HHS Public Access

Author manuscript

*JAMA Intern Med*. Author manuscript; available in PMC 2015 May 05.

Published in final edited form as:

*JAMA Intern Med*. 2015 May 1; 175(5): 853–856. doi:10.1001/jamainternmed.2015.17.

# The Usefulness of Diagnostic Testing in the Initial Evaluation of Chronic Kidney Disease

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Chronic kidney disease (CKD) affects approximately 13% of adults in the United States and is associated with significant morbidity, mortality, and costs.[1–3] There is a broad differential for CKD, including diabetes mellitus, hypertension, glomerulonephritis, tubulointerstitial disease, urologic causes, and unknown causes.[2] To our knowledge, a comprehensive assessment of the tests used in CKD evaluation has not been conducted. We determined how often laboratory and imaging tests were obtained in the initial evaluation of CKD and whether these tests affected diagnosis and/or management.

## Methods

We conducted a retrospective cohort study of patients referred for initial evaluation of CKD from January 1, 2010, to January 1, 2013, to nephrology clinics affiliated with Brigham and Women's Hospital and Massachusetts General Hospital in Boston, Massachusetts; 1487 patients were included (Table 1). Partners Institutional Review Board approved the study and waived the need for informed consent. Electronic medical records were abstracted. We used methods to ensure the validity and reliability of data, including review of 10 initial medical records by 2 of us (M.L.M. and S.S.W.) to refine criteria.[4] Tests obtained at another clinic before the nephrology clinic visit were documented.



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**Conflict of Interest Disclosures:** Dr Waikar served as a consultant to Abbvie, CVS Caremark, Harvard Clinical Research Institute, and Takeda; provided expert testimony or consultation for litigation related to nephrogenic systemic fibrosis (GE Healthcare) and mercury exposure; and has received grants from the National Institute of Diabetes and Digestive Kidney Diseases, Genzyme, Merck, Otsuka, Pfizer, and Satellite Healthcare. No other conflicts are reported.

**Author Contributions:** Drs Mendu and Waikar had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
*Study concept and design:* Mendu, Aizer, Steele, Waikar.
*Acquisition, analysis, or interpretation of data:* All authors. *Drafting of the manuscript:* Steele, Mendu.
*Critical revision of the manuscript for important intellectual content:* All authors. *Statistical analysis:* Mendu, Aizer.
*Administrative, technical, or material support:* Mendu, Leaf, Waikar.
*Study supervision:* Robinson, Steele, Waikar.

We reviewed nephrology progress notes to ascertain the presumed cause of CKD and whether a test had been documented to affect the diagnosis and/or management. A test was considered to have affected diagnosis and/or management if it was specifically stated to have contributed to, confirmed, or established the underlying diagnosis of and/or any management decision related to CKD. This definition included documentation of negative and positive test results and diagnoses related to CKD. A second reviewer (E.R.) blindly abstracted a random sample of 36 patients' records (2.4% of patients). The degree of interrater agreement, assessed by the prevalence-adjusted, bias-adjusted statistic,[5,6] was a mean (SE) of 0.89 (0.02).

## Results

Among the 1487 patients included, common comorbidities were hypertension (79.0%) and diabetes (58.4%), and CKD stages were 3b (39.5%) and 3a (28.7%) (Table 1). Frequently obtained tests included measurement of calcium (94.8%), hemoglobin (84.0%), phosphate (83.5%), urine sediment (74.8%), and parathyroid hormone (74.1%) levels; urine dipstick for blood (69.9%) and protein (69.7%); serum protein electrophoresis (68.1%); and renal ultrasonography (67.7%) (Table 2). Determination of the hemoglobin $A_{1c}$ level, urine total protein to creatinine ratio, and urine microalbumin to creatinine ratio had relatively high yields, affecting diagnosis in 15.4%, 14.1%, and 13.0% of the patients and management in 10.1%, 13.7%, and 13.3%, respectively. Serum protein electrophoresis and renal ultrasonography, although frequently performed, had much lower yields, affecting diagnosis in 1.4% and 5.9% and management in 1.7% and 3.3% of the patients, respectively. Results of tests to detect antineutrophil cytoplasmic antibody and antiglomerular basement membrane antibody did not affect the diagnosis or management in any patients.

## Discussion

In this analysis of patients undergoing initial evaluation of CKD, we found that many tests are obtained frequently despite low rates of effect on diagnosis and management. Certain tests, such as serum protein electrophoresis and screening for antinuclear antibody, C3, C4, hepatitis C, hepatitis B, and antineutrophil cytoplasmic antibody, were obtained often (13.4%–68.1%) despite infrequently affecting diagnosis or management (0–1.7%). In contrast, hemoglobin $A_{1c}$ and urine protein quantification tests affected the diagnosis and management in 13.0% to 15.4% of the patients. These findings are limited by the retrospective study design, subjective nature of evaluating clinical usefulness, potential underestimation of the benefit of negative test results, and representation from only 2 academic medical centers in the northeastern United States. Further investigation incorporating community-based patients and identifying subgroups benefiting from more extensive evaluation is needed. However, this study suggests that reflexively ordering several tests for CKD evaluation and management may be unnecessary. An evidence-based, targeted approach based on pretest probabilities of disease for diagnosis and management may be more efficient and reduce costs.

