ACUTE RENAL FAILURE MORTALITY IN HOSPITALIZED AFRICAN AMERICANS: AGE AND GENDER CONSIDERATIONS

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The aging kidney is at risk for both toxic and hemodynamic-induced acute damage, resulting in a high incidence of acute renal failure (ARF) in elderly patients. The effect of age and or gender in ARF mortality in African Americans (AA) was studied in a 3-year, computer assisted retrospective review. In an inner city medical center, 100 patients classified as ARF at discharge or expiration were included in the study. Patients were classified into 3 age categories : <40, 40–64, and >64 years. The incidence of ARF was 35%, 28% and 37%, respectively. Patients >64 years of age were less likely to be dialyzed. Both pre- and postrenal causes of ARF were more common in patients >64 years of age than in younger patients. Hospital length of stay increased progressively with age. Mortality was lower in patients >64 years of age than in younger patients. The incidence of ARF was higher in male than female patients and the incidence of sepsis was higher in female than male patients. Dialytic need was greater in male patients, but mortality was higher in female than male patients. Multivariate logistic regression showed that in the presence of sepsis, oliguria and mechanical ventilatory support, the relative risk of mortality associated with advanced age was 16.5, the relativbe risk of mortality associated with female gender was 0.2. In summary, hospitalized elderly African-American patients have a high incidence of ARF, and patients less than 40 years of age are equally at risk. Although mortality was higher in female patients, gender and advanced age did not independently contribute to high mortality. Neither age nor gender considerations should supplant sound clinical judgment in the management of and decision making in elderly African-American patients with ARF. (*J Natl Med Assoc.* 2002;94:127–134.)

Key words: acute renal failure ♦ mortality ♦ African American ♦ age ♦ gender

The aging kidney undergoes both functional and structural changes, including reduction in the number of glomeruli and development of focal sclerosis in the remnant nephrons,[1] development of proteinuria,[2] and inability to concentrate the urine.[3] These changes cumulatively will translate into a progressive decline in glomerular filtration rate with aging and a propensity to volume depletion.[4] At the same time, the relationship between the serum creatinine and glomerular filtration rate is also changing such that a serum creatinine of 1 mg/dL (88.4 μmol/L) in an 80-year-old patient most likely

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represents a glomerular filtration rate of ≤50 mL/min. Thus, it is not surprising that elderly patients are at increased risk for the development of acute renal failure (ARF). Indeed, the incidence of ARF in the elderly has progressively increased over the last 15 to 50 years.[5–7] However, the effect of age on ARF mortality has remained controversial. Advanced age has been reported to be an adverse predictor of ARF mortality by many studies,[8–11] whereas other studies have observed the contrary.[6,12–18]

The overwhelming predominance of males in both the incidence and prevalence of ARF has been well documented,[5–8,11,14,16–18] however, the role of gender in ARF mortality has not been clarified. Although some authors have reported a significantly higher mortality in their male patients with ARF,[5,11,18] others could not show gender differences in mortality.[16,17] Most of these published reports were from Europe and Japan with no indigenous black population, hence, the absence of data on the effect of advancing age and gender on ARF mortality in African Americans. In this retrospective study, we evaluated the incidence, prognosis, and outcome of de novo ARF and assessed their relationship to age and gender as they pertain to hospitalized African-American patients.

METHODS

This is a 3-year (1994 to 1996) computer-assisted retrospective review of all cases classified as acute renal failure, acute tubular necrosis, or acute tubulointerstitial nephritis at the time of hospital discharge or expiration. The location was a 900-bed urban medical center that serves as a secondary and tertiary care facility. Annual admissions to the adult medical/surgical services during the study period approximated 15,000 (96% African American). Two hundred forty cases of acute renal failure were initially identified, however, only 100 of these satisfied the inclusion criteria. To be included in the study, patients must be of African-American ethnic origin, have no prior history of renal disease, be age 18 years or older; have a rise in serum creatinine of at least 44.2 μmol/L (0.5 mg/dL) and ≥176 μmol/L (2.0 mg/dL) during hospitalization, and have admission creatinine of at least 176 μmol/L (2.0 mg/dL) when no prior history of renal disease was available. All cases of glomerulonephritis, obstetric related renal failure, and acute-on-chronic renal failure were excluded. Patients with incomplete medical records, those who left the hospital prematurely without follow-up arrangements, and those whose elevation in serum creatinine resolved within 48 h were excluded.

