Retrospective Comparison of Renal Ultrasonographic and Clinical Findings in Patients with Rhabdomyolysis

Jae-Joon Chung*, Eun-Suk Cho, Jeong Min Choi, Jeong-Sik Yu
Department of Radiology, Research Institute of Radiological Science, Yonsei University College of Medicine, Seoul, Korea

Abstract

**Background:** This study evaluated the ultrasonographic and clinical findings of two groups with rhabdomyolysis, who showed abnormal or normal ultrasonographic findings of kidneys. **Methods:** Two groups (n = 78) of abnormal (A) and normal (B) renal ultrasonographic findings were included. Multiple laboratory findings were assessed within 2 days before or after ultrasonography. Student’s t-test or Mann–Whitney U-test was used for statistical analysis. **Results:** The variable causes of rhabdomyolysis were intense exercise, burn, operation, shivering, and drug intoxication, etc. Group A (n = 26; M:F = 19:7) showed enlarged both kidneys, increased parenchymal thickness, and increased (n = 23, 88.5%) or decreased (n = 3, 11.5%) cortical echogenicity. Group A also showed elevated blood urea nitrogen (BUN), creatinine, potassium, and prolonged activated partial thromboplastin time (aPTT), compared with those in Group B (n = 52; M:F = 36:16), and these results were statistically significant (P < 0.01). The myoglobin in serum and urine, creatine kinase, prothrombin time, dark urine, and microscopic hematuria were not statistically different between the two groups. **Conclusion:** Patients with elevated BUN, creatinine, potassium, and prolonged aPTT showed the ultrasonographic findings of acute kidney injury, but other parameters were not statistically different between the two groups.

**Keywords:** Acute kidney injury, kidney, rhabdomyolysis, ultrasonography

Introduction

Rhabdomyolysis is a syndrome that occurs when skeletal muscle cells disrupt and release creatine kinase (CK), lactate dehydrogenase, and myoglobin (MB) into the interstitial space and plasma. The main causes of rhabdomyolysis include direct muscular injury, intense exercise, drugs, toxins, infections, hyperthermia, seizures, metabolic, electrolyte abnormalities, and endocrinopathy. Rhabdomyolysis can be asymptomatic, present with mild symptoms such as muscular enzyme elevation, or manifest as a severe syndrome with acute kidney injury and high mortality. Acute kidney injury is known to occur in 33%–50% of patients with rhabdomyolysis, and it is the main cause of mortality in these patients.

Rhabdomyolysis is usually diagnosed based on clinical symptoms and supporting laboratory tests. However, in difficult cases, several imaging studies may prove useful for diagnosis. Renal ultrasonography (US) is the most appropriate method for imaging renal disease; however, there is known to be considerable overlap in renal size and renal cortical echogenicity between normally and abnormally functioning kidneys. In patients with acute kidney injury related to symptomatic rhabdomyolysis, US can be used as the first imaging study to evaluate renal function and renal size. However, discrepancies between renal ultrasonographic findings and clinical findings have been discussed in patients with rhabdomyolysis.

This study was performed to retrospectively compare the ultrasonographic and clinical findings between two groups with abnormal and normal ultrasonographic kidney findings in patients with clinically diagnosed rhabdomyolysis and to suggest that which laboratory data would be related with abnormal renal ultrasonographic finding in patients with rhabdomyolysis.

**Address for correspondence:** Prof. Jae-Joon Chung, Department of Radiology, Gangnam Severance Hospital, Yonsei University College of Medicine, 211 Eonju-ro, Gangnam-gu, Seoul 06273, Korea. E-mail: jjchung@yuhs.ac

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**Materials and Methods**

This retrospective study was approved by our institutional review board (IRB No. 3-2017-0247 approved on Oct. 27th, 2017), and the requirement for informed consent was waived. We reviewed the electronic medical records based on the diagnostic codes of all patients who had both abdominal US and clinical diagnosis of rhabdomyolysis in the time period between January 2007 and December 2016. Diagnosis of rhabdomyolysis was made when the patients complained of muscle pain or weakness and dark urine with elevated level of CK (normal range: 22–232 U/L), MB (normal range: 12.8–69.3 mcg/L) in serum and urine, potassium (normal range: 3.6–4.8 mmol/L), and creatinine (normal range: 0.8–1.4 mg/dL) in serum and urine.

Out of a total of 334 patients, 256 were excluded, due to a lack of corresponding laboratory data within 2 days before or after renal US (n = 142), poor renal US imaging quality (n = 45), underlying chronic renal disease (n = 31), obstructive uropathy (n = 19), hemodialysis (n = 12), or peritoneal dialysis (n = 7). Thus, a total of 78 consecutive patients were finally enrolled in this study. The patients with underlying chronic renal disease had a gradual loss of renal function and elevated serum creatinine level over than 1.5 mg/dL for 3 months or more, which did not include the patients under hemodialysis or peritoneal dialysis.

