Hemorrhagic Shock in Polytrauma Patients: Early Detection with Renal Doppler Resistive Index Measurements

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Purpose: To investigate whether renal Doppler resistive index (RI) changes occur early during posttraumatic bleeding and may be predictive of occult hypoperfusion—and thus hemorrhagic shock—in patients with polytrauma.

Materials and Methods: This study was approved by the institutional ethics committee, and informed consent was obtained from all patients. The renal Doppler RI was measured in 52 hemodynamically stable adult patients admitted to the emergency department (ED) because of polytrauma. Renal Doppler RI, hemoglobin, standard base excess, lactate, systolic blood pressure, pH, heart rate, and inferior vena cava diameter values were recorded at admittance and correlated with outcome (progression or nonprogression to hemorrhagic shock). Logistic regression analysis was performed to assess the risk factors for progression to hemorrhagic shock.

Results: Twenty-nine patients developed hemorrhagic shock, and 23 did not. At univariable analysis, the hemorrhagic shock group, as compared with the nonhemorrhagic shock group, had higher renal Doppler RI (mean, 0.80 ± 0.10 [standard deviation] vs 0.63 ± 0.03; \( P < .01 \)), injury severity score (mean, 36 ± 11 vs 26 ± 5; \( P < .01 \)), and standard base excess (mean, −4.0 mEq/L ± 4 vs 1 mEq/L ± 3; \( P = .04 \)) values. At logistic regression analysis, a renal Doppler RI greater than 0.7 (vs less than or equal to 0.7) was the only independent risk factor for progression to hemorrhagic shock (odds ratio, 57.8; 95% confidence interval: 10.5, 317.0) (\( P < .001 \)).

Conclusion: In polytrauma patients who are hemodynamically stable at admittance to the ED, renal cortical blood flow redistribution occurs very early in response to occult bleeding and might be noninvasively detected by using the renal Doppler RI. A renal Doppler RI greater than 0.7 is predictive of progression to hemorrhagic shock in polytrauma patients.

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Traumatic injury is the leading cause of death worldwide among persons aged 5–44 years (1) and accounts for 10% of all deaths (2). Despite improvements in trauma care, uncontrolled bleeding is the leading cause of potentially preventable early in-hospital deaths, contributing to 30%–40% of trauma-related deaths. About 30% more deaths occur within the second or third hour after injury owing to occult major internal hemorrhage (3). Commonly used parameters suggested for the initial assessment of blood loss in otherwise hemodynamically stable patients, such as the injury severity score (ISS) (4), markers of hypoperfusion such as lactate level and base deficits (5–7), arterial blood pressure, hemoglobin and hematocrit levels (8), heart rate (9), and respiratory rate, have been found to have poor sensitivity (10). Previous studies have shown that in patients treated for trauma, inferior vena cava (IVC) diameter and collapsibility index values are good indicators of blood loss despite normal vital signs at emergency department (ED) admission. These findings suggest that IVC diameter is better correlated to circulating blood volume than to blood pressure (11,12).

In animal models, marked increments of renal vascular resistance occur in response to hemorrhage (13,14), mainly owing to cortical vasoconstriction (15,16). In humans, this mechanism can reduce renal blood flow by more than 1 L/min during initial hemorrhagic shock and thereby act as a reservoir against severe hypoperfusion of core organs (17).

In humans and animals, various quantitative and semiquantitative Doppler parameters have been proposed to quantify renal blood flow. Among these, the Doppler resistive index (RI) of an intrarenal artery is the most frequently used for clinical investigations because this measurement does not require estimations of the Doppler angle or the vessel cross-sectional area (18). Moreover, animal studies have shown that the renal Doppler RI is dependent on the perfusion pressure (19) and is increased by hypotension in the presence of hypovolemia or normovolemic anemia (20,21). To our knowledge, the effects of early hemodynamic changes on the renal Doppler RI had not been previously investigated in patients with trauma.

The purpose of the present study was to investigate whether renal Doppler RI changes occur early with post-traumatic bleeding and whether the renal Doppler RI may enable accurate prediction of occult hypoperfusion and thus be predictive of the development of hemorrhagic shock in polytrauma patients.

