

## Increased Prevalence and Decreased Mortality of Patients With Acute Kidney Failure

*Soliyeva M.O.*

*Andijan State Medical Institute , Uzbekistan*

**Annotation:** Acute renal failure (ARF) remains one of the most enigmatic syndromes in nephrology, with reported incidence rates varying from 0.9 to 20% and mortality rates between 25 to 80% (1). There is little doubt that these discrepancies are caused by large differences in the definition of ARF (2), case-mix (3), and experience with treatment of ARF and its concomitant pathology. In this issue of JASN, two papers describe the epidemiologic and prognostic evolution of ARF over the last decade (4,5). Both papers are based on a retrospective analysis of databases containing a very large number of patients and, interestingly, covering to some extent similar patient populations. The main message of both papers is that, in contrast to other recent data (6), the death rates attributable to ARF are declining over time despite a rise in the occurrence of ARF in the same period. One study (5) is based on the US Renal Data System and covers Medicare patients who were identified by International Classification of Diseases, 9th Edition, Clinical Modification (ICD9-CM) discharge codes, while the other (4) covers a nationwide inpatient sample database of hospital discharges.

**Key words:** renal , kidney, pathology, patient.

Why the Increase in ARF Prevalence? Why are the reported values for prevalence (from 15 to 35 per 1000 hospitalizations [5] versus from 61 to 288 per 100,000 population [4]) and death rates (decreasing from 49.7% to 40.3% [5] and from 40.4% to 20.3% [4], respectively) so very different in both studies, although they are based on samples extracted from similar populations? Either the two samples had in fact quite different characteristics, calling into question the extrapolation to the overall US population, or there is a bias, most likely related to differences in definitions of ARF used in these databases at different time points. That the latter may play a role is suggested by the validation test in the study by Waikar et al. (4). The sensitivity of that registry for ARF was only 17.4% in 1994, and “rose” to 29.3% in 2002. This observation implies that: (1) administrative databases are not very sensitive for the diagnosis ARF, and many cases, most likely the less severe ones, may have been missed, resulting probably in underestimated prevalences; (2) the increase in sensitivity over time means that the interpretation of the instructions on data collection for these databases has not remained constant over the registration period. This is not only a likely explanation for the increase in ARF prevalence, but since more “less severe” ARF cases were probably recently included, it could also at least partly explain the improved outcomes. However, the difference in “reporting sensitivity” might not completely explain the increased prevalence of ARF. Among other reasons, increased age of the population is often the most proposed explanation. However, panel B of Figure 1 of the paper of Xue et al. (5) reveals that the increased prevalence is present in all age categories. In the paper by



Waikar et al. (4), age was also not different in the different time periods. A more likely explanation is a change in the spectrum of ARF itself. One recent national survey showed major differences between patients with and without a discharge diagnosis of ARF (7). Older age, male gender, much higher frequency of comorbidities, diagnostic and therapeutic interventions, and nonrenal organ dysfunction were observed in the ARF patients. In addition, HIV and related treatments, more frequent nonrenal organ transplantations, and more aggressive diagnostic and therapeutic interventions also contribute to the changing spectrum (8). Another explanation is the increasing prevalence of diabetes patients who are increasingly being treated with angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and aldosterone antagonists, which all carry an increased risk for ARF, particularly during episodes of dehydration (9,10). Optimism or “self applause” is thus not warranted yet, as it is highly possible that the increase in ARF is to a large extent iatrogenic. In addition, the increased awareness on the part of nonnephrologist intensive care unit (ICU) specialists of the potential presence of ARF has probably also increased. This increased awareness has been accompanied by a more widespread use of so-called “nonrenal indications” for dialysis (11,12) and an “earlier start” of dialysis in ICU patients. Unfortunately, the evaluation of the beneficial impact of these strategies is also prone to the same confounders as the ones present in the analysis of the epidemiology of ARF. All these considerations might explain why the prevalence of both ARF and, more particularly, dialysis requiring ARF has increased. Why the Decrease in Mortality Rates? Although there might be few reasons to celebrate the increasing prevalence of ARF, nephrologists could still be proud of the decreasing mortality rates, as reported in both articles. However, some skepticism and caution should also prevail here. First of all, the reported mortality rates in these two studies are still horrifying: Nearly 2 out of 3 patients suffering from ARF will not be alive 90 d after the onset of ARF. This overall result is not only sobering but the “improvement” could be more artificial than real. As pointed out before, it is possible that in recent years less severe cases of ARF have been registered in both data bases, explaining the better survival. In the paper by Waikar et al. (4), the mean Deyo-Charlson severity index for the period 1993 to 1997 was comparable to that for the period 1998 to 2002. Table 3 of that paper gives us the comorbidity-adjusted odds ratio for mortality, with the period 1988 to 1992 as reference. The observation that, in this timeframe, data on the race of 50% of the patients is missing lowers to some extent the confidence in using this period as a reliable reference. But still, when looking at the 1993 to 1997 and 1998 to 2002 cohorts, there appears to be an improvement in outcome. In the paper by Xue et al. (5), a decreasing trend of comorbiditycorrected mortality rate has also been observed. There is, however, a striking increase in ICU stay and sepsis diagnosis, one of the comorbid conditions corrected for, so that it is not unlikely that, over time, patients were more rapidly admitted into ICU with less comorbidity. It is also possible that the basis for the diagnosis of “sepsis” in 1992 in these administrative databases was different from that in 2002 (13). In that regard, the observation reported in Table 2 that more patients were diagnosed with “sepsis” than were hospitalized in the ICU is puzzling and could mean that some of these “septic patients” were not ill enough to be admitted in the ICU. The diagnosis of “sepsis” in one episode may thus not be the same as in another episode. But, if we accept that indeed the prognosis of ARF has improved over the last decade, which factors then have contributed to this success? All of the “golden oldies,” like dopamine, renal vasodilators, growth factors, and diuretics, have been evaluated during this decade and benchmarked as “not effective” (14,15), or even potentially deleterious. For the new drugs, there is little doubt that “the magic bullets” that may work well in animal studies to treat ARF have failed when tested in real clinical conditions (1,16). There has, however, been some progress made. This is illustrated by the positive influence of the use of norepinephrine on the outcome of ARF and sepsis, at least as observed in mainly uncontrolled trials



