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Spot Urine Protein/Creatinine Ratio Testing at a Large University Medical Center: Evidence for Overuse of This Low-Value Diagnostic Test

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We and others have documented the remarkable unreliability of spot urine (single void) protein/creatinine ratio (PCR) testing as an estimate of proteinuria magnitude.[1] However, the extent to which spot PCR testing has displaced 24-hour urine PCR testing has not been examined previously. Here, we analyze this experience at the Ohio State University Wexner Medical Center. Our site is relevant because we are a large academic medical center, and our nephrology group has long championed the cause of estimating proteinuria magnitude from the PCR of an overnight collection (first morning void) or from an intended 24-hour urine collection that is approximately 50% of a complete 24-hour urine collection. To our chagrin, spot urine (single void) testing constitutes almost all of the testing to quantitate proteinuria at our institution. Here, we quantify this overuse, and describe how it likely compromised clinical care. Also discussed are steps to marginalize the utilization of this test, as it has very low clinical value.

Random, single-void (spot) urine PCR is often a highly unreliable estimate of proteinuria magnitude.[1] The problem is that in patients with glomerular proteinuria, the urine protein excretion rate is highly variable hour by hour, but the urine creatinine excretion rate is relatively stable.[1] Therefore, short collections (e.g., spot collections) reveal this PCR variability, whereas long collections (e.g., all or most of a 24-hour collection) conceal this PCR variability, because the PCR of the long collections can be viewed as the integrated mean of each of the spot collections that make up the intended 24-hour collection.

The other major flaw inherent in spot PCR testing is that, as we have recently shown, serial spot PCR testing cannot be trusted to reliably determine proteinuria trend.[1] This limitation was shown in our *post hoc* analysis of Abatacept and Cyclophosphamide Combination Efficacy and Safety Study (ACCESS), a randomized double-blind intervention trial in which 103 patients with severe lupus nephritis had 24-hour urine PCR (24-hour PCR) and spot PCR measured concurrently, during up to 15 months of follow-up care.[1] We found that spot PCRs were unreliable in identifying proteinuria trend in about half the patients.[1] Unfortunately, those who produced unreliable spot PCRs could be identified only in retrospect. In other words, there were no baseline predictors of which patients would produce unreliable spot PCRs. Therefore, spot PCR testing results were useless in clinical decision-making. Indeed, the degree of unreliability of spot PCRs was such that serious management errors likely would have occurred if the clinician had trusted the spot PCR test results.[1]

The only sure way to assess proteinuria magnitude and proteinuria trend is to use intended 24-hour urine collections in which the creatinine content of the collection indicates that the patient provided ≥50% of a complete 24-hour collection. We and others have shown that this level of collection produces a PCR that is not significantly different from the PCR of a complete 24-hour urine collection.[1]

An acceptable alternative to an intended 24-hour collection is a first morning void that represents

