

# Collective occurrence of rhabdomyolysis after high-intensity resistance training— A prospective study

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## Research article

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# Abstract

Background: Rhabdomyolysis is a syndrome characterized by muscle necrosis and release of intracellular muscle components into systemic circulation. Common causes include high-intensity exercise, crush injury, high fever, drugs, and inflammation. Here, we have a prospective observational study of collective rhabdomyolysis caused by infrequent short-term high-intensity exercise.

Methods: The patients were a group of adolescents, of which 35 developed severe muscle pain and dark-brown urine after military training and were hospitalized, while others developed mild symptoms and returned to school after relief of symptoms following outpatient treatment. We used SPSS 13.0 to calculate the sample mean and standard deviation of various laboratory indicators.

Results: The average serum creatinine kinase was  $33532.43 \pm 39982.95$  U/L, and average serum lactate dehydrogenase was  $1816.97 \pm 1413.59$  U/L at the time of admission. When they were discharged, the above two indicators became  $1902.2 \pm 1366.37$  U/L and  $210.31 \pm 61.27$  U/L. Signs and symptoms improved in all patients after the intravenous injection of average 5000ml within 5.5 days of normal saline and balance solution and implementation of a bed rest regimen. No complications occurred (e.g., acute renal failure, disseminated intravascular coagulation, or electrolyte imbalance). All patients were relieved of symptoms and discharged after an average of 5.47 days of hospitalization. Of these, 20 patients were prescribed medical treatment and returned to the clinic within 1 month after discharge.

Conclusions: Suddenly and dramatically increase the amount of exercises in a short period of time is easy to cause rhabdomyolysis. We hope that everyone can avoid similar situations.

## Background

Rhabdomyolysis (RM) is caused by movement, extrusion, hyperthermia, drugs, inflammation, and other sources of striated muscle destruction and disintegration. It causes leakage of muscle-cell components, such as creatine kinase and myoglobin, into the blood circulation, which is associated with a series of syndromes that cause internal environmental disorders, including acute kidney injury (AKI).

## Methods

Patients were aged 10–16 (average 13.94) years from a city middle school who attended military training. The students had undergone outdoor high-intensity military training on the morning of December 6, 2017, including outdoor long-distance running (3–8 km), 80–400 squats, and other activities. The outdoor temperature was 32°–35°C, and the relative humidity was 95%. Most students (approximately 60) experienced muscle soreness in the thighs, calves, and abdomen; some had dark-brown urine. After 3 days of rest, muscle pain, brown discoloration of urine, and other symptoms had resolved in most students; however, 35 students were hospitalized owing to persistent dark-brown discoloration of urine.

The 35 patients (8 boys and 27 girls) with mean age  $13.94 \pm 0.92$  years, mean weight  $50.36 \pm 5.98$  kg, and mean height  $163.38 \pm 5.76$  cm had no unique medical histories, no chronic conditions, no histories of smoking or drinking, no histories of specific medications (e.g., statins), and no histories of allergies. They underwent routine blood analyses (creatinine kinase [CK], lactate dehydrogenase [LDH], creatine kinase isoenzyme [CK-MB], aspartate aminotransferase [AST], alanine aminotransferase [ALT], and blood electrolytes [ $K^+$ ,  $Na^+$ ,  $Cl^-$ ,  $Ca^{2+}$ , and  $P$ ]), routine urinalyses (creatinine, urea nitrogen, uric acid), and blood gas analysis. All patients met the following diagnostic criteria: (1) appearance of symptoms after a large number of exercises; (2) presence of corresponding clinical manifestations of rhabdomyolysis, such as muscle pain, tenderness, swelling and weakness, general malaise, brown discoloration of urine, oliguria, anuria, and fever; (3) CK levels five-fold greater than the normal range; and (4) the absence of other causes for CK elevation.