Materials and Methods

Study Subjects

This study was approved by the institutional ethics committee, and informed consent was obtained from all patients. This was a prospective observational study involving 52 patients admitted to the ED of an urban level 1 trauma center (San Martino Hospital, Genoa, Italy) between January 1, 2009, and June 30, 2010, because of polytrauma (ISS > 16) (22) without clinical signs of hemorrhagic shock. Hemorrhagic shock was defined as low blood pressure (systolic blood pressure < 90 mm Hg), low urine output (<30 mL/h), and a blood lactate level greater than 2 mmol/L (23).

Patients were excluded if they had one of the following: (a) age younger than 18 years or older than 65 years, (b) hemoglobin level of 10 g/dL or less, (c) penetrating trauma, (d) vasoactive drug support, (e) abnormal creatinine level (>1.2 mg/dL) or history of renal disease, (f) diabetes, (g) or free abdominal fluid diagnosed by means of focus assessment sonography for trauma (FAST).

Study Protocol

The patients underwent a clinical examination according to the Advanced Trauma Life Support recommendations (24). FAST was performed within 10 minutes after the clinical examination. Arterial and venous blood samples were drawn for laboratory testing and cross-matching immediately before the FAST procedure. If the FAST results were negative for free abdominal fluid, the renal Doppler RI was determined while the patient was being treated and waiting to undergo computed tomography (CT). If the FAST results were positive, an abdominal CT scan was obtained immediately, and surgery was performed—depending on the hemodynamic balance—and the patient was excluded from the study. All hemodynamically stable patients underwent further evaluation for intrathoracic and intraabdominal sources of hemorrhage with CT.

Advance in Knowledge

- In normotensive polytrauma patients, a renal Doppler resistive index (RI) greater than 0.7 at admittance into the emergency department was predictive of hemorrhagic shock within the first 24 hours (odds ratio, 57.8; 95% confidence interval: 10.5, 317.0) (P < .001).

Implication for Patient Care

- A high renal Doppler RI is an early sign of hypoperfusion in apparently stable polytrauma patients and may facilitate accurate prediction of the occurrence of hemorrhagic shock and thus help to activate early surgical and/or radiologic interventions.

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Abbreviations:

ED = emergency department
ISS = injury severity score
IVC = inferior vena cava
RI = resistive index

Author contributions:

Guarantors of integrity of entire study, F.C., C.B., A.V., P.M.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, F.C., S.P., F.A., P.M., P.P.; clinical studies, F.C., C.B., A.V., F.A., P.M., P.P.; statistical analysis, F.C., C.B., F.A., P.M., P.P.; and manuscript editing, F.C., C.B., F.A., P.M., P.P.

Potential conflicts of interest are listed at the end of this article.
Measurements

**Color Doppler ultrasonography.**—All ultrasonographic (US) examinations were performed with the patient supine and by using a 3.5-MHz convex probe for examination of the kidney and a sector-array probe with a 2–4-MHz transducer for examination of the IVC.

After a general preliminary examination of the abdominal cavity and organs, Doppler US measurements of the interlobar arteries were obtained by an internal medicine physician (F.C., 15 years experience in Doppler US). The US examinations were considered technically adequate if the following criteria were met: (a) a clear two-dimensional image with definition of the renal parenchyma was obtained, (b) a good color image with representation of the intrarenal vascular blood flow was obtained, and (c) at least three consecutive Doppler time-velocity spectra for each renal area (upper, middle, and lower regions) were examined. Waveforms were recorded and the renal Doppler RI was calculated according to the protocol of Planiol and Pourcelot (25). For each of the three renal areas, three Doppler measurements were taken. The mean values for the three areas were then averaged to derive an index for the whole organ (Figs 1, 2).

To minimize sampling error, the pulsed wave Doppler spectrum was increased by using the lowest frequency shift range that did not cause aliasing and the wall filter was set on a low frequency (100 MHz). Venous flow studies of the kidney were limited to evaluation of the patency of the vessels to exclude the presence of occlusion or thrombosis.

To evaluate the IVC, the probe was placed at a subxyphoid location and the sagittal section of the IVC was imaged. Measurements were taken at both inspiration and expiration during spontaneous tidal breathing, proximally to the junction with the hepatic vein that lies approximately 2 cm before the right atrium where the anterior and posterior walls of the IVC are well seen and parallel to each other. On the short-axis view, the M-mode cursor of the two-dimensional sector was used to generate a time motion recording of the circular size of the IVC. The difference between the IVC measurement during expiration (IVCₑ) and the IVC measurement during inspiration (IVCᵢ) was derived, and the IVC collapsibility index was calculated as \((IVCₑ - IVCᵢ)/IVCₑ\) to assess the intravascular volume in relation to the central venous pressure (26).

