stem cell data are significant because they suggest that undifferentiated ES cells are also capable of contributing to regeneration by providing the missing $\alpha 3$(IV) chain in a manner similar to the blood and BM cells.

Although the successful treatment of mice, including increased survival rates, is significant, it is still a big step to use such stem cells in clinical trials. This article, however, represents significant movement toward the development of cell-based therapies for the treatment of kidney disease and has implications beyond Alport syndrome.

DISCLOSURES

None.

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See related article, "Stem Cell Therapies Benefit Alport Syndrome," on pages 2359–2370.

Critical Care Nephrology: It's Not Just Acute Kidney Injury

Paul M. Palevsky*† and Steven D. Weisbord*†‡

*Renal Section and ‡Center for Health Equity Research and Promotion, VA Pittsburgh Healthcare System, Pittsburgh, Pennsylvania; and †Renal Electrolyte Division, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

J Am Soc Nephrol 20: 2281–2282, 2009.
doi: 10.1681/ASN.2009080875

The care of the critically ill with kidney disease represents a growing proportion of patients treated by nephrologists in the hospital. As a result, critical care nephrology, melding together the expertise of nephrologists and intensivists, has emerged as a distinct subdiscipline during the past decade.[1–3] Critical care nephrology is a topic at national and international meetings, has a proposed core curriculum for trainees,[4] and even has its own textbook[5]; however, a casual perusal of the literature in critical care nephrology rapidly reveals an almost exclusive focus on issues pertaining to acute kidney injury (AKI) with relative neglect of the patient with ESRD and superimposed critical illness. In a nearly 1800-page textbook of critical care nephrology, discussion of critically ill patients with ESRD are covered in fewer than a dozen pages.[5]

The need for critical care nephrology to broaden its perspective and provide increased focus on patients who have ESRD and are critically ill is highlighted by the findings of Strijack *et al.* in this issue of *JASN*.[6] Using a prospectively maintained database of all adult patients admitted to intensive care units (ICUs) in Winnipeg, Manitoba, Canada, they found patients with ESRD accounted for nearly 3.4% of all ICU admissions and estimated the annual rate of ICU admission among adult patients with ESRD was more than 25 times that of the general adult population. The ESRD patients were younger, less likely to be male, and more than twice as likely to have diabetes as compared with the general ICU population. Although rates of coronary artery disease were similar, patients with ESRD had more than two-fold the rate of peripheral vascular disease, were more likely to require ICU care for nonsurgical disease, had more than double the rate of sepsis than the general ICU population, and had substantially higher severity of illness scores, even after subtracting the renal component. The patients with ESRD composed nearly 40% of patients who received renal replacement therapy (RRT). The remainder, representing patients with AKI, had even higher severity of illness scores with more than double the frequency of sepsis as compared with the patients with ESRD. Overall hospital mortality was ap-

Published online ahead of print. Publication date available at www.jasn.org.

The views expressed in this article are those of the authors and do not necessarily represent the views of the Department of Veterans Affairs.

Correspondence: Dr. Paul M. Palevsky, Room 7E123 (111F-U), VA Pittsburgh Healthcare System, University Drive, Pittsburgh, PA 15240. Phone: 412-360-3932; Fax: 412-360-6130; E-mail: palevsky@pitt.edu

proximately 10% in critically ill patients without ESRD or AKI, 16% in the patients with ESRD, and more than 40% in the patients with AKI. In contrast to patients with AKI, ESRD status was not independently associated with mortality risk, and ICU length of stay and resource use were similar to those of the overall ICU population. ICU readmission rates, however, were approximately twice as high in both the patients with ESRD and the patients with AKI as in the general ICU population.

This study confirms and extends the findings of previous studies evaluating ICU use and outcomes in patients with ESRD.[7–11] The majority of past studies were small, single-center analyses with limited inference to generalize. The only previous analysis of a large regional data set used the Intensive Care National Audit and Research Centre (ICNARC) Case Mix Programme database from Great Britain.[11] This analysis found patients with ESRD composed 1.3% of all 276,731 admissions to 170 adult ICUs in England, Wales, and Northern Ireland between 1995 and 2004. On the basis of the period prevalence of ESRD, the ICU use rate was approximately six admissions per 100 ESRD patient-years, a rate slightly less than half that observed by Strijack *et al.*[6] A variety of reasons may account for this, including differences in case mix, criteria for ICU admission, and other ICU practice patterns as reflected by differences in age, frequency of nonsurgical ICU admissions, and ICU and hospital mortality rates in both general ICU and critically ill patients with ESRD. Although ESRD status was associated with an increased odds of in-hospital death (1.82; 95% confidence interval 1.13 to 1.37) in the ICNARC data set, after adjustment for demographics and case-mix factors, the odds of death (1.24; 95% confidence interval 1.69 to 1.96) were markedly attenuated, suggesting that underlying comorbidity rather than renal failure *per* se was the major determinant of increased mortality risk in patients with ESRD.

These data emphasize the need to include patients with ESRD in the spectrum of critical care nephrology. Patients with ESRD develop critical illness more frequently than the general population and have a greater severity of illness than those without renal disease. Moreover, patients with ESRD often present a unique set of clinical issues related to fluid and electrolyte management, mineral homeostasis, bleeding diatheses, and drug dosing that require the multidisciplinary expertise of nephrologists and critical care providers. Although renal failure seems to be, at most, only a minor contributor to the increased mortality risk associated with critical illness in patients with ESRD, the simple fact remains: Mortality in patients who have ESRD and develop critical illness is unacceptably high. To improve the care and outcomes of critically ill patients with ESRD, practitioners and investigators need to broaden the focus of critical care nephrology to include this patient population.

ACKNOWLEDGMENTS

Dr. Weisbord is supported by a Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development Service Career Development Transition Award and by Merit Review Project IIR 07-190.

DISCLOSURES

None.

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See related article, "Outcomes of Chronic Dialysis Patients Admitted to the Intensive Care Unit," on pages 2441–2447.

Allograft Biopsies: Studying Them for All They're Worth

Isaac E. Stillman*†‡ and Martha Pavlakis†‡§
*Department of Pathology, †Renal Division, Department of Medicine, and §Transplant Institute, Beth Israel Deaconess Medical Center, Boston, Massachusetts; and ‡Harvard Medical School, Boston, Massachusetts

J Am Soc Nephrol 20: 2282–2284, 2009.
doi: 10.1681/ASN.2009090930

Advances in short-term renal allograft survival, as a result in large part of the use of calcineurin inhibitors (CNIs), have not

Published online ahead of print. Publication date available at www.jasn.org.

Correspondence: Dr. Isaac E. Stillman, Department of Pathology, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Boston, MA 02215. Phone: 617-667-4344; Fax: 617-667-7120; E-mail: istillma@bidmc.harvard.edu