The Impact of Renal Tissue Procurement at Bedside on Specimen Adequacy and Best Practices

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ABSTRACT

Objectives: Renal biopsy is the gold standard for the diagnosis of both native and allograft renal diseases. We studied the impact of tissue procurement at bedside (TPB) omission on the adequacy of renal biopsies.

Methods: We compared 120 renal biopsies collected during 2015 using TPB with 111 renal biopsies collected during 2016 when TPB was discontinued. Adequacy criteria were applied as follows: by light microscopy, 10 glomeruli and two arteries for allograft biopsies and seven glomeruli for native biopsies. At least one glomerulus was considered adequate for immunofluorescence and electron microscopy in both groups.

Results: The rate of inadequacies in allograft biopsies increased significantly, from 12.50% to 21.61% (P < .05), when TPB was discontinued.

Conclusions: Elimination of TPB service had a negative impact on allograft specimen adequacy. Repeat biopsies add cost and delay patient care. Institutions should take this into consideration when considering omission of TPB.

Percutaneous renal needle core biopsy is considered to be the gold standard for the diagnosis of most renal diseases. The procedure involves collecting one or more needle core biopsies, which are then submitted for evaluation by light microscopy (LM), immunofluorescence (IF), and electron microscopy (EM). As the major structure of interest in most diagnostic renal biopsies is the glomerulus, it is ideal, if not essential, that at least one or more glomeruli are present for study by each of these modalities. The exact number of glomeruli that need to be sampled to reasonably exclude a diagnosis varies depending on the disease in question, the structures involved, and the distribution of the lesion throughout the kidney. To diagnose a diffuse disease that involves all the glomeruli of the kidney, a single glomerulus would be enough, while to diagnose a focal disease where some of the glomeruli will be normal a greater number of glomeruli are needed for examination. Moreover, what constitutes an adequate biopsy depends on whether the procedure is performed on a native kidney or on an allograft kidney.

Allograft biopsies are evaluated using the Banff criteria, which lays out both the criteria for specimen adequacy and the grading system for the various lesions seen in the allograft biopsy. On the other hand, for native renal biopsies, there are no widely accepted numerical criteria for adequacy. In some institutions, a biopsy with material sufficient to render a diagnosis is considered adequate while others use internally decided adequacy criteria. Many institutions use the cutoff of seven or eight glomeruli in LM sections for native kidney biopsies.

The primary method that ensures the presence of glomeruli for all three modalities is the on-site evaluation of the biopsy core(s) by a trained technologist, referred
to as tissue procurement at bedside (TPB) in our institution. The rapid evaluation allows for additional tissue to be requested prior to the termination of the biopsy procedure, if necessary. TPB also provides the opportunity to divide the biopsy under the dissecting microscope for LM, IF, and EM, maximizing the utilization of the cores. Depending on how busy the renal service is, TPB can represent substantial investment of man-hours, which may be difficult to justify.\(^5\) TPB was performed at our institution for many years before being discontinued in January 2016, due to a manpower shortage.

IF and EM are critical tools in the evaluation of renal diseases. IF remains the primary tool used by nephropathologists to examine a variety of antigens in both allograft and native biopsies.\(^7\) EM is performed routinely on native kidney biopsies and contributes meaningfully to the diagnosis in many cases.\(^7\) For the allograft kidney, EM is occasionally omitted but has been demonstrated to provide important evidence that can support the diagnosis of antibody-mediated rejection and glomerular diseases.\(^7\,8\)

In our study we compare two consecutive years of renal biopsies, the first calendar year with TPB (2015) and the second year without (2016). The goal of this investigation was to determine if lack of TPB significantly affects the adequacy of our biopsy material.

### Materials and Methods

This was a single center, retrospective study. The authors searched the laboratory information system for all percutaneous renal core biopsies performed between January 1, 2015, and December 31, 2016. Biopsies for focal lesions, such as tumors, were excluded. The pathology reports were reviewed and the following data were extracted: the number of glomeruli present in sections for LM, IF, and EM; the number of arteries present in allograft biopsies; and the number of cores collected.

A single core was obtained to limit the possibility of hemorrhage postbiopsy in a minority of cases in both years at the request of the treating physician. In these cases, if TPB was performed, the technologist still divided the specimen under the dissecting microscope to maximize tissue availability for each diagnostic modality.

Biopsies performed between January 1, 2015, and December 31, 2015, were evaluated at the bedside under a dissecting microscope by either a nephropathologist or a technologist trained by the nephropathologist. The cores were divided under the dissecting microscope prior to being placed in fixative. Biopsies collected between January 1, 2016, and December 31, 2016, were placed in fixative (Zamboni for LM and EM and Michel solution for IF) by the interventional radiologist or nephrologist without being evaluated under the dissecting microscope.

Based on a review of the literature and current published guidelines concerning biopsy adequacy, cutoffs were defined as follows for each modality:\(^4\):

- **LM**: 10 glomeruli for allograft biopsies and seven glomeruli for native biopsies
- **LM**: two arteries for allograft biopsies
- **IF**: at least one glomerulus for both allograft and native biopsies
- **EM**: at least one glomerulus for both allograft and native biopsies.

To quantify the degree to which the biopsy was inadequate, the following scoring system was devised: biopsies were given one point for each of the above modalities found to be deficient. The inadequacy rate was calculated as the total number of inadequacies, up to four for allograft or three for native per biopsy, divided by the total number of possible inadequacies for the group. When calculating the average number of cores present for histologic evaluation, cases with fragmented cores were excluded to not artificially inflate the average.

A two-tailed two-proportions was used with an \(\alpha\) of 0.05. Fisher exact test was applied to determine the statistical significance between data obtain from 2015 and 2016.

