Cystatin C and serum creatinine in estimating acute kidney injury of shock patients

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BACKGROUND: Serum creatinine (SCr) is the most commonly used parameter to estimate renal function impairment, but there are some shortcomings. Many factors including age, gender, drug, diet, muscle mass and metabolic rate can influence SCr, leading to an inaccurate estimation of kidney impairment. Studies have shown that cystatin C (CysC) is not affected by factors such as muscle mass, age, gender, diet, inflammation or tumor. The present study was undertaken to compare the sensitivity of CysC and SCr in evaluating renal function impairment at early stage of shock.

METHODS: Seventy-one patients aged 38.3±21.4 years, who had been treated at the Emergency Medicine Department of the First Affiliated Hospital, Sun Yat-sen University between February 2006 and June 2007, were studied. They were divided into groups A, B, C, and D according to the shock time. Serum sample was drawn from each patient at 1, 2, 3, 4 hours after shock to determine SCr and CysC. CysC and SCr were determined again at 72 hours and 7 days after shock.

RESULTS: CysC increased earlier than SCr in the 71 patients, and CysC decreased slower than SCr when shock was corrected. CysC increased at 1 hour after shock. There was a negative correlation between CysC, SCr and glomerular filtration rate (GFR), especially at early stage of shock.

CONCLUSIONS: There is renal injury at early stage of shock. CysC is more sensitive than SCr in assessing renal function at the early stage of shock.

KEY WORDS: Cystatin C; Serum creatinine; Shock; Acute kidney injury

INTRODUCTION

The ideal endogenous marker would be characterized by stable production rate, stable circulating levels (unaffected by pathological changes), lack of protein binding, free glomerular filtration, and lack of reabsorption or secretion; to date, no such marker has yet been identified. Some substances such as creatinine, urea, β2-microglobulin and retinol-binding protein have been used as endogenous markers of glomerular filtration rate (GFR), by measuring either their plasma levels or their renal clearance. Among them, the most useful markers for assessing GFR are serum creatinine and renal creatinine clearance (CCr). This is secondary to their correlations with the renal clearance of some exogenous substances (inulin, creatinine-EDTA, iothalamate) that are considered 'gold standards' for determining GFR.

In shock, renal function impairs due to inadequate perfusion to the kidney, so monitoring renal function is extremely important in the management of patients. GFR, which can be measured by determining the clearance of various substances, is the 'gold standard' parameter for monitoring renal function. The ideal endogenous marker would be characterized by stable production rate, stable circulating levels (unaffected by pathological changes), lack of protein binding, free glomerular filtration, and lack of reabsorption or secretion. To date, however, no such marker has yet been identified.

Serum creatinine (SCr) is the most commonly used parameter to estimate the impairment of renal function, but there are some shortcomings. Many factors, including...
age, gender, drug, diet, muscle mass and metabolic rate, can influence SC, leading to an inaccurate estimation of kidney impairment.\cite{1,2} SCr increases as glomerular filtration rate (GFR) decreases to 75 ml/min per 1.73 m². A series of studies have shown that cystatin C (CysC) is not affected by factors such as muscle mass, age, gender, diet, inflammation or tumor.\cite{3-5} CysC increases as GFR decreases to 88 ml/min per 1.73 m². The present study was undertaken to compare the sensitivity of CysC and SCr in evaluating the renal function impairment at early stage of shock.

**METHODS**

Seventy-one patients, aged 38.3±21.4 years, who had been treated at the emergency medicine department of the First Affiliated Hospital, Sun Yat-sen University between February 2006 and June 2007 were studied. Inclusion criteria were systolic pressure <90 mmHg, shock index (pulse rats/ systolic pressure) >1.0, and the manifestations of hypovolemia (thirst, pallor, and increased heart rate). Exclusion criteria were chronic nephrosis, abnormal renal function without nephrosis, diabetes, erythematous, kidney neoplasma, and multiple organ failure. The patients were classified according to the acute kidney injury (AKI) stages set by Armstrong Conference in September 2005 (Table 1).

The 71 patients were divided into four groups according to the shock time. They were group A (n=35), shock time 0.5-1 hour; group B (n=21), shock time 1-2 hours; group C (n=9), shock time 2-3 hours; group D (n=6), shock time 3-4 hours. There were no significant differences in the demographic characteristics and clinical conditions of the patients.

Serum sample was taken from each patient at 1, 2, 3, 4 hours after shock to determine SCr and CysC. CysC and SCr were determined again at 72 hours and 7 days after shock. Body surface area was calculated by the Stevenson formula:

\[
\text{Body surface area(m}^2) = 0.016 \times \text{height(cm)} + 0.0128 \times \text{body weight(kg)} - 0.1529
\]

GFR was calculated by detected CysC value and the Hoek formula.\cite{7}

\[
\text{GFR(ml/min)} = -4.32 + 80.35 \times \frac{1}{\text{CysC}}
\]

Corrected GFR (ml/min/1.73m²-1) = GFR₀ × 1.73/body surface area (m²)

The standard GFR of a person of 1.73 m² body surface area is 125 ml/minute.\cite{6}

Decreased GFR was counted through comparing the corrected GFR and the standard GFR.

\[
\text{Decreased GFR} = 1 - \frac{\text{corrected GFR}}{\text{standard GFR}}
\]

The patients were reclassified according to SCr and decreased GFR.