Abdominal US for both kidneys was performed using an IU 22 (Philips Medical Systems, Bothell, WA, USA) with a 1–4 MHz convex transducer and an Acuson Sequoia 512 (Acuson Corporation, Mountain View, CA, USA) with a 4 MHz convex transducer. Renal US was performed by the many different radiologic doctors with 1–27 years of experience in abdominal radiology and US.

Renal ultrasonographic actual images on the picture archiving and communication system were retrospectively reviewed by one board certificated radiologist (JJC) who had over 27 years of experience in abdominal radiology and US. Abnormal renal ultrasonographic findings of acute kidney injury in patients with rhabdomyolysis were decided when kidneys were enlarged, and there was evidence of increased parenchymal thickness and increased or decreased cortical echogenicity. Enlarged renal size was defined when the longitudinal length of each kidney was more than 12 cm. Renal parenchymal thickness was defined as the distance between the sinus fat and the renal capsule at the mid-portion of each kidney. Increased parenchymal thickness was defined when the value was >12 mm. Abnormal renal cortical echogenicity was defined when renal cortical echogenicity was diffusely increased or decreased compared to that of the liver or spleen.

A total of 78 patients were retrospectively divided into two groups: Group A with abnormal renal ultrasonographic findings and Group B with normal renal ultrasonographic findings. It is known that elevated levels of creatine kinase (CK; found in the skeletal muscles, brain, and heart), MB in blood and urine (by-product of muscle breakdown), potassium (leaked from injured bone and muscles), and creatinine in blood and urine (breakdown product created by muscle) are signs of muscle damage. Moreover, prothrombin time (PT) and activated partial thromboplastic time (aPTT) are prolonged in case of disseminated intravascular coagulopathy, which is a kind of complications of rhabdomyolysis. Therefore, blood urea nitrogen (BUN), creatinine, potassium, PT, aPTT, CK, MB in serum and urine, dark brownish urine, and microscopic hematuria were retrospectively assessed in regard to renal ultrasonographic findings and clinical laboratory data within 2 days before or after renal US.

Patient age, PT, aPTT, potassium, urinary MB, serum MB, BUN, creatinine, CK, and CK-MB were statistically analyzed using Student’s t-test (P < 0.001). Gender, dark urine, and hematuria were analyzed using the Mann–Whitney U-test. Each method was for quantitative and qualitative results.

**Results**

The most common cause of rhabdomyolysis in this study was intense exercise (n = 36, 46.2%), followed by flu (n = 10, 12.8%), intense shivering from generalized tonic seizure (n = 8, 10.3%), drug intoxication (n = 7, 9.0%), burn (n = 5, 6.4%), and operation or trauma (n = 4, 5.1%) [Table 1]. The duration between initiating causes and symptom onset was 4.3 days and 4.4 days in Group A and Group B, respectively, and the results are not statistically different.

On renal US of Group A (n = 26; M:F = 19:7; mean age, 48.7 years), both kidneys were enlarged, with evidence of increased parenchymal thickness or diffusely increased [n = 23, 88.5%, Figures 1 and 2] or decreased [n = 3, 11.5%, Figure 3] cortical echogenicity, suggestive of acute and diffuse renal disease. All patients in Group B (n = 52; M:F = 36:16; *A 70-year-old female complained of weakness of the upper extremities, high fever (42°C) and cough, and tachycardia for 3 days and was diagnosed with probable viral pneumonia. *A 36-year-old female complained of severe dizziness and syncope for a 5 min 8 h ago. After then, she suffered severe myalgia of the upper extremities. Except this event, there was no predisposing factor before diagnosis of rhabdomyolysis

| Table 1: Related causes of rhabdomyolysis in the patients |
| --- |
| Causes | Group A | Group B | Total (%) |
| Intense exercise | 9 | 27 | 36 (46.2) |
| Flu | 5 | 5 | 10 (12.8) |
| Seizure | 1 | 7 | 8 (10.3) |
| Drug intoxication | 1 | 6 | 7 (9.0) |
| Burn | 3 | 2 | 5 (6.4) |
| Operation/trauma | 1 | 3 | 4 (5.1) |
| Brain infarction/encephalitis | 1 | 1 | 2 (2.6) |
| Pneumonia | 0 | 1 | 1 (1.3) |
| Extremity edema | 1 | 0 | 1 (1.3) |
| Alcohol | 0 | 1 | 1 (1.3) |
| Bee biting | 1 | 0 | 1 (1.3) |
| Polymyositis | 1 | 0 | 1 (1.3) |
| Syncope | 0 | 1 | 1 (1.3) |
| Total | 24 | 54 | 78 (100.0) |

* A 70-year-old female complained of weakness of the upper extremities, high fever (42°C) and cough, and tachycardia for 3 days and was diagnosed with probable viral pneumonia. * A 36-year-old female complained of severe dizziness and syncope for a 5 min 8 h ago. After then, she suffered severe myalgia of the upper extremities. Except this event, there was no predisposing factor before diagnosis of rhabdomyolysis.
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4.7 mmol/L and 39.1 s, respectively, which were significantly larger than those in Group B (4.0 mmol/L and 31.5 s, \( P < 0.01 \)).