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## Table 1

Patient Demographics and Clinical Characteristics

| Characteristic | No. (%) |
|---|---|
| Male sex | 914 (61.4) |
| Age, median (IQR), y | 70 (61–79) |
| Married or with partner | 845 (56.8) |
| English speaking | 1402 (94.3) |
| Race | |
| White | 1084 (72.9) |
| African American | 189 (12.7) |
| Hispanic | 149 (10.0) |
| Other | 65 (4.4) |
| Comorbidities | |
| Hypertension | 1175 (79.0) |
| Diabetes mellitus | 868 (58.4) |
| Coronary artery disease | 382 (25.7) |
| History of cancer | 359 (24.1) |
| Gout | 207 (13.9) |
| Anemia | 182 (12.2) |
| Obesity | 164 (11.0) |
| Congestive heart failure | 142 (9.6) |
| Benign prostatic hypertrophy | 139 (9.3) |
| Kidney stones | 130 (8.7) |
| Connective tissue disease | 60 (4.0) |
| Nephrectomy | 44 (3.0) |
| Monoclonal disease | 41 (2.8) |
| Lupus erythematosus | 18 (1.2) |
| History of hydronephrosis | 18 (1.2) |
| History of renal artery stenosis | 13 (0.9) |
| Proteinuria[a] | 625 (42.0) |
| CKD stage[b] | |
| 1 or 2 | 183 (12.3) |
| 3a | 427 (28.7) |
| 3b | 589 (39.5) |
| 4 | 276 (18.6) |
| 5 | 12 (0.8) |
| Medications before initial visit | |
| Statin | 865 (58.2) |
| ß-Blocker | 810 (54.5) |

| Characteristic | No. (%) |
|---|---|
| ACE inhibitor | 608 (40.9) |
| Calcium channel blocker | 531 (35.7) |
| Proton pump inhibitor | 426 (28.7) |
| Thiazide diuretic | 378 (25.4) |
| Loop diuretic | 307 (20.6) |
| Angiotensin receptor blocker | 306 (20.6) |
| Vitamin D supplement | 245 (16.5) |
| Nonsteroidal anti-inflammatory drugs | 203 (13.7) |
| Allopurinol | 147 (9.9) |
| Renal replacement during study | |
| Dialysis | 40 (2.7) |
| Transplant | 4 (0.3) |

Abbreviations: ACE, angiotensin-converting enzyme; CKD, chronic kidney disease; IQR, interquartile range.

[a] Urine dipstick for protein result of 1+ or greater, microalbuminuria (≥30 mg/g), urine protein to creatinine ratio greater than 0.2.

[b] Based on most recent estimated glomerular filtration (eGFR) rate before study enrollment period. CKD stage 1–2, eGFR, greater than 60 mL/min/1.73 $m^2$; stage 3a eGFR, 45 to 59 mL/min/1.73 $m^2$; stage 3b eGFR, 30 to 44 mL/min/1.73 $m^2$; stage 4 eGFR, 15 to 29 mL/min/1.73 $m^2$; and stage 5 eGFR, less than 15 mL/min/1.73 $m^2$.

## Table 2

Frequency and Yield of Diagnostic Testing Obtained in the Initial Evaluation of CKD