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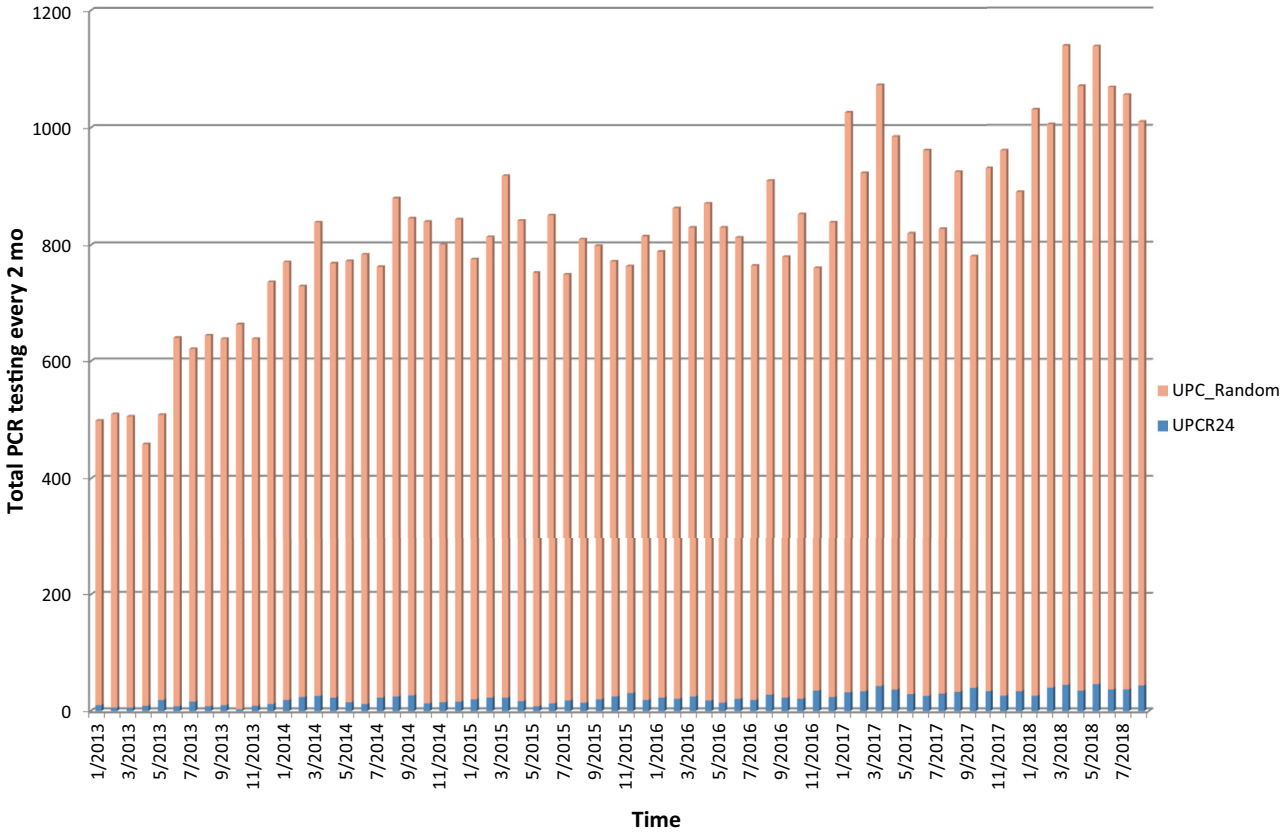

Figure 1. Change in protein/creatinine ratio (PCR) testing over time in the Ohio State University Wexner Medical Center laboratories since 2013. The height of the bars indicates the total number of PCR testings (spot and 24-hour) each 2 months since 2013. The red bars show the spot PCR (UPC_Random), and the blue bars show the 24-hour PCR (UPCR24) utilization.

all of the urine formed during sleep time. Although this method underestimates proteinuria magnitude by about 20%,[1] that degree of inaccuracy is acceptable. Unacceptable urine collections are those that represent only a few hours of urine production, as shown by Koopman *et al.*[1] in a unique study done in patients with primary glomerulopathy. In an effort to minimize proteinuria variability, patients were maintained supine for 3 days, on a constant diet, and receiving no medications. Urine was collected each 3 hours during the study. Despite these measures, PCR variability of the individual collections was remarkable.

Since our original descriptions of spot PCR variability, numerous other studies have corroborated our work.[1] Nevertheless, it would be a fair statement that the Nephrology Division of the Ohio State University Wexner Medical Center is *ground zero* for documenting the remarkable inadequacy of spot PCR testing. We have dutifully shared these insights with our Ohio State University Wexner Medical Center colleagues and house officers. So, it was of interest for us to examine the utilization of spot PCR and 24-hour PCR at our institution over the past 5 years.