Other parameters including PT, CK, serum MG, urine MG, gender, age, dark urine, and microscopic hematuria were not statistically different between the two groups with rhabdomyolysis.

**DISCUSSION**

A classic triad of rhabdomyolysis consists of muscle aches, weakness, and dark-colored urine. Additional specific symptoms include muscle tenderness, swelling, cramping, stiffness, weakness, and loss of function of the relevant muscles.\(^{[1-4]}\) Other nonspecific symptoms may include fever, malaise, abdominal pain, nausea, and vomiting.\(^{[2,8-10]}\) A definitive diagnosis is made by laboratory tests including serum CK and urine MG.\(^{[11-14]}\)

Acute kidney injury is common among rhabdomyolysis patients, although it can present several days after the initial impact. About 33%–50% of rhabdomyolysis patients will develop acute kidney injury,\(^{[1,15,16]}\) and 7%–10% of all occurring acute kidney injury are due to rhabdomyolysis.\(^{[4,17,18]}\) However, the mechanisms for this condition are diverse and not fully understood. Renal US is particularly important in the evaluation of acute kidney injury if the diagnosis of rhabdomyolysis is unclear or the clinical course is not as expected.

In general, the cortex and medulla of the kidney have the same echogenicity, although the medulla may be slightly darker.\(^{[7,19,20]}\) If increased cortical echogenicity is noted, i.e., the echogenicity is equal to or greater than that of a normal liver, this is typically abnormal, with the exception of neonates. Increased echogenicity of the renal parenchyma was reported to have 96% specificity and 67% positive predictive value for

| Group | Group B \( (n = 52) \) | \( P \) |
|-------|----------------|------|
| Female/male \( (n) \) | 7/19 | 16/36 | NS |
| Mean age \( \text{years} \) | 49 ± 20 | 42 ± 20 | NS |
| BUN \( \text{mg/dL} \) | 44.2 ± 33.9 | 18.8 ± 41.7 | <0.01 |
| Cr \( \text{mg/dL} \) | 4.0 ± 4.6 | 0.8 ± 0.3 | <0.01 |
| K \( \text{mmol/L} \) | 4.7 ± 0.8 | 4.0 ± 0.5 | <0.01 |
| CK \( \text{IU/L} \) | 64,421 ± 177,406 | 26,221 ± 31,982 | NS |
| PT \( \text{sec} \) | 13.4 ± 1.7 | 12.9 ± 1.8 | NS |
| aPTT \( \text{sec} \) | 39.1 ± 13.1 | 31.5 ± 6.4 | <0.01 |
| Urine MB \( \text{IU/L} \) | 6074.4 ± 10,780.2 | 6462.9 ± 12,945.3 | NS |
| Serum MB \( \text{IU/L} \) | 3301.3 ± 2,098.6 | 4605.4 ± 6724.6 | NS |
| Dark urine \( \% \) | 3/26 (11.5) | 10/52 (19.2) | NS |
| Microscopic hematuria \( \% \) | 11/26 (42.3) | 4/52 (7.7) | NS |
| Increased CE on US \( \% \) | 23/26 (88.5) | - | - |
| Decreased CE on US \( \% \) | 3/26 (11.5) | - | - |
| Normal CE on US \( \% \) | - | 52/52 (100) | - |

BUN: Blood urea nitrogen, Cr: Creatinine, K: Potassium, CK: Creatine phosphokinase, PT: Prothrombin time, aPTT: Activated partial thromboplastin time, MB: Myoglobin, CE: Cortical echogenicity, US: Ultrasonography, NS: Not significant

mean age, 41.6 years) showed normal range of renal size, parenchymal thickness, and cortical echogenicity.

The mean values of BUN and creatinine in Group A were 44.2 mg/dL and 4.0 mg/dL, respectively, which were larger than those in Group B (18.8 mg/dL and 0.8 mg/dL), and these results were statistically significant \( (P < 0.01) \) [Table 2]. In addition, the mean values of potassium and aPTT in Group A were 4.7 mmol/L and 39.1 s, respectively, which were significantly larger than those in Group B (4.0 mmol/L and 31.5 s, \( P < 0.01 \)).