Demographic, biochemical, and clinical profiles of all patients were examined by further in-depth hard copy chart review. Oliguria was considered present when urine output was 400 mL/day or less. Preexisting chronic renal insufficiency was defined as documented serum creatinine 150 μmol/L or more (1.7 mg/dL) in the previous 12 months. The length of hospital stay (LOS) was defined as the number of days between date of admission and date of discharge or expiration. Multiorgan failure was defined and scored according to the format suggested by Marshall et al.[19]

Analysis

Patients were classified into three age categories: <40, 40–64, and >64 years of age. Variables are reported as mean ± SD where appropriate. ANOVA with factorial analysis and Fisher's protected least significant differences (which evaluates all possible pair-wise comparison with multiple t-statistics) was used to compare some characteristics, whereas nominal variables were evaluated by contingency tables with raw data and chi-square analysis. Multivariate logistic regression models were employed to examine the effect of age and gender on mortality in the presence of eight other variables. These variables include peak plasma creatinine, serum albumin, cholesterol and electrolytes, volume depletion, mechanical ventilation, sepsis, and oliguria. Goodness-of-fit statistics was provided by likelihood ratio test, which yielded a $p < 0.05$. The estimated exper-

Table 1. Comparison of Demographic and Select Clinical Profiles of the Patients by Age Category

Variables	<40	40–64	>64	p-value
*n**	35	28	37	
Gender (M,%)	28 (80)	18 (64)	21 (57)	
Weight (kg)	62.3 ± 14.7	70.3 ± 20.3	63.6 ± 12.2	
Peak creatinine (μmol/L)	583 ± 380	495 ± 301	424 ± 336	NS
Dialysis (%)	17	7	<1	0.09
Mech vent (%)	29	46	24	NS
Sepsis (%)	34	57	47	NS
Oliguria (%)	31	46	43	NS
MOF (%)	29	46	24	NS
Etiology of ARF:				
Intrarenal (%)	71†	75†	41	0.014
Prerenal (%)	23	25	43†	0.014
Postrenal (%)	6	0	16†	0.014

**n* = number of patients; MOF = multiorgan failure; Mech vent = mechanical ventilation.
†The component with significantly higher value.

imental coefficients and their 95% confidence interval (CI) provided the relative risk of death. Kaplan-Meier plots were utilized to evaluate the effect of gender and advanced age (>64) on survival. Censoring occurred at 120 days based on a 90-day maximum hospital stay with 30 days post discharge follow-up. Statistical software package Statview (SAS Institute Inc., Cary, NC, 1998) was employed in all analyses.

RESULTS

Table 1 shows male predominance in all age categories. Patients more than 64 years of age had the highest incidence of pre- and postrenal ARF, although they were least dialyzed. The differences among the age groups were only statistically significant with respect to etiology of ARF. Patients in the 40–64 age group had the lowest incidence of ARF, although they were more likely to require ventilatory support, develop sepsis, and be oliguric.

The mean hospital LOS progressively increased as age increased, although not significantly so (Fig. 1). The mean LOS between the male and female patients was similar 15 ± 18 vs. 15 ± 14, respectively (p = NS). Multiple regression analysis did not show a significant relationship between age and LOS ($r = 0.16$; p = NS).