**Clinical and laboratory data.**—The following patient data were collected and recorded: sex, age, mechanism of injury according to the Advanced Trauma Life Support classification (24), ISS, time between departure from the trauma scene and arrival at the hospital, time from hospital admittance to US, systolic blood pressure, heart rate, blood lactate level, standard base excess, arterial pH, hemoglobin concentration, platelet count, intensive care unit admittance, length of hospital stay, and hospital mortality.

The patients were further assigned to one of two groups: patients who did not develop hemorrhagic shock within the first 24 hours (no hemorrhagic shock group) and those who did (hemorrhagic shock group).

**Statistical Analyses**

Differences between the two groups were assessed for significance by using the Student t test for unpaired data and the Fisher exact test for frequencies. All variables that yielded \(P < .05\) were submitted for multiple-variable logistic regression analysis and then entered into sensitivity receiver operating characteristic analysis for assessment of the diagnostic accuracy of the test. Sensitivity, specificity, and positive and negative predictive values were determined. \(P < .05\) was considered to indicate statistical significance. The Hosmer-Lemeshow test...
was used to assess the goodness of fit of the logistic regression model (27). Likelihood ratios and pre- and posttest probabilities were calculated to analyze the efficiency of the diagnostic method. The power of the study based on observed means and standard deviations, with \( \alpha < .05 \), was greater than 80%. Statistical analyses were performed by using Statistica 7.1 (StatSoft, Tulsa, Okla) and SPSS, version 18.0 (SPSS, Chicago, Ill), software packages.

### Results

During the 18-month study period, 263 patients were admitted to the ED because of polytrauma. Twenty-one (8%) of these patients died at ED admission; 118 (45%) were excluded because of oral-tracheal intubation and/or vasovagal drug administration at admission; 42 (16%) were excluded because of clear signs of hemorrhagic shock; and 30 (11%) were excluded because of age, history of renal disease or diabetes, penetrating trauma, or hemoglobin level lower than 10 g/dL. Of the 52 (20%) patients who met the inclusion criteria, 29 developed hemorrhagic shock within the first 24 hours after hospital admittance. Seven of these 29 patients died of multisystem organ failure, 11 underwent explorative laparotomy for suspected intraabdominal injuries, nine underwent angiography for arterial hemorrhage that required therapeutic intervention, and two who had venous hemorrhage from pelvic fracture were treated conservatively, with no potential for angiography or surgical treatment. None of the 23 patients who did not develop hemorrhagic shock died or required emergency surgery.