Other parameters including PT, CK, serum MG, urine MG, gender, age, dark urine, and microscopic hematuria were not statistically different between the two groups with rhabdomyolysis.

![Figure 1](image1.png)

*Figure 1:* A 65-year-old male with edema of the hands and feet after general weakness for 1 week. On renal ultrasonography, the right kidney is enlarged (12.8 cm), with diffusely and slightly increased cortical echogenicity and hypoechoic renal pyramids, suggesting acute kidney injury (blood urea nitrogen/creatinine = 97.2/18.7 mg/dL, K = 6.4 mmol/L, and activated partial thromboplastin time = 33.1 s). K: Potassium

![Figure 2](image2.png)

*Figure 2:* A 28-year-old female with oliguria and dyspnea after a burn injury 5 days prior. On renal ultrasonography, the right kidney showed swollen renal parenchyma (12.5 cm), increased cortical thickness (22 mm), increased cortical echogenicity, and hypoechoic renal pyramids (blood urea nitrogen/creatinine = 53.2/5.78 mg/dL, K = 4.8 mmol/L, and activated partial thromboplastin time = 35.3 s). K: Potassium
the presence of parenchymal kidney disease,[19] which is caused by the increased presence of materials of sound reflection, inflammatory infiltrates,[21] proteinaceous casts, or fibrous tissues.[22] In patients with acute kidney injury, 39.5% showed increased renal cortical echogenicity and 61.7% showed no ultrasonographic abnormality.[23]

Increased renal cortical echogenicity, however, may occur in both acute kidney injury and chronic kidney disease and so cannot be used to reliably distinguish between the two. Therefore, the morphological appearance of kidneys does not always match the renal diagnosis or renal function.[19,20,22] Considerable overlap in renal size and renal cortical echogenicity exists between normally and abnormally functioning kidneys. In our study, 88.5% of Group A with abnormal renal ultrasonographic findings showed increased cortical echogenicity, and the remaining 11.5% showed decreased cortical echogenicity. Mean renal length averages 11 cm in healthy adults, and 10–12 cm is a useful range for normal renal length at average body height.[26] In our study, abnormal renal size was also defined when the longitudinal length of each kidney was over than 12 cm.

The mean parenchymal thickness and renal length were similar in acute kidney injury patients and a normal control group.[1] In our study, patients with elevated BUN, creatinine, and potassium and prolonged aPTT showed renal ultrasonographic findings of acute kidney injury with an enlarged size, increased parenchymal thickness, and increased or decreased cortical echogenicity. It is known that hyperkalemia results from the release of potassium from damaged muscle cells. Levels of potassium may increase rapidly, but the levels of potassium decrease as they are excreted in the urine. Hyperkalemia is more common in patients with oliguric acute kidney injury. Prolonged aPTT can be detected when disseminated intravascular coagulation which is a kind of complications of rhabdomyolysis may be initiated by released components of necrotic muscle tissue, resulting in diffuse internal hemorrhage.

Therefore, we suggest that renal US should be performed in rhabdomyolysis patients with elevated BUN, creatinine, and potassium or prolonged aPTT for better imaging of possible acute kidney injury.

Many studies have attempted to determine whether renal parenchymal echogenicity could be useful for distinguishing different forms of acute kidney injury.[27] For example, it was originally reported that ischemic acute tubular necrosis might be characterized by normal or decreased echogenicity, presumably from edema, while nephrotic acute tubular necrosis was characterized by increased echogenicity.[27] Therefore, in our study, 88.5% of Group A showed increased cortical echogenicity, which was likely because serum MB has a direct nephrotoxic effect due to its activity as a peroxidase-like enzyme in cases like rhabdomyolysis, resulting in the similar change as shown in the nephrotic acute tubular necrosis.

There were some limitations to our study. First, our study was a retrospective analysis and was completed at a single institution, which may lead to selection bias. Second, confirmative diagnosis using a muscle or kidney was not performed for any of the cases. Third, other laboratory data related to rhabdomyolysis were not included in our study. Fourth, the ultrasonographic images were obtained by many different radiologic doctors because of the retrospective nature of the study.

**Conclusion**

In patients with elevated serum creatinine level, renal US should be recommended to rule out pre- or post-renal causes of acute kidney injury and to evaluate the causes of elevated serum Cr level which can be from chronic kidney disease or acute kidney injury.

On renal US of Group A, both kidneys were enlarged with increased parenchymal thickness and diffusely increased or decreased cortical echogenicity, suggestive of acute and diffuse renal disease. The mean values of BUN, creatinine, potassium, and aPTT in Group A were significantly larger than those in Group B. Therefore, in patients with elevation of these laboratory parameters, renal US should be recommended to evaluate the suspicion of acute kidney injury related to rhabdomyolysis.

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**Conflicts of interest**

There are no conflicts of interest.

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