The prevalence of multiple adverse prognostic indicators according to gender is illustrated in Table 2. Although the incidence of ARF was higher among the male patients (67% vs. 37%), female patients were more likely to be septic (64% vs. 37%; $p = 0.01$), require mechanical ventilatory support, and have multiorgan failure (MOF). The need for dialysis and occurrence of oliguria were more frequently observed in male patients. There was no significant age difference between the genders in the etiologic causes of ARF (Fig. 2). Although female patients with both intrarenal and postrenal ARF were older (56 ± 18 and 67.5 years of age, respectively), patients with postrenal ARF were older than those with intrarenal ARF (62.9 ± 18 vs. 48.9 ± 18; $p = 0.005$). The mean difference in ages between patients with pre- and postrenal ARF was –1.9; p = NS.

Figure 3 shows the relationship between age, gender, and mortality. There were no significant differences in age between surviving and expired female patients (55 ± 20 vs. 61 ± 21; p = NS). Similarly, the mean difference in age between surviving and expired male patients was 4.7 years (p = NS). Male patients who died were much younger than their female counterparts, although overall, female mortality was higher than male mortality (46% vs. 36%; p =

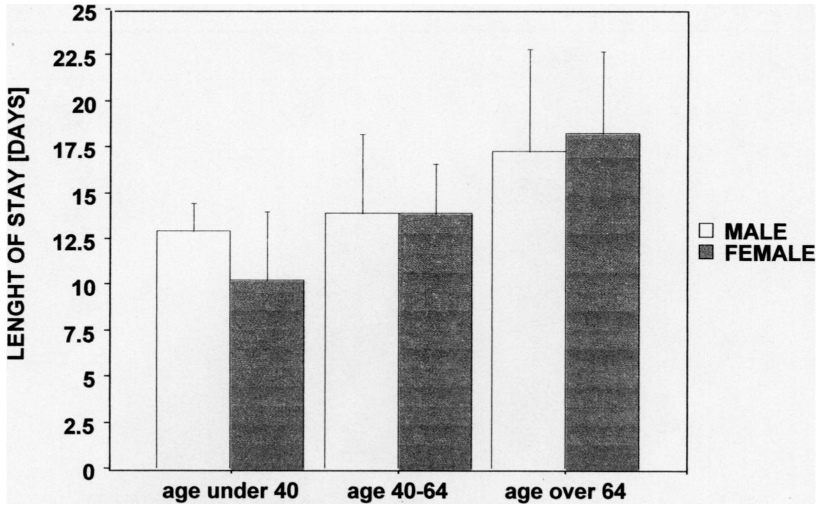

Figure 1. The effect of advancing age and gender on hospital length of stay.

NS). The patients who were 40–64 years of age had the highest mortality of 50% compared with 40% and 30% in the <40 and >64 age groups (p = NS), respectively. The reduced survival in the 40–64 age group is clearly displayed in Fig. 4. Most of our younger patients had acquired immunodeficiency syndrome (AIDS), which was associated with the highest overall mortality. The distribution of underlying morbid conditions and associated mortality is shown in Table 3. Re-analysis of the mortality data with exclusion of patients with pre- and postrenal ARF revealed that patients 40 to 64 years of age continued to be associated with the highest mortality, compared with patients <40 and >64 years of age, respectively (62% vs. 48% and 53%, p = NS). The mean age of the patients who died was 49.6 ± 19. Patients in the >64 age group had the best survival. Although univariate logistic regression analysis showed that the relative risk of mortality associated with advanced age was 1.0 (CI = 0.9–1.03; p = NS), in the presence of oliguria, sepsis, and mechanical ventilation, multivariate logistic regression showed that the relative risk of mortality associated with patients >64 years of age was 16.5 (CI = 1.2–226, p = 0.036). The relative risk of mortality associated with female gender utilizing the same multivariate logistic regression was 0.2 (CI = 0.02–2.3; p = NS). The risk of mortality was equally present in both male and female patients, as depicted in Fig. 5. Male patients had better survival than female patients, although the difference was not statistically significant (p = 0.24).