The patients who developed hemorrhagic shock, as compared with those who did not, had significantly higher ISS (mean, 36 ± 11 [standard deviation] vs 26 ± 5; \( P < .01 \)), renal Doppler RI (mean, 0.80 ± 0.10 vs 0.63 ± 0.03; \( P < .01 \)), and standard base excess (mean, \(-4.0 \) mEq/L ± 4 vs \( 1 \) mEq/L ± 3; \( P = .04 \)) values (Table 1). The patients with hemorrhagic shock also had a higher rate of intensive care unit admission (21 of 29 vs four of 23 patients, \( P < .01 \)).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hemorrhagic Shock Group (n = 29)*</th>
<th>No Hemorrhagic Shock Group (n = 23)*</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female patients†</td>
<td>22/7</td>
<td>17/6</td>
<td>.56</td>
</tr>
<tr>
<td>Age (y)</td>
<td>38 ± 17 (18–65)</td>
<td>41 ± 15 (18–65)</td>
<td>.44</td>
</tr>
<tr>
<td>Male patients</td>
<td>37 ± 14 (18–64)</td>
<td>40 ± 15 (18–65)</td>
<td>.53</td>
</tr>
<tr>
<td>Female patients</td>
<td>40 ± 24 (18–65)</td>
<td>44 ± 16 (21–62)</td>
<td>.74</td>
</tr>
<tr>
<td>Time from trauma to hospital (min)‡</td>
<td>28 ± 17</td>
<td>30 ± 19</td>
<td>.79</td>
</tr>
<tr>
<td>Time from ED admittance to US (min)</td>
<td>7 ± 5</td>
<td>7 ± 3</td>
<td>.69</td>
</tr>
<tr>
<td>Mechanism of trauma†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVA</td>
<td>7</td>
<td>9</td>
<td>...</td>
</tr>
<tr>
<td>PMHBC</td>
<td>16</td>
<td>10</td>
<td>...</td>
</tr>
<tr>
<td>Fall</td>
<td>6</td>
<td>2</td>
<td>...</td>
</tr>
<tr>
<td>Crash injury</td>
<td>0</td>
<td>2</td>
<td>...</td>
</tr>
<tr>
<td>ISS</td>
<td>36 ± 11</td>
<td>26 ± 5</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>pH</td>
<td>7.36 ± 0.05</td>
<td>7.37 ± 0.05</td>
<td>.34</td>
</tr>
<tr>
<td>Standard base excess (mEq/L)</td>
<td>(-4.0 ± 1 )</td>
<td>1 ± 3</td>
<td>.04</td>
</tr>
<tr>
<td>Lactate level (mmol/L)</td>
<td>3 ± 1</td>
<td>2 ± 1</td>
<td>.05</td>
</tr>
<tr>
<td>Hemoglobin level (g/dL)</td>
<td>12 ± 1.5</td>
<td>13 ± 1.5</td>
<td>.05</td>
</tr>
<tr>
<td>Platelet count (&lt;10³/L)</td>
<td>245 ± 86</td>
<td>257 ± 62</td>
<td>.65</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>112 ± 14</td>
<td>114 ± 9</td>
<td>.82</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>97 ± 20</td>
<td>89 ± 15</td>
<td>.24</td>
</tr>
<tr>
<td>Renal Doppler RI</td>
<td>0.80 ± 0.10</td>
<td>0.63 ± 0.03</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>IVC (mm)</td>
<td>15 ± 4</td>
<td>16 ± 4</td>
<td>.59</td>
</tr>
<tr>
<td>IVC (mm)</td>
<td>12 ± 3</td>
<td>13 ± 4</td>
<td>.36</td>
</tr>
<tr>
<td>Collapsibility index (%)</td>
<td>24</td>
<td>20</td>
<td>.18</td>
</tr>
</tbody>
</table>

* Unless otherwise noted, data are means ± standard deviations, with ranges in parentheses. IVC = inferior vena cava; SAP = systolic arterial pressure.
† Data are numbers of patients.
‡ Time between departure from the trauma scene and arrival at the hospital.

In the multivariable logistic regression model, only the renal Doppler RI was demonstrated to be significantly predictive of early hemorrhagic shock and bleeding (Table 2). The Hosmer-Lemeshow goodness-of-fit \( \chi^2 \) value was 2.47 (df = 8) (\( P = .96 \)). The \( R^2 \) for the final model was 0.64.

Areas under the receiver operating characteristic curves (Fig 3) were
rate may reach 60% despite the large amounts of total blood transfused (30). This is because even major occult bleeding may occur during the early phases after trauma without being recognized owing to the complex triage and screening procedures in overcrowded EDs. A delay in the diagnosis of occult bleeding can result in a greater than threefold increase in hospital mortality, and several studies have shown that early hemodynamic monitoring and aggressive resuscitation can reduce mortality among polytrauma patients (31). Different scoring systems (32,33) and markers of hypoperfusion, such as serum lactate and standard base excess measurements (7,34), have been proposed for identifying patients who will require massive transfusions. Although predictive in the general trauma population, these methods are not suitable for predicting occult bleeding during the early phases in hemodynamically stable patients with blunt trauma. Use of the ISS and other anatomic scores requires knowledge of all anatomic injuries, and this determination may take hours after the ED admission. For this reason, these scores might not be useful for early screening (35). Lactate levels have proved to be useful in predicting surgical intervention and hospital mortality rates but not bleeding or transfusion requirements (36). Moreover, in most of these studies, the patients were not

**Table 3**

<table>
<thead>
<tr>
<th>Predictive Variable</th>
<th>Value Cutoff</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>AUC*</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Doppler RI</td>
<td>0.7</td>
<td>90</td>
<td>87</td>
<td>90</td>
<td>87</td>
<td>0.98 (0.1, 1.00)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ISS</td>
<td>25</td>
<td>97</td>
<td>17</td>
<td>87</td>
<td>80</td>
<td>0.74 (0.60, 0.88)</td>
<td>.011</td>
</tr>
<tr>
<td>Standard base excess (mEq/L)</td>
<td>-2.8</td>
<td>58</td>
<td>72</td>
<td>75</td>
<td>54</td>
<td>0.74 (0.60, 0.89)</td>
<td>.007</td>
</tr>
</tbody>
</table>

Note.—Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) are percentages.