As shown in Figure 1, the overwhelming majority of proteinuria testing was spot PCR, even among inpatients. The latter finding is remarkable because *convenience to the patient* is the most common reason given for testing spot urine collections rather than 24-hour urine collections. This concern, however, is not relevant to inpatient testing.

A relevant concern regarding the present work is the extent to which the spot PCRs actually represent the PCRs of a complete overnight collection. The latter would be a reliable estimate of 24-hour protein.[1] However, based on our experience at our institution, very few of the spot PCRs depicted in Figure 1 reflect the PCRs of complete overnight collections.

It is respectfully suggested that steps need to be taken to eliminate spot PCR testing. It can be cogently argued that spot PCR testing is among the most useless of routine clinical tests. How else would one describe a test that is highly inaccurate in many/most patients, and of which its unreliability can be determined only in retrospect? Also, this low-value diagnostic test incurs significant cost. At the Ohio State University Wexner Medical Center, the list

price for either spot or 24-hour PCR testing is $75. Over recent years, the utilization of spot PCR testing has been rising (see Figure 1). In the most recent year, more than 6000 spot PCR tests were performed by our clinical laboratory. None of those spot PCRs can be trusted, but unfortunately, spot PCR test results *are* trusted. Undoubtedly, this trust has resulted in serious management errors, as previously discussed.[1]

Some might argue that doing spot PCR testing at the time of the outpatient encounter is better than not doing spot PCR testing. This strategy is flawed. There are dangers inherent in basing clinical decisions on spot PCR test results.[1] That danger can be avoided by not utilizing spot PCR test results. Instead, the physician should instruct the patient to provide either a 24-hour urine collection or an overnight urine collection at a time deemed appropriate by the physician. If the physician feels compelled to do something at the time of the outpatient visit, urine dipstick testing for protein and specific gravity can be performed. This is a rough estimate of the urine PCR. Of course, that test result, like the spot PCR, should not be used in clinical decision-making.

It has been our experience that patients can be easily trained to bring in intended 24-hour urine collections or an overnight collection to each of their clinic visits. Tips for the patient in providing these collections have been discussed previously.[1] However, this approach is seldom used at our institution.

Although ours is only a single-center study, it is our belief, based on our interactions with physicians locally and nationally, that massive overuse of spot PCR testing is a pervasive problem. We suggest further that this editorial describes an object lesson in what can happen when a diagnostic test is adopted, essentially by acclamation, based on specious evidence (statistically significant correlation between spot PCR and 24-hour PCR, when these measures are compared over a wide range of abnormal values[1]). The diagnostic test then becomes entrenched because it is acknowledged by clinical guidelines from authoritative sources, in this case, Kidney Disease: Improving Global Outcomes[3] (KDIGO) and the American College of Rheumatology[4] (ACR).

The following actions are suggested:

(i) Medical insurers should deny payment for spot PCR testing in adults.
(ii) Medical insurers should, however, pay for PCR testing on urine collections made over a substantial period of time. Shidham and Hebert showed that 3-hour urine collections are inadequate.[2] However, an overnight (morning void) collection, or collections >6 hours, provide reasonably good estimates of 24-hour PCR.[1] So, it would seem reasonable to deny payment unless the urine collection period is ≥6 hours in duration, based on its creatinine content.

Summary

(i) It is plausible that spot PCR is the most unreliable clinical test currently available.
(ii) There is no role for spot PCR testing in adults for clinical purposes. To the best of our knowledge, the reliability of spot PCR testing in children has not been rigorously studied.
(iii) The only role for spot PCR testing is in research, for example, when comparing proteinuria levels between large groups. In that situation, the errors inherent in spot PCRs will be equally distributed between the groups being compared and, therefore, offsetting.
(iv) The Kidney Disease Improving Global Outcomes (KDIGO) and the American College of Rheumatology (ACR) guidelines should state specifically that spot PCR testing should not be used in clinical management.

DISCLOSURE

All the authors declared no competing interests.

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