Table 2. Comparison of Demographic and Select Clinical Profiles by Gender

Variable	Male	Female	p-value
n	67	33	
Age (yr)	52 ± 19	58 ± 20	NS*
Dialysis (%)	13	0	0.02
Sepsis (%)	37	64	0.01
Mech vent (%)	6	18	NS
Oliguria (%)	42	36	NS
MOF (%)	27	42	NS

*NS = not significant; Mech vent = mechanical ventilation; MOF = multiorgan failure.

DISCUSSION

The physiologic and structural changes associated with the aging kidney predispose elderly patients to acute renal injuries either by toxic metabolites or by hemodynamic perturbations. Hence, it is uniformly accepted that the incidence of ARF is greatest among elderly pa-

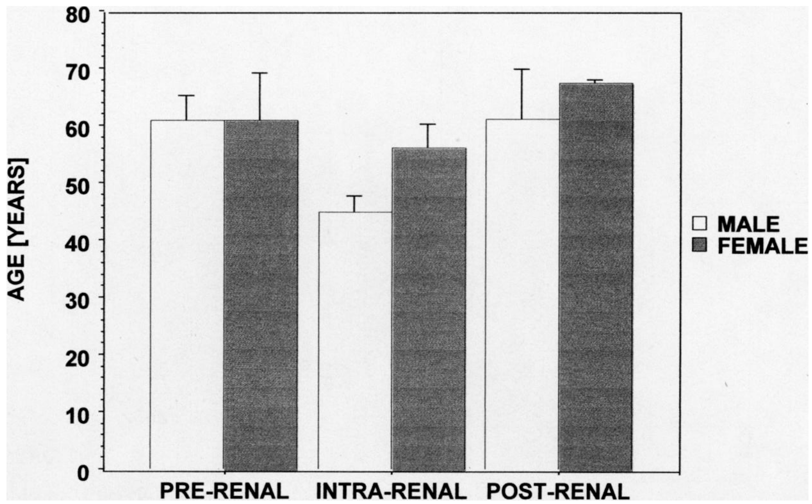

Figure 2. The mean ages of the patients according to etiologic causes of acute renal failure and gender. Only one female patient had postrenal ARF.

tients.[5–7,20] One study observed an incidence of 36% among their patients over 70 years of age.[20] In this study, we observed a bimodal distribution in the incidence of ARF of 35% in those patients less than 40 years of age and 37% in those patients more than 64 years of age. This finding differs from previous reports that have shown a progressive increase in incidence of ARF with increasing age.[7,20,21] The high incidence observed in our patients less than 40 years of age was probably due to our large population of patients with AIDS. Many inner city hospitals have observed a progressive increase in hospitalization for patients with AIDS.[22] The majority of these patients are African American and often develop terminal ARF as a result of sepsis or toxic nephropathy with associated MOF.[22] The mean age of our patients was 54 ± 20. This is consistent with the observation that the mean age of patients with

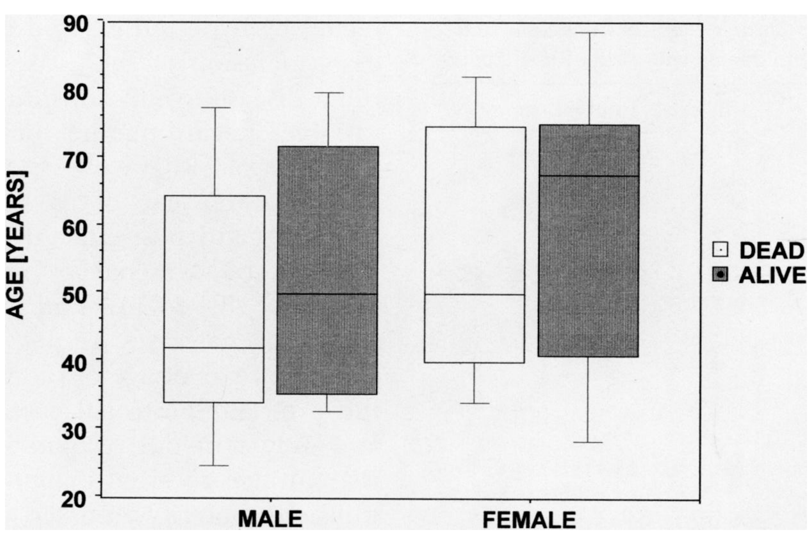

Figure 3. The relationship between age and gender with mortality. The box represents 25% to 75% of cases. The horizontal line in the box represents the median.

