Board; Renal Physicians Association: Member, Quality, Safety and Accountability Committee; Quality Insights Renal Network 4: Chair, Medical Review Board; UpToDate: Section Editor, Acute Kidney Injury; *Journal of Intensive Care Medicine*: Member, Editorial Board. K.L. Johansen reports the following: Consultancy: Akebia, GSK, Vifor; Advisory or Leadership Role: GSK; and Other Interests or Relationships: Associate Editor, *Journal of the American Society of Nephrology*. J.A. Kellum reports the following: Consultancy: AM Pharma, Astellas, Astute Medical, Baxter, bioMerieux, RenalSense; Ownership Interest: J3RM, Klotho, Photophage, Spectral Medical; Research Funding: Astute Medical, Astellas, Baxter, bioMerieux, RenalSense; Patents or Royalties: Astute Medical, Cytosorbents, J3RM, Klotho, Photophage; and Advisory or Leadership Role: Editor: Critical Care Clinics of North America; Editorial Boards; Nephrology Dialysis Transplantation; Critical Care; Critical Care Medicine; Blood Purification. K.D. Liu reports the following: Employer: University of California San Francisco; Consultancy: AM Pharma, Biomerieux, BOA Medical, Neumora, Seastar Medical; Ownership Interest: Amgen (hold stock only); and Other Interests or Relationships: UpToDate. All remaining authors have nothing to disclose.

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Supplemental Material

This article contains the following supplemental material online at http://links.lww.com/KN9/A376.

Supplemental Table 1. Occurrence of impairments in the eight health attributes among 1-year survivors in the three patient subgroups.

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