### Results

A total of 120 renal biopsies (52 allograft, 68 native) were collected in 2015 using TPB and 111 biopsies (59 allograft, 52 native) were collected in 2016 without TPB. Both the allograft and native groups were compared year to year. The rate of inadequacies was higher in the 2016 allograft kidney biopsies when compared to the 2015 group (21.61% and 12.50%, respectively) \(\text{Table I}\). This difference was statistically significant \(P = .012\).

Statistically significant differences were also seen in the analysis of the individual modalities. In 2016, 17 allograft biopsies had less than 10 glomeruli present
Discussion

The percutaneous renal biopsy is a well-established procedure that physicians rely upon to diagnose and monitor therapy for renal diseases. High-quality specimens with an adequate number of glomeruli and, additionally, in the case of allografts, an adequate number of arteries, are essential for accurate evaluation to occur. The vast majority of biopsies provide actionable information to the clinician. Correct treatment of the disease process may hinge on the biopsy result, and any delay in diagnosis may adversely impact patient outcomes.

Historically, renal biopsies have been performed primarily by nephrologists. Over the years though, more of these biopsies are being performed by interventional radiologists who may not be as cognizant of the adequacy criteria or their impact on interpretation of the renal biopsy. Despite the benefits of image guidance in the radiology suite, TPB is the only method to ensure that adequate material is obtained.

Even though the renal biopsy is generally considered a safe procedure, complications, mostly related to bleeding, are well described in the literature and occur in around 10% of patients. Taking this into account, a single biopsy procedure that obtains sufficient specimen should be the goal of the team caring for the patient. Usually, multiple cores are collected to provide sufficient material for all diagnostic modalities. Studies have demonstrated that collecting a single core does not significantly reduce the complication rate when compared to collecting multiple cores. Taking only a single core may be a consideration in circumstances where there is concern about complications but this should be avoided when possible. The decision to collect a single core should involve a discussion between the nephropathologist, the primary care team, and the service performing the biopsy to achieve a balance between patient safety and need for an adequate sample.

Furthermore, adequate biopsies help to constrain costs for the patient and institution. Looking specifically at the inpatient setting, a repeat biopsy will result in a minimum of one to two additional hospital days, at a cost of on average US$2,000 per day, if a diagnosis can be made on LM findings alone. When IF or EM studies are required the delay may grow, further increasing the cost. By comparison, providing TPB is relatively inexpensive, occupying on average 30 minutes of the pathologist’s or technologist’s time based on our institutional experience. If well-coordinated with the clinical services, this should cause minimal disruptions to daily work flows.

An additional benefit to TPB is the educational opportunity it can provide to the fellows and residents from nephrology and interventional radiology who are involved in collecting and handling these specimens. In providing this service, the importance of specimen adequacy and handling can be discussed with the involved trainees who may be asked to provide this service themselves later in their careers. In our institution, nephropathology fellows as well as pathology residents receive theoretical and practical training from the staff nephropathologist covering all aspects of the biopsy procedure, evaluation of tissue adequacy, tissue processing, and slide interpretation. At institutions fortunate enough to sponsor a nephropathology fellowship, the fellow, as part of their training, will likely play a central role overseeing and managing TPB.

Most other investigations have classified renal biopsies as either adequate or inadequate, with some including suboptimal as a third group. We have taken a slightly different approach in our study, choosing to assign points for each inadequacy occurring in any of the three modalities. The idea behind this approach was that a biopsy that was deficient in multiple modalities had an increased likelihood of being of lower diagnostic quality.

TPB is used in many centers to help ensure specimen adequacy. The impact of bedside tissue evaluation on specimen adequacy has been investigated by several authors. The results are somewhat mixed but...
in general demonstrate increased adequacy rates when TPB is utilized. While there are well-established criteria to define adequacy for renal allograft biopsies, no such guidance is available for renal native biopsies, and these authors have each defined their own adequacy criteria. Development of adequacy criteria for native biopsies would help to standardize practice and allow for more easily comparable data in future studies of these tissue specimens.

Our study demonstrates a significant difference in the inadequacy rates of the allograft biopsies collected without TPB compared to those with TPB. When TPB is omitted, it is impossible to ensure that sufficient material will be present for LM, IF, and EM. Paradoxically, in our study, we did not find a significant change in the inadequacy rate of native kidney biopsies when performed without TPB despite the more technically difficult nature of this procedure. This is most likely due to the increase in the number of intact cores collected from an average of 2.76 to 3.49. Having more material available for evaluation seems to have masked any increase in the inadequacy rate caused by the absence of TPB. We did not identify a cause for the increased number of cores collected in this group.

In the event that it is not possible to provide TPB, it may be helpful to give guidance to the clinician who is performing the biopsy about the number of cores to collect. Guidelines from the Banff group and the Ad Hoc Committee on Practice Guidelines have suggested that a minimum of two cores should be obtained for allografts in order to provide sufficient sensitivity in detecting rejection. Goldstein et al found that three or four cores allowed for a histologic diagnosis to be reached in both native and allograft biopsies. In their study, three cores resulted in a diagnosis in 84% of cases and four cores increased that number to 94%. The effect of TPB discontinuation on the rate of biopsy complications and its impact on the quality of the diagnosis were not evaluated in our study and therefore are possible limitations of this investigation. The authors plan to address these limitations in a separate study. We also plan to conduct a cost analysis for the operation of a TPB service.

In conclusion, use of TPB helps to ensure the adequacy of renal biopsies. Our study demonstrated that discontinuation of TPB lead to a significant increase in the rate of inadequacy in our allograft biopsies. This can result in increased risks to the patient and potential cost increases for the health care system. Health care systems should keep this in mind when considering either instituting or discontinuing a TPB service.

References