(17), the impact of early resuscitation (18) and of activated protein C in severely ill septic patients with a high risk of dying (19), and the maintenance of euglycemia in critically ill patients (20,21). With regard to ARF requiring dialysis, it seems unlikely that the dose of dialysis recommendations, based on the landmark study of Ronco et al. (22), have yet influenced clinical practice enough to improve outcomes, but this will come. Even if more centers are now using more continuous techniques (continuous venovenous hemofiltration) as renal replacement therapy, the evidence that this improves outcomes is still lacking (23). If the outcome of ARF patients is really improving, it is most likely the result of “better” general and supportive care. This “improved care,” although difficult to define, may be due to greater attention to clinical details, and more consistent involvement of interested “organ specialists” in the care of these often very ill patients. This mix of “intensivist” and “organ specialist” knowledge is, in our opinion, the most important progress of the last decade, but its impact is of course quite difficult to measure (24). This integrated care is not only important for further improvement of the outcome of the ARF patient, but it is crucial for nephrologists as well. If we still want to be involved in the care of these patients, and we must be, then our physical presence in the ICU is required, even at hours that are less convenient. In addition, the curriculum for training fellows in nephrology must include intensive training in ICU medicine. In conclusion, we sincerely hope that the optimistic results described in both of these papers (4,5) will be confirmed in future prospective clinical studies. In addition, in view of the hypothesis that the rising prevalence of ARF is due to a more aggressive diagnostic and therapeutic approach to the disease, prevention of ARF in patients at risk is still the most efficient way to improve the outcome of this syndrome with its high associated mortality and economic cost.

### References

1. Lameire N, Van BW, Vanholder R: Acute renal failure. *Lancet* 365: 417–430, 2005
2. Mehta RL, Chertow GM: Acute renal failure definitions and classification: Time for change? *J Am Soc Nephrol* 14: 2178–2187, 2003
3. Mehta RL, Pascual MT, Soroko S, Savage BR, Himmelfarb J, Ikizler TA, Paganini EP, Chertow GM: Spectrum of acute renal failure in the intensive care unit: The PICARD experience. *Kidney Int* 66: 1613–1621, 2004
4. Waikar SS, Curhan GC, Wald R, McCarthy EP, Chertow GM: Declining mortality in patients with acute renal failure, 1998 to 2002. *J Am Soc Nephrol* 17: 1143–1150, 2006
5. Xue JL, Daniels F, Star RA, Kimmel PL, Eggers PW, Molitoris BA, Himmelfarb J, Collins AJ: Incidence and mortality of acute renal failure in Medicare beneficiaries, 1992 to 2001. *J Am Soc Nephrol* 17: 1135–1142, 2006
6. Ympa YP, Sakr Y, Reinhart K, Vincent JL: Has mortality from acute renal failure decreased? A systematic review of the literature. *Am J Med* 118: 827–832, 2005
7. Liangos O, Wald R, O’Bell JW, Price L, Pereira BJ, Jaber BL: Epidemiology and outcomes of acute renal failure in hospitalized patients: A national survey. *Clin J Am Soc Nephrol* 1: 43–51, 2006

