Renal Biopsies in Acute Kidney Injury: Who Are We Missing?

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What one finds on a renal biopsy is a function of whom one chooses to biopsy. This is especially true with regards to acute kidney injury (AKI). AKI is a common entity in the hospital setting (1), even given the problems of definition and terminology that have recently received attention (2), and its causes are highly dependent on the population studied. Despite its enormous clinical impact, there have been few series of renal histology data published on the etiologies leading to AKI. Our need for more data is further complicated by the fact that the overwhelming majority of AKI cases are never biopsied. Why is this so? In many cases, the clinical context suggests the cause, often either “acute tubular necrosis” (ATN) or “prerenal,” with a reasonable degree of certainty. In others, the lack of efficient therapeutic options coupled with the risks and costs of a biopsy make it appear unwise. There are other considerations as well. In current practice, most nephrologists choose to biopsy when they are not confident as to the cause of the AKI or when the renal injury has an obscure etiology. Is this appropriate?

This is one context in which to approach the important contribution by Lopez-Gomez et al. appearing in this issue, detailing the latest findings from the Spanish Registry of Glomerulonephritis, one of the largest in the world and one from which we have earlier reports (3–5). An important advantage of this registry is that the indication for biopsy was recorded, allowing identification of those biopsies performed in the setting of AKI, which comprised 16% of the cases. Another advantage is that the findings were stratified by age. Not surprisingly, AKI as a biopsy indication was far more common in the elderly, although they were not the most commonly biopsied. Whether this represents reluctance on the part of the nephrologists to biopsy the elderly is unclear.

Given their indications for biopsy in the setting of AKI (which we assume are similar to other countries) and the fact that we are dealing with a Glomerulonephritis Registry, 90% of their patients had an “active urinary sediment,” an unusual finding in what are typically thought to be the most common causes of AKI (ATN or “prerenal”). This underscores the intense selection bias resulting from clinical practice inherent in any particular registry study of AKI. Presumably, clinical evaluation led to the elimination of prerenal and postrenal causes of AKI. In essence, then, this study answers the question: “what will one find on biopsy of patients with AKI who are thought not to have ATN, but presumably glomerulonephritis?” The results deserve examination in the light of this formulation. Accordingly, one might be reassured that ATN was found in only 5% of these cases, despite its far larger presumed prevalence in patients with AKI overall (6). Nevertheless, the development of ATN is often multifactorial, and its histologic findings can be subtle, raising the possibility that some cases of ATN were classified under other entities. Of course, in that case it is also likely that those entities played a role in the development of the ATN. It is also notable that the percentage of ATN was similar in all three ages, a finding that does not appear to reflect clinical experience.

This report is a rare opportunity to document the causes of AKI in a selected biopsy population. However, what this study cannot answer, and what deserves asking, is the inverse question: how many patients clinically thought to have ATN actually don’t, and have a different renal disease instead? We may know less than we think we do. In other words, how many patients have treatable forms of AKI that are being missed as a result of current biopsy practice? Despite the impossibility of fully answering this question, there are several studies suggesting significant discordance between prebiopsy and postbiopsy diagnoses in the setting of AKI. Haas et al. studied the elderly and found the clinical diagnosis to be incorrect in 34% of cases biopsied, many of them involving potentially treatable entities (7). In a more recent biopsy study, Uezono et al. found that, among elderly patients presenting with acute or rapidly progressive renal injury, 71% had pauci-immune, myeloperoxidase–antineutrophil cytoplasmic antibody-positive, crescentic glomerulonephritis and 17% had interstitial nephritis; both groups benefited from therapeutic intervention (8). Histopathologic and prebiopsy clinical diagnoses differed in 15% of patients, and the complication rate after biopsy was low (3%) (8). Unfortunately, the Spanish Registry did not correlate clinical and pathologic diagnosis nor report on outcome. Furthermore,
we don’t know how many of their patients were initially thought to have ATN, did not get better, and when eventually biopsied, were found to have another entity. Clinical experience suggests that that is not a very rare scenario, and delay in diagnosis may affect outcome. Given the relative safety of the modern renal biopsy, the question as to whether current biopsy practice is appropriate deserves further investigation.

Some of the findings in this study may be relevant to this issue. Most of the pathologic diagnoses were entities that are both difficult to recognize without biopsy and are treatable. Vasculitis was the most common cause (23%). Given that, it is unfortunate that antineutrophil cytoplasmic antibody results were unavailable. Acute interstitial nephritis was next at 11%. For reasons that remain unclear, crescentic immune complex disorders and anti-GBM disease were lumped together in this study and comprised 10% of the biopsies (12% when the separately listed anti-GBM antibody category is added). At least 10% of the other causes found met these criteria. Interestingly, IgA nephropathy comprised 8.8% of cases, underscoring that it can be a significant cause of AKI. How many of these cases were of the more acute and reversible form of IgA associated AKI, as opposed to irreversible scarring, is unclear. The prevalence of diabetic nephropathy was surprisingly low. The results, when stratified by age, permit additional observations: vasculitis was prominent in the elderly and thrombotic microangiopathy in the young (although the prevalence of thrombotic microangiopathy in adults/elderly appeared somewhat low). Interestingly, the prevalence of AKI as an indication for biopsy increased over the course of the study period. This may represent an increase in incidence or a change in practice patterns, but we do not have solid data to choose one of the two possibilities.

An important caveat when examining the findings relates to the way that the patients were classified clinically. Apparently, each patient was given only one designation, for example, nephritic syndrome or AKI, but not both. Perhaps they chose the AKI designation only when other possibilities were absent. Either way, how this might affect the significance of these data for patients typically not biopsied is uncertain.

Despite many of these and other issues, this biopsy registry report provides crucial and useful data in a field where there is still far too limited knowledge. For that alone, we should thank our Spanish colleagues. May they serve as an inspiration to others!

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Disclosures
None.

References

See related article, “Renal Biopsy Findings in Acute Renal Failure in the Cohort of Patients in the Spanish Registry of Glomerulonephritis,” on pages 674–681.