

AKI Is Around the World but Public Recognition Is Lacking

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The interest in AKI by nephrologists and critical care physicians, from pathogenesis to therapy, has never been higher. Numerous epidemiologic, clinical, and basic science studies have zeroed in on what is today a leading cause of hospital morbidity and mortality. Unfortunately, this is not true for translational studies that would provide progress in the ability to affect the incidence and course of this disease entity. The importance of AKI is compounded by the association of AKI with the development CKD following AKI, an increased risk for AKI in patients with CKD, and acceleration of CKD to ESRD (1).

Together, these synergistic interactions are resulting in global social and economic problems (2). In this issue of *CJASN*, Susantitaphong and several members of the ASN Acute Kidney Injury Advisory Group report on a worldwide meta-analysis of AKI (3). This exhaustive review details 8 years of large, well described cohort studies, using the recent Kidney Disease Improving Global Outcomes definition for AKI, and provides yet more compelling data regarding the unacceptable health care consequences of AKI. The overall hospital incidence of AKI was >21% for adults and 33% for children, with corresponding mortality rates of nearly 24% and 14%, respectively. The increased incidence and reduced overall mortality result from a more liberal and inclusive definition of AKI. Of note, the mortality rate was inversely related to the income of individual countries and the percentage of Gross Domestic Product spent on total health care.

These statistics leave little room for denying the well published but unfortunately poorly appreciated worldwide health importance and humanitarian burden of AKI. Limited public recognition and insufficient government and commercial funding have hampered the ability of health care professionals, scientists, and engineers to develop and advance the approaches needed to study, prevent, diagnose, quantify the severity of injury from, and treat kidney diseases. To generate government emphasis and funding, the public needs to understand that everyone is at risk for developing AKI and, therefore, CKD and ESRD. Recent data indicate that >50% of all United States citizens develop CKD stage 3a and beyond, making them a target for AKI and subsequent CKD and ESRD (4).

We have made a mistake by describing individuals as “at risk” for AKI. This implies that if you are not “at

risk” you need not worry. This is just not true; the term should be “at increased risk” or “at high risk.” AKI results from myriad causes, including sepsis, prescribed and environmental nephrotoxins, trauma, surgery, and bladder outlet obstruction, to name a few. Unlike diseases such as hypertension and hypercholesterolemia, for which genetic factors play an important etiologic role, everyone is at risk for AKI. However, hypertension, diabetes, obesity, and aging certainly increase the risk of developing AKI and kidney disease, and these individuals require enhanced surveillance. Until the public, lawmakers, and health care professionals are fully aware of this health threat, kidney disease prevention and therapeutic efforts will not advance appropriately, and dialysis will remain one of medicine’s fastest-growing and costly markets (5).

Fortunately, the National Institutes of Health (NIH), the U.S. Food and Drug Administration (FDA), and “industry” have recognized the unmet needs for diagnostic procedures, prevention, and therapy. The National Institute of Diabetes and Digestive and Kidney Diseases was first to seize upon the importance of AKI and its overall health care impact and kidney health (6). However, the United States government is investing less in medical research, and, given its prevalence and financial burden, kidney disease is markedly underfunded. Additionally, recent automatic budget cuts instituted by the United States government have reduced overall funding for the NIH by \$1.6 billion. These limited and dwindling federal dollars have hampered the ability of the NIH to vigorously support the initiatives necessary to turn the tide in this disease. This is not to dismiss the progress made in addressing ongoing and unacceptable health disparities in kidney disease. Development and refinement of dialysis and transplantation represent remarkable successes in clinical care. This success has focused much of the community’s attention on a small select population of patients requiring end-stage renal replacement therapy. Even some members of Congress and their staff are unaware that nephrology represents anything outside of dialysis and transplant therapies. Moving forward, we need to bring the same level of effort to preventing kidney injury and kidney disease and to minimizing loss of kidney function early in the disease process. Otherwise, the flow of patients with ESRD will

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continue and probably even increase given the epidemic in obesity and diabetes.

Lacking the ability to detect and quantify injury in AKI has greatly impaired the ability to define sensitive surrogate endpoints that would allow for successful clinical studies early in the disease process. All too often, clinical studies have had to focus on patients with late stages of AKI who already possess a marked disease burden and may be far less likely to respond to treatment. This has minimized the ability to translate highly successful therapies from preclinical studies into the clinic. Major diagnostic areas, such as functional studies, especially imaging, have lagged behind other medical fields (7). Given that the discipline of nephrology was built on functional studies and structural functional relationships, this is very puzzling. Unfortunately, the commercial environment for developing diagnostic techniques is not favorable, and a diagnostic procedure, besides being effective in advancing care, often must also reduce overall costs to be considered positively for adoption.

These deficiencies have also resulted in nephrologists using population studies and estimating equations in attempts to develop diagnostic approaches and therapies for individual patients. AKI is a complex disease process involving many different cell types and cell responses and a host of different causes. To think we will find one biomarker that can be used in isolation seems naïve. To think we can use one approach, such as urinary biomarkers, to diagnose, classify, and determine the extent of injury in individual patients with AKI seems wishful, and to think effective therapies can be developed before having these quantitative diagnostic approaches seems optimistic at best.

On the brighter side, biotechnology and pharmaceutical companies have fully recognized that AKI, and synergism between AKI and CKD, offers areas of tremendous opportunity for both improving patient care and the associated financial rewards. They have identified unmet needs for developing diagnostic devices, drugs, and biologics. As a result, these commercial entities are starting to make major global investments in AKI and CKD. This is particularly exciting because translation of basic information into clinically useful technology and therapies requires commercial commitment (8). In addition, the FDA is now working more closely with industry to foster advancement in the AKI arena. I am hopeful the American Society of Nephrology Kidney Health Initiative with the FDA will provide a forum where health care professionals, patient groups, the FDA, NIH, and industry can work for the betterment of patient care. This should be an extremely exciting time, one long overdue.

Finally, captivating the next generation of nephrology professionals requires that we correct the present public awareness, funding situations, and lack of therapeutic advances. Research, innovation, and therapeutic advances have brought incredible excitement to many other areas of medicine, prompting many students to choose other specialties over nephrology (9). The situation is particularly concerning in the United States, where medical student

interest in nephrology is at an all-time low. Although numerous steps are necessary to alleviate this situation, developing effective therapies to improve kidney health care, based on sound diagnostic tests, will go a long way toward attracting the best and brightest to nephrology, further maximizing the prevention and treatment of kidney disease.

In summary, existing epidemiologic and clinical data indicate that AKI should stimulate a global outcry for a health care designation requiring immediate attention. However, until the general public fully understands the health care implications of AKI, their likelihood of developing AKI, and possible consequences, the funding to support the necessary initiatives will not be forthcoming and progress will be unacceptable.

Disclosures

B.A.M. is a founder, stock holder, and medical director of FAST Biomedical and the current president of the American Society of Nephrology.

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See related article, “World Incidence of AKI: A Meta-Analysis,” on pages 1482–1493.