## Results

The main laboratory indicators are shown in the Table 1 below:

Patient number	CK(Admission)	CK(Discharged)	LDH(Admission)	LDH(Discharged)	ALT(Admission)	ALT(Discharged)	AST(Admission)	AST(Discharged)
	U/L		U/L		U/L		U/L	
01	15641	1738	318	215	98	52	260	51
02	5936	461	3069	196	68	24	60	27
03	69343	4106	1440	282	431	176	667	118
04	99291	4896	1977	215	464	121	892	77
05	59252	3756	3751	29	41	107	223	48
06	4319	1095	712	226	80	17	56	28
07	5264	1045	3533	197	34	18	46	28
08	6910	2438	3616	216	60	39	59	78
09	126441	1388	1463	266	608	233	2326	94
10	38549	1973	2356	260	602	271	2193	146
11	30045	2852	1069	202	92	95	337	70
12	8588	1054	315	170	37	44	120	55
13	15645	865	516	226	77	70	210	49
14	17505	1292	586	202	78	82	217	55
15	1127	433	3785	197	25	13	44	22
16	8057	448	324	174	38	36	100	39
17	65000	769	1508	174	208	138	246	68
18	167283	3878	4574	319	580	277	2730	339
19	30796	3457	906	123	124	130	340	250
20	72773	4112	2034	261	478	124	783	173
21	19865	1302	2154	228	103	32	119	50
22	3484	1798	2821	270	44	10	50	33
23	593	167	95	238	31	12	21	18
24	11815	3405	81	221	24	44	113	74
25	26154	406	3752	175	365	43	277	27
26	18621	4159	925	377	25	40	275	118
27	2671	947	219	169	19	30	43	43
28	58283	1349	4254	146	304	39	261	37
29	10333	1025	1361	208	78	27	130	58
30	4891	641	4149	179	60	28	52	35
31	113639	3585	2753	290	356	214	1015	199
32	26159	1576	764	122	82	193	266	157
33	22361	3004	173	241	68	99	328	109
34	3169	544	2184	143	81	51	51	121
35	3832	613	57	204	20	32	48	37
Average	33532.43	1902.2	1816.97	210.31	168.09	84.6	427.37	83.74
Standard deviation	39982.95	1366.37	1413.59	61.27	186.26	75.38	658.04	69.52

Table 1: Laboratory examination of patients at admission and discharge

CK:Creatine kinase(Enzyme coupling); LDH:Lactate dehydrogenase(Continuous monitoring); ALT:Alanine aminotransferase(Continuous monitoring); AST:Aspartate aminotransferase(Continuous monitoring)

Routine urinalysis showed protein within the range of 1+–2+ and occult blood within the range of 2+–3+; the number of red blood cells in the urine sediment was 20–38/high magnification field of view. The morphology of these red blood cells was primarily in the form of normal red blood cells.

All patients were treated with a large amount of fluid replacement, and correction of electrolyte and acid-base imbalances with intravenous infusion of 5% sodium bicarbonate injection(for urinary alkalization) and compound sodium chloride injection. 24 patients also received liver protection with intravenous infusion of magnesium isoglycyrrhizinate injection or polyene phosphatidylcholine injection. None of the 35 patients had any complications, such as acute renal failure or multi-organ system failure. The average hospital stay was 6.74 days (median, 7 days). A total of 19 patients participated in the return visit in January after discharge. The blood and urine results were shown in Table 2.

Patient number	CK U/L	LDH U/L	ALT U/L	AST U/L	Urin RBC /HPF
01	132	144	19	20	1
02	197	200	34	22	1
03	2267	230	163	120	0
04	197	200	34	22	0.1
05	111	180	<10	15	5
06	78	148	11	18	4
07	437	180	18	22	4
08	67	186	14	16	1
09	129	170	21	19	3
10	424	288	136	51	12
11	156	197	15	23	0
12	568	186	32	28	NA
13	94	NA	NA	NA	NA
14	140	188	<10	16	1
15	66	165	14	14	NA
16	107	NA	NA	NA	NA
17	784	276	109	53	1
18	1580	193	79	69	3
19	173	187	25	14	NA

Table 2:Patients returned to the hospital after one month of discharge, laboratory examination

CK:Creatine kinase(Enzyme coupling); LDH:Lactate dehydrogenase(Continuous monitoring); ALT:Alanine aminotransferase(Continuous monitoring); AST:Aspartate aminotransferase(Continuous monitoring) ; RBC: Red blood cell;

/HPF: Every high power field.