* AUC = area under the receiver operating characteristic curve. Numbers in parentheses are 95% confidence intervals.

**Discussion**

The main findings of this study were as follows: (a) more than half the polytrauma patients who were hemodynamically stable at ED admission developed complications due to early unrecognized occult bleeding; (b) the patients who developed hemorrhagic shock had higher renal Doppler RI, ISS, and standard base excess values at ED admission compared with those who did not develop hemorrhagic shock; and (c) multivariate analysis revealed the renal Doppler RI to be an independent significant predictor of occult hemorrhagic shock with high sensitivity and specificity.

Generally, among all patients admitted to the ED because of polytrauma, a relatively small number of patients in stable hemodynamic condition at ED admission eventually require massive transfusion (29 of 263 patients in our group). Yet, about 40% of them die within the first 6 hours after admission (28,29), and the total mortality...
stratified on the basis of hemodynamic stability; thus, conclusions cannot be generalized (34). However, initially elevated lactate levels and standard base excess values might be affected by numerous nonhypoxic causes of metabolic acidosis.

The concept of compensated shock and hemodynamic instability does not imply the presence of hypotension (37). Even if the arterial blood pressure is normal, substantial maldistribution of blood flow to the vital organs may be present; this condition, termed cryptic shock, eventually may lead to organ dysfunction. Measurements of regional circulation have been shown in experimental models to be predictive of outcome (38). In critically ill patients, organ failure may result from inadequate tissue perfusion and oxygenation, contributing to increased mortality. Methods that are currently available for monitoring regional circulation are tonometry, laser Doppler flowmetry, indocyanine green clearance, lidocaine metabolism, and sublingual microcirculation tests (39); however, these techniques are time consuming and not immediately available in emergency settings.

Patients with occult bleeding generally have relative hypovolemia or normovolemic anemia, which may result in vasoconstriction and increased vascular resistance (40,41). Because increased tissue resistance to perfusion slows the diastolic velocity more than it slows the systolic velocity, these changes cause an increase in the RI that can be measured in parenchymal organs such as the kidneys (16).

The lack of a difference in the caval index or diameter between the two groups in our study is in contrast to previously published data (12-42). This may be because only patients who were initially hemodynamically stable and without biochemical signs of hypoperfusion and had a very short delay between departure from the trauma scene to ED admission and US examination were included. Thus, we hypothesize that most of the patients were normovolemic at arrival in the ED despite having occult bleeding.

We found that early changes in the renal cortical blood flow and renal Doppler RI were present independently of hemodynamic instability in normotensive patients after major trauma. The major advantages of using the renal Doppler RI measurement are that it is inexpensive, repeatable, and noninvasive and it could be rapidly performed in the ED in combination with other vital sign and gas-analytic parameter assessments as a completion of the focus assessment sonography for trauma examination.

Our study had limitations. First, the small sample size did not permit direct application of these findings to current clinical practice. Second, the study was focused on traumatic hemorrhagic shock, so the role of the renal Doppler RI cannot be generalized to other types of shock. Third, because renal Doppler RI measurements are operator dependent, a long training period might be required before one becomes adequately skilled to perform the procedure. Fourth, the renal Doppler RI might not be a reliable prognostic indicator in patients with preexisting conditions of renal failure such as diabetes, severe hypertension, history of renal disease, or renal dysfunction. Fifth, the presence of renal artery stenosis might affect the renal Doppler RI—possibly rendering this measurement nonuseful. In this study, we were unable to collect information regarding the presence of renal arterial stenosis; however, because the mean age of the group that developed hemorrhagic shock was 38 years, it is unlikely that the enrolled patients had renal arterial stenosis.

In conclusion, our study results support the hypothesis that renal Doppler RI measurement may represent a clinically useful noninvasive method for the early detection of occult hemorrhagic shock.

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