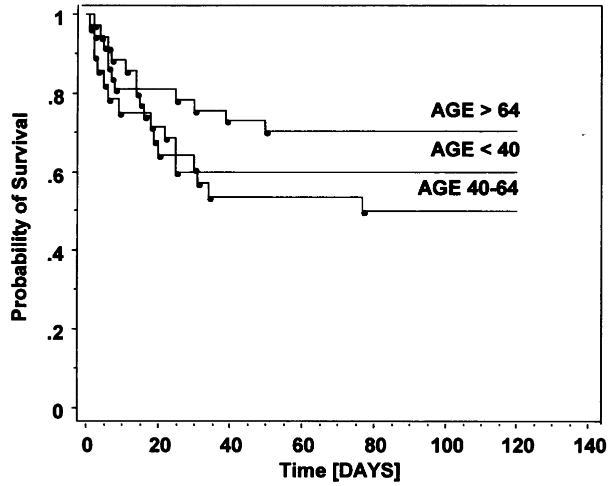

Figure 4. Kaplan-Meier plot showing the probability of survival according to age categories. The dots represent mortality (event) times.

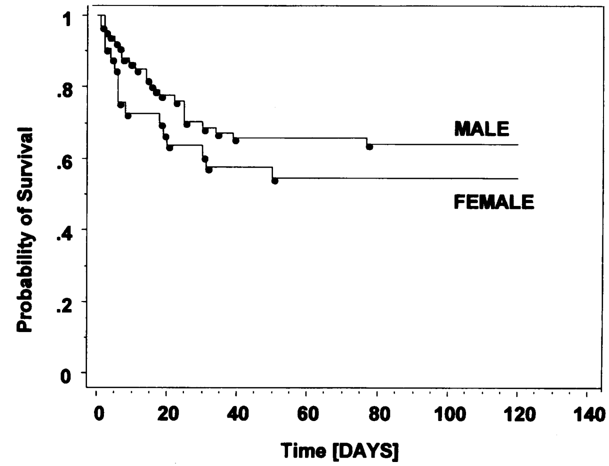

Figure 5. Kaplan-Meier plot showing the probability of survival according to gender. The dots represent mortality (event) times.

ARF has progressively increased from 44 years old in 1975–1979 to 58 years old in 1985–1989.[7]

The predominance of male patients represented in the incidence of ARF has been confirmed by many studies.[5–8,11,14,16–18] This study is in agreement with those studies. The high incidence of prostate-related obstructive renal disease[14] and the reduction in obstetric-related ARF[5] are only partial explanations. Obstetric-related ARF constituted 20% to 30% of ARF cases in the 1950s and almost none in the 1980s.[5] We excluded obstetric-related ARF from our study because none of the cases satisfied our inclusion criteria. Patients with preexisting renal disease and those with glomerulonephritis were also excluded in accordance with other published reports.[16,18,20] Studies that included glomerulonephritis often required confirmatory renal biopsies. Renal failure that resolved within 24 to 48 h were thought to be insignificant and, as such, were excluded.[16] African Americans are disproportionately affected by hypertensive and diabetic renal disease, inclusion of such cases with preexisting renal disease would constitute a confounding variable. Regarding the incidence of various etiologies of ARF, we observed that our patients more than 65 years of age were more likely to have pre- and postrenal ARF (43% and 16%, respectively). Pascual et al.[6] reported incidences of 28% to 30% and 11% to 20% in pre- and postrenal cases, respectively, in their patients 65 years of age or older. The majority of the pre- and postrenal cases were reversible, and only 1 of our 37 patients more than 64 years of age received dialysis. The decision to withhold dialysis was based on severity of underlying medical conditions and family requests for no further intervention. There was

