An Approach To The Evaluation Of An Elevated Serum Creatinine

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Citation

Abstract
Serum creatinine can be an effective means of assessing renal function. This paper offers an approach to the evaluation of an elevated creatinine that can be undertaken by primary care physicians.

An evaluation should begin by excluding potentially surreptitious etiologies of the elevation, including medications and physiologic states. The serum creatinine should then be used to estimate glomerular filtration rate (GFR) using one of the GFR estimation equations. If the GFR is decreased, workup to include history and physical, urinanalysis and renal ultrasound should be performed. The results of these studies may lead to further workup and/or referral.

Serum creatinine is one of the most common assays measured by primary care physicians. Generally correlated with renal function, it offers a rapid, effective test. Knowing what to do with the results of an elevated study is, however, less clear. Few guidelines regarding the appropriate workup or approach to an elevated creatinine are available.

The gold standard measurement of kidney function is the glomerular filtration rate (GFR).1 Serum creatinine is a simple and effective means of estimating GFR. Elevations of serum creatinine are thus important within the context of their relationship with GFR, and should be evaluated with this in mind. This paper offers one approach to the evaluation of an elevated serum creatinine.

PHYSIOLOGY
In the steady state, serum creatinine is an ideal marker of glomerular filtration.2 The steady state is dependant upon constant generation and excretion, the perturbations of which can affect clinical correlations between serum levels and glomerular filtration. In addition, 5 to 10% of excreted creatinine is secreted in the proximal tubule, rather than being filtered through the glomerulus.3 Changes in secretion can thus affect serum levels without changes in filtration. When evaluating elevated serum creatinine levels, consider whether recent changes in generation or secretion may have occurred. Some common alterations are listed in Table 1.

Figure 1
Table 1: Potential Etiologies of Elevated Serum Creatinines

<table>
<thead>
<tr>
<th>Condition</th>
<th>Change in Serum Creatinine</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin or</td>
<td>Increase</td>
<td>Inhibits urinary creatinine secretion</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle wasting</td>
<td>Decrease</td>
<td>Decreased creatinine generation</td>
</tr>
<tr>
<td>Prolonged vigorous</td>
<td>Increase</td>
<td>Increased creatinine production</td>
</tr>
<tr>
<td>Exercise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma lactic acid</td>
<td>Increase</td>
<td>Interference with pyruvic acid assay for creatinine</td>
</tr>
<tr>
<td>Ingestion of large</td>
<td>Increase</td>
<td>Transient increase in creatinine generation</td>
</tr>
<tr>
<td>amounts of protein</td>
<td></td>
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</tbody>
</table>

ESTIMATE GFR
Use the serum creatinine to estimate GFR. A variety of methods to estimate GFR have been developed. The National Kidney Foundation currently recommends that the estimation equation from the Modification of Diet in Renal Disease study be used, especially when the GFR is less than 60 mL/min/1.73m².4 Other GFR estimation equations tend to overestimate GFR at lower levels, as does creatinine clearance. The MDRD GFR estimation equation is listed on Figure 1.
Figure 2
Figure 1: The Modification of Diet in Renal Disease Glomerular Filtration Rate Estimation Equation

Because of the complexity of the equation, online GFR calculators are available. The NKF website (www.kidney.org) has downloadable calculators for PCs and PDAs.

For patients with GFRs greater than 60 mL/min/1.73m², the MDRD equation may underestimate the appropriate GFR. Creatinine clearance or direct GFR measures may be more appropriate in this population. One commonly used equation is the Cockcroft-Gault (Figure 2).

Figure 3
Figure 2: Cockcroft-Gault Equation

EVALUATE ETIOLOGIES

Complete a history and physical, check renal ultrasound and urinalysis. The goals of these tests are twofold: 1) to determine whether renal insufficiency is acute or chronic, and 2) to determine the potential cause. A history and physical examination, combined with an ultrasound and urinalysis provide an excellent means of initially evaluating potential etiologies of renal disease.

A complete history should include questions about drug use (including over-the-counter, prescription and herbal products), edema, nocturia, overt hematuria, elevated blood pressure, family history of kidney disease, diabetes and polya. Mild renal insufficiency may present with few physical findings, but careful examination for signs of vasculitis, lupus, diabetes, endocarditis and hypertension should be undertaken.

Urinalysis can be helpful in detecting proteinuria, hematuria and an active urinary sediment. Even when the urinalysis is negative it is helpful, as it suggests the patient may have an extrarenal etiology for the rise in serum creatinine. Proteinuria is usually indicative of glomerular disease. Hematuria may be of glomerular or urological origin. An active urinary sediment (cellular casts) indicates active glomerular disease.

Renal ultrasound reports should include renal sizes, echogenicity and the presence of absence of hydronephrosis. Patients with hydronephrosis should be referred to urology in a timely manner. Large kidneys are often indicative of diabetic nephropathy, focal segmental glomerular sclerosis or myeloma kidney. Small kidneys are often suggestive of longstanding renal disease.

If evidence of obstruction or post-renal disease, refer to urology. Patients with obstructive renal disease often present with hydronephrosis on renal ultrasound, isosthenuria (urine specific gravity approximately 1.010), and bland urinary sediment.

If hematuria alone is present, consider referral to urology. It is often difficult to discern between an intrarenal and extrarenal etiology for hematuria. Intrarenal hematuria will often present with increased numbers of dysmorphic red blood cells, while extrarenal disease often will not. Bladder cancer is a common etiology of hematuria among patients over 50 years of age. Ruling this out as a part of working up hematuria is essential.

Patients with proteinuria need to be carefully assessed. A variety of means of assessing proteinuria can be undertaken. They include a twenty-four hour urine collection and the protein/creatinine ratio.

Proteinuria is a common indication of diabetic nephropathy. Other signs of diabetic nephropathy include normal to large kidneys on ultrasound, a lack of an active urine sediment or hematuria. Patients with symptoms consistent with these findings should be managed appropriately (control blood sugars, control blood pressure and prescribe ACEI/ARB).

Patients with significant proteinuria who do not have diabetes should be referred to a nephrologists and UPEP and ANA should be ordered.

Active urine sediment should prompt nephrology referral and/or review as it may be indicative of glomerulonephritis. In addition to nephrology referral, physicians should order vasculitis studies (Antineutrophilic cytoplasmatic antibody, C3, C4, cryoglobulins, antineutrophilic antibody, etc.) and possibly urine protein electrophoresis.

Patients with a GFR less than 30 mL/min/1.73m² should prompt input from nephrology, either in the form of a referral or review.
SUMMARY

Evaluation of an elevated serum creatinine should begin by excluding potentially surreptitious etiologies of the elevation. The serum creatinine should then be used to estimate GFR using one of the GFR estimation equations. If the GFR is decreased, workup to include history and physical, urinanalysis and renal ultrasound should be performed. Based upon these studies, further workup and/or referral can be undertaken.

Figure 4
Figure 3: Elevated Creatinine Algorithm

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References

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