**RESULTS**

Table 2 shows that the shock time was less than 1 hour, CysC began to increase, and the positive detection rate was 100%. With the shock time prolonged, CysC increased more obviously, and the recovery time was much slower.

<table>
<thead>
<tr>
<th>Stages</th>
<th>Creatinine</th>
<th>Urine volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 at risk</td>
<td>SCr increased ≥ 26.5 μmol/L or SCr increase &gt;50% or GFR decreased &gt; 25%</td>
<td>Or &lt;0.5 ml/kg per hour for more than 6 hours</td>
</tr>
<tr>
<td>Stage 2 injury</td>
<td>SCr increased &gt;200%-300% or GFR decreased &gt; 50%</td>
<td>Or &lt;0.5 ml/kg per hour for more than 12 hours</td>
</tr>
<tr>
<td>Stage 3 failure</td>
<td>SCr increased &gt;300% or GFR decreased &gt;75% or SCr ≥353.6 μmol/L or increased ≥ 44.2 μmol/L</td>
<td>Or &lt;0.3 ml/kg per hour for more than 24 hours or oliguria 12 hours</td>
</tr>
</tbody>
</table>

Table 2. CysC and the positive detection rate at different time points (mean±SD, mg/L, %)

<table>
<thead>
<tr>
<th>Group</th>
<th>1h</th>
<th>2h</th>
<th>3h</th>
<th>4h</th>
<th>72h</th>
<th>7d</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (n=35)</td>
<td>CysC Xc</td>
<td>1.14±0.11</td>
<td>1.10±0.10</td>
<td>0.971</td>
<td>1.10±0.10</td>
<td>0.971</td>
</tr>
<tr>
<td>B (n=21)</td>
<td>1.21±0.10</td>
<td>1.47±0.32</td>
<td>1.49±0.31</td>
<td>1.49±0.31</td>
<td>1.50±0.32</td>
<td>1.00</td>
</tr>
<tr>
<td>C (n=9)</td>
<td>1.28±0.18</td>
<td>1.50±0.33</td>
<td>2.15±0.35</td>
<td>1.98±0.31</td>
<td>1.50±0.32</td>
<td>1.00</td>
</tr>
<tr>
<td>D (n=6)</td>
<td>1.28±0.19</td>
<td>1.54±0.38</td>
<td>2.24±0.67</td>
<td>3.42±0.73</td>
<td>1.87±0.39</td>
<td>100</td>
</tr>
</tbody>
</table>
As the shock time was less than 1 hour, SCr increased only in half of the patients, and the positive detection rate was 51%-67% (Table 3). Only when the shock time was more than 2 hours, SCr increased in all patients. With the shock time prolonged, SCr increased more obviously, and the recovery time was much slower.

One hour after shock, the detection of SCr indicated only some of patients in the stage 1 of acute kidney injury. As the shock time prolonged, SCr increased significantly, and acute kidney injury reached stage 2 or stage 3 (Table 4).

The renal function began to impair when the shock time was less than 1 hour. With the shock time prolonged, the renal function deteriorated, and developed into renal failure when the shock time was more than 2 hours (Table 5).

CysC and SCr were negatively related to corrected GFR. When the shock time was more than 2 hours, the correlation coefficient of CysC and SCr were similar ($P>0.05$). The correlation coefficient of CysC and SCr was different at shock time one hour ($P<0.05$). The results indicated that CysC is more sensitive in detecting early kidney injury (Table 6).

### DISCUSSION

The kidney is one of the organs which are often injured during shock. At the early stage of shock, insufficient blood perfusion to the kidney causes the decrease of glomerular filtration rate. At this time if the circulating blood volume is sufficient, the renal function recovers with normal perfusion; otherwise, acute renal failure (ARF) will appear.\[^{[8,9]}\] In the treatment of shock, pressor agents are often used to increase the blood pressure, but this causes the decrease of renal blood flow and the increase of the incidence of ARF. In the past 30 years, the incidence of ARF has gradually increased by 11% per year. Therefore, it is necessary to detect kidney injury during the treatment of shock. At present, serum creatinine (SCr) is the most commonly used parameter to estimate renal function impairment, but SCr is influenced by age, gender, drug, diet, muscle

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### Table 3. Scr and positive detection rate at different time points (mean ±SD, μmol/L, Xc %)

<table>
<thead>
<tr>
<th>Group</th>
<th>1h</th>
<th>2h</th>
<th>3h</th>
<th>4h</th>
<th>72h</th>
<th>7d</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (n=35)</td>
<td>110.3±18.4</td>
<td>51.4</td>
<td>110.1±18.1</td>
<td>51.4</td>
<td>110.2±17.1</td>
<td>51.4</td>
</tr>
<tr>
<td>B (n=21)</td>
<td>114.2±19.3</td>
<td>57.1</td>
<td>139.1±24.2</td>
<td>76.2</td>
<td>140.9±13.4</td>
<td>76.2</td>
</tr>
<tr>
<td>C (n=9)</td>
<td>118.2±19.3</td>
<td>55.6</td>
<td>159.6±12.4</td>
<td>100</td>
<td>239.4±89.1</td>
<td>100</td>
</tr>
<tr>
<td>D (n=6)</td>
<td>119.3±17.5</td>
<td>66.6</td>
<td>168.2±16.4</td>
<td>100</td>
<td>287.8±87.6</td>
<td>100</td>
</tr>
</tbody>
</table>

*SC.