| | No. (%)[a] | | | |
|---|---|---|---|---|
| **Test Obtained** | **Frequency (N = 1487)** | **Abnormal Results[b]** | **Affected Diagnosis[c]** | **Affected Management[d]** |
| **Primarily for Diagnosis** | | | | |
| Urine | | | | |
| Sediment | 1112 (74.8) | 104 (9.4) | 39 (3.5) | 37 (3.3) |
| Dipstick for protein | 1036 (69.7) | 356 (34.4) | 25 (2.4) | 23 (2.2) |
| Dipstick for blood | 1039 (69.9) | 159 (15.3) | 19 (1.8) | 22 (2.1) |
| SPEP | 1012 (68.1) | 84 (8.3) | 14 (1.4) | 17 (1.7) |
| Renal ultrasonography | 1007 (67.7) | 270 (26.8) | 59 (5.9) | 33 (3.3) |
| Urine microalbumin to creatinine ratio | 901 (60.6) | 494 (54.8) | 117 (13.0) | 120 (13.3) |
| Urine total protein to creatinine ratio | 811 (54.5) | 415 (54.8) | 114 (14.1) | 111 (13.7) |
| UPEP | 526 (35.4) | 23 (4.4) | 6 (1.1) | 8 (1.5) |
| ANA | 423 (28.5) | 218 (51.5) | 4 (0.9) | 5 (1.2) |
| Uric acid | 390 (26.2) | 172 (44.1) | 12 (3.3) | 38 (9.7) |
| Serum-free light chains | 374 (25.2) | 168 (44.9) | 5 (1.3) | 8 (2.2) |
| C3 | 360 (24.2) | 25 (6.9) | 5 (1.4) | 5 (1.4) |
| C4 | 359 (24.1) | 29 (8.1) | 4 (1.1) | 4 (1.1) |
| HBV[e] | 262 (17.6) | 1 (0.4) | 1 (0.4) | 1 (0.4) |
| HCV | 259 (17.4) | 3 (1.2) | 2 (0.8) | 2 (0.8) |
| ANCA | 205 (13.8) | 5 (2.4) | 0 | 0 |
| Hemoglobin $A_{1c}$ | 188 (12.6) | 72 (38.3) | 29 (15.4) | 19 (10.1) |
| Rheumatoid factor | 156 (10.5) | 19 (12.2) | 1 (0.6) | 3 (1.9) |
| DsDNA | 128 (8.6) | 9 (7.0) | 1 (0.8) | 2 (1.6) |
| Anti-Ro antibody | 77 (5.2) | 8 (10.4) | 2 (2.6) | 4 (5.2) |
| Anti-La antibody | 77 (5.2) | 5 (6.5) | 2 (2.6) | 4 (5.2) |
| Cryoglobulins | 74 (5.0) | 3 (4.1) | 4 (5.4) | 4 (5.4) |
| Kidney biopsy | 70 (4.7) | 70 (100) | 70 (100) | 70 (100) |
| Anti-GBM | 52 (3.6) | 0 | 0 | 0 |
| Abdominal CT | 33 (2.2) | 18 (55.5) | 11 (33.3) | 6 (18.2) |
| Creatine kinase | 30 (2.0) | 7 (23.3) | 1 (3.3) | 1 (3.3) |
| Renal nuclear scan | 24 (1.6) | 22 (91.7) | 16 (66.7) | 8 (33.3) |
| LDH | 19 (1.3) | 12 (63.2) | 1 (5.3) | 2 (10.5) |
| Haptoglobin | 15 (1.0) | 4 (26.7) | 1 (6.7) | 3 (20) |
| Antiphospholipid antibody | 12 (0.8) | 4 (33.3) | 1 (8.3) | 2 (16.7) |
| HIV | 6 (0.4) | 0 | 0 | 0 |
| Abdominal | | | | |
| MRI | 4 (0.3) | 3 (75) | 0 | 0 |

| Test Obtained | No. (%)[a] | | | |
|---|---|---|---|---|
| | Frequency (N = 1487) | Abnormal Results[b] | Affected Diagnosis[c] | Affected Management[d] |
| MRA | 4 (0.3) | 0 | 0 | 0 |
| **Primarily for Management** | | | | |
| Calcium | 1410 (94.8) | 123 (8.7) | 5 (0.4) | 8 (0.6) |
| Hemoglobin | 1249 (84.0) | 373 (29.9) | 0 | 90 (7.2) |
| Phosphate | 1242 (83.5) | 214 (17.2) | 3 (0.2) | 19 (1.5) |
| Parathyroid hormone | 1102 (74.1) | 619 (56.2) | 0 | 97 (15.7) |
| 25-Hydroxyvitamin D | 817 (54.9) | 352 (43.1) | 0 | 119 (14.6) |
| Iron | 551 (37.1) | 52 (9.4) | 0 (0.2) | 84 (15.2) |
| LDL-C | 163 (11.0) | 65 (39.9) | 0 | 11 (6.7) |

Abbreviations: ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibody; Anti-GBM, antiglomerular basement membrane antibody; CKD, chronic kidney disease; CT, computed tomography; DsDNA, double-stranded DNA; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; LDH, lactate dehydrogenase; LDL-C, low-density lipoprotein cholesterol; MRA, magnetic resonance angiogram; MRI, magnetic resonance imaging; SPEP, serum protein electrophoresis; UPEP, urine protein electrophoresis.

[a] The denominator for the percentages provided is the number of tests ordered.

[b] Defined for most laboratories based on the reference range established by the laboratory. For urine sediment, any finding other than an acellular sediment or epithelial cells was considered to be abnormal. For SPEP, UPEP, and serum-free light chains, any abnormal immunoglobulin finding was considered to be abnormal. For parathyroid hormone, Kidney Disease Outcomes Quality Initiative target plasma levels based on CKD stage were used to define abnormal laboratory values.[2] An abnormal finding for imaging was defined as any abnormality documented in the final report, with the exception of simple cysts and nonobstructive stones for renal ultrasonography.

[c] Defined as any test result that was noted in the nephrology progress notes to have contributed to, confirmed, or established any diagnosis.

[d] Defined as any test result that were noted in the nephrology progress notes to have contributed to any management decision.

[e] It is recommended that patients with advanced CKD (≥stage 4) receive hepatitis B vaccination before dialysis is initiated, and it is possible that some of these patients had hepatitis B serology tests performed for that reason; the serology tests were performed in 44 patients with CKD stage 4 and in 2 patients with CKD stage 5.