## Discussion

This report presents a case of collective rhabdomyolysis, which developed following rigorous exercise in a group of patients who underwent military training.

Rhabdomyolysis constitutes a group of common clinical syndromes with complex and diverse causes. Rhabdomyolysis was first described in 1946, and much of the subsequent literature focused on military trainees undergoing significant physical stress<sup>[1]</sup>. In 1997, the incidence of rhabdomyolysis in adults was estimated at 26,000 cases annually, with myriad and often multifactorial causes<sup>[2]</sup>. Strenuous exercise has been reported as one of the most frequent causes, both on China and the world; however, the collective incidence of rhabdomyolysis owing to strenuous exercise has rarely been reported. Exertional rhabdomyolysis has one common cause: too much, too fast, and too soon of an exercise too novel<sup>[3]</sup>. Patients who are physically untrained seem to have a greater risk of developing clinically significant exertional rhabdomyolysis, although rhabdomyolysis has been known to occur in trained athletes<sup>[4][5]</sup>. The serum aminotransferase level is usually elevated in rhabdomyolysis, and these enzymes originate from the skeletal muscle<sup>[6]</sup>. When performing high-intensity exercise, rhabdomyolysis is more likely to occur in individuals who do not routinely exercise, rather than in athletes. General education in Southeast Asian countries (e.g., China, South Korea, and Japan) is based on exam-oriented education. Students are expected to spend considerable amounts of time focused on classroom learning and homework, while physical exercise is considered as “wasting time” and “not relating to learning.” This has led to a general lack of daily physical activity among students in Southeast Asia, especially among girls. Pre-school military training is mandatory for Chinese public schools (primary, secondary, and university). Students are required to undergo 1–2 weeks of paramilitary training to cultivate their strong will and collectivism. A lack of daily

exercise, combined with short-term high-intensity training, has led to increased incidence of rhabdomyolysis during military training. However, because of the self-limiting nature of the disease, adolescent patients have fewer complications and sequelae.

## Conclusion

This study reveals a collective rhabdomyolysis event and we hope that people (especially from East Asian countries) will pay more attention to the daily physical exercise of adolescents and avoid the type of exercise like: suddenly and dramatically increase the amount of exercises in a short period of time. Adolescents have fewer complications and sequelae, but it does not mean that the syndrome never cause harm to their bodies.

Limited to economic conditions and other factors, the study did not check the blood and urine myoglobin, and 15 patients had not returned to the clinic after discharge. Moreover, owing to political factors, there are few reports of collective rhabdomyolysis—the education departments will bear the pressure of public opinion for them. To avoid potential repercussions, this report was published more than 2 years after the occurrence of the case. For the reason of the research institution is a primary medical institution in China, serum and urine myoglobin, and renal biopsy are not available for execution.

## List Of Abbreviations

U/L: Units per litre

RM: Rhabdomyolysis

AKI: Acute kidney injury

CK: Creatine kinase(Enzyme coupling)

LDH: Lactate dehydrogenase(Continuous monitoring)

ALT: Alanine aminotransferase(Continuous monitoring)

AST: Aspartate aminotransferase(Continuous monitoring)

K<sup>+</sup>: Serum potassium concentration(Ion-selective electrode)

Na<sup>+</sup>: Serum sodium ion concentration(Ion-selective electrode)

Cl<sup>-</sup>: Serum chloride ion concentration(Ion-selective electrode)

Ca<sup>2+</sup>: Serum calcium ion concentration(O-cresolphthalein complex ketone)

P: Serum inorganic phosphorus concentration(Phosphomolybdate method and enzyme)

## Declarations

Ethics approval and consent to participate

The name(s) of the ethics committee(s)/institutional review board(s) (IRBs): Medical Ethics Committee of Yueqing Hospital Affiliated to Wenzhou Medical University

Committee's reference number: YQYY201700003

Disclaimer: This study has obtained the consent of the parent(s) or guardian of all participants, and the research institution has obtained written informed consent from parent(s) or guardian for participants under 16 years old.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests

The authors declare that they have no competing interests.

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Not applicable.

Authors' contributions

HT analyzed and interpreted the patient data, and was a major contributor in writing the manuscript. XC,LW,