### Table 4. SCr level (μmol/L) and stages of acute kidney injury

<table>
<thead>
<tr>
<th>Group</th>
<th>1h</th>
<th>2h</th>
<th>3h</th>
<th>4h</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (n=35)</td>
<td>91.9-128.7</td>
<td>0-1</td>
<td>92-128.2</td>
<td>0-1</td>
</tr>
<tr>
<td>B (n=21)</td>
<td>94.9-133.5</td>
<td>0-1</td>
<td>114.9-163.3</td>
<td>1-2</td>
</tr>
<tr>
<td>C (n=9)</td>
<td>98.9-137.5</td>
<td>0-1</td>
<td>147.2-172</td>
<td>1-3</td>
</tr>
<tr>
<td>D (n=6)</td>
<td>101.8-136.8</td>
<td>0-1</td>
<td>135.8-200.6</td>
<td>1-3</td>
</tr>
</tbody>
</table>

### Table 5. Calculation of GFR decrease according to the Hoek formula and Stevenson formula

<table>
<thead>
<tr>
<th>Group</th>
<th>1h</th>
<th>2h</th>
<th>3h</th>
<th>4h</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (n=35)</td>
<td>32.3-55.6</td>
<td>1-2</td>
<td>28.8-58.5</td>
<td>1-2</td>
</tr>
<tr>
<td>B (n=21)</td>
<td>32.1-58.6</td>
<td>1-2</td>
<td>50.1-67.2</td>
<td>1-2</td>
</tr>
<tr>
<td>C (n=9)</td>
<td>37.1-60.5</td>
<td>1-2</td>
<td>51.2-68.0</td>
<td>2</td>
</tr>
<tr>
<td>D (n=6)</td>
<td>42.4-61.5</td>
<td>1-2</td>
<td>53.6-68.8</td>
<td>2</td>
</tr>
</tbody>
</table>

### Table 6. Correlation of CysC, SCr and corrected GFR at deferent time points in shock patients

<table>
<thead>
<tr>
<th>Shock time</th>
<th>n</th>
<th>R value CysC</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A+B+C+D (n=71)</td>
<td>-0.83</td>
<td>-0.57</td>
<td>0.032</td>
</tr>
<tr>
<td>B+C+D (n=36)</td>
<td>-0.84</td>
<td>-0.79</td>
<td>0.28</td>
</tr>
<tr>
<td>C+D (n=15)</td>
<td>-0.85</td>
<td>-0.81</td>
<td>0.40</td>
</tr>
<tr>
<td>D (n=6)</td>
<td>-0.89</td>
<td>-0.84</td>
<td>0.41</td>
</tr>
</tbody>
</table>

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mass and metabolic rate. In addition, clinically a 24-hour urine sample is collected to calculate creatinine clearance using the following formula: $CCr (\text{mL/min}) = (\text{urine volume} \times \text{urine creatinine})/(\text{serum creatinine} \times 1440)$. However, measurement of creatinine clearance can cause erroneous findings in many situations, particularly when urine collection technique is poor. Thus SCr is not sensitive enough to estimate the early change of GFR, especially the slight impairment of the proximal renal tubule.

Levels facilitate its glomerular filtration. Subsequently, diseases, or inflammatory diseases. The use of serum cystatin C as a marker of GFR is well documented, its concentration is not influenced by infections, liver diseases, or inflammatory diseases. The use of serum cystatin C as a marker of GFR is well documented, and some authors have suggested that it may be more accurate than serum creatinine for this purpose. Moreover, its concentration is not influenced by infections, liver diseases, or inflammatory diseases. The use of serum cystatin C as a marker of GFR is well documented, and some authors have suggested that it may be more accurate than serum creatinine for this purpose.

The results of CysC and SCr in the present study were consistent to those of other research on hypertension, diabetes and kidney transplantation.

In the present study, we classified the stages of acute kidney injury according to CysC, SCr and decreased GFR and compared their relationship with renal function. The results revealed that renal function injury appeared at shock time less than 1 hour. The severity of acute renal injury was positively correlated with the shock time and the shock severity. Renal function returned to be normal in the patients when the shock time less than 1 hour. When the shock time was more than 2 hours, the positive detection rate of CysC and SCr was 100%, and the AKI was in stage 2 or stage 3. At 7 days after shock, CysC in all patients and SCr in half of the patients were still higher than normal. With the shock time was prolonged, CysC and SCr increased obviously, and CysC was more sensitive in detecting renal injury at early stage.

**REFERENCES**


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