Table 3. Underlying Chronic Medical Conditions and Associated Mortality in Patients with Acute Renal Failure

Condition	*n*	Total mortabity (%)
Hypertension	21	3
Diabetes mellitus	10	8
AIDS*	27	31
CHF	7	15
Myocardial infarction	2	5
Carcinoma	9	10
COPD	3	5
Liver disease	3	2.5
CVA	4	8
Unknown†	14	2.5

*AIDS = acquired immunodeficiency syndrome; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; CVA = cerebrovascular accident.
†Unknown cases represent patients with no obvious chronic medical condition.

no denial of dialysis based on age considerations.

Prognostic indicators of adverse outcomes in ARF, such as sepsis, oliguria, comorbid conditions, and mechanical ventilation, have been well characterized.[8,10,11] We have reported similar findings.[23] Unresolved, however, is the role of age as an independent prognostic indicator of poor outcome in ARF. Many studies have reported that advanced age connotes poor outcome.[5,8,10,11] Bullock et al.[8] noted a relative risk of 1.65 for every 10-year increase in age. They observed a mortality of more than 70% in their patients who were 60 years of age or older. We observed a mortality of 30% in our patients more than 65 years of age. However, in agreement with other studies, we were unable to show that advanced age independently constituted adverse outcome.[6,12,13,15–18] Even when the pre- and postrenal ARF cases were eliminated, the mortality was only 53% among our elderly patients more than 65 years of age. The high mortality of 62% observed in the patients who were 40 to 64 years of age was probably related to the high prevalence of the poor prognostic indicators in this group as discussed above. Our observed relative risk of 1.0 for mortality associated with advanced age was consistent with the 0.99–1.09 for patients more than 65 years of age reported by Pascual et al.[6] The role of gender is also controversial in ARF mortality. Some authors have noted that male patients have a higher risk of mortality.[5,11,18] Turney et al.[5] observed a male survival of 44.7% as compared to 52.3% in their female patients, whereas Chertow et al.[18] reported that male gender was associated with mortality relative risk of 2.01. We observed a higher female mortality of 46% vs. 36% for male patients, and a female gender-associated mortality relative risk of 0.2. The higher female mortality was probably related to the higher incidence of sepsis, mechanical ventilatory support, and MOF within that cohort. Other published studies have not found a significant difference in gender-related mortality.[16,17] In the African-American population, cardiovascular-related mortality in male patients has been consistently reported to be higher than that of female patients over the last 30 years.[24] We have no explanation for the higher incidence of sepsis, mechanical ventilation, and MOF among our female patients.

Our rigorous inclusion criteria, which excluded a large number of patients, and our arbitrary age classification have imposed limits upon this study. There are no uniform criteria for either the definition of ARF or age classification in the literature. The lack of unanimity in the definition of ARF, the severity of concomitant illness, and the categorization of etiologies confound interpretation of demography in ARF.[25] The retrospective nature of this study compelled us to adopt what we considered to be "intermediate" selection and classification criteria. Our findings may not be applicable to other hospital settings, but should be reproducible at similar inner city hospitals with a large population of African-American patients and patients with AIDS. In the excellent review by Elasy and Anderson[25] they concluded that the diversity in outcomes reported in the elderly ARF population reflect differences in comorbidity.

In conclusion, our study confirms the high incidence of ARF in elderly African-American patients, which has been previously observed in white patients. In addition, we found an earlier peak that occurs in patients less than 40 years of age, thus a bimodal incidence of ARF in African-American patients. The male predominance in African-American patients is similar to reports among white patients, however, the role of age and gender as independent predictors of mortality in ARF warrants further exploration. Good clinical judgment grounded in ethical principles should determine the provision of optimal care to all patients with ARF. Management decisions should not be based on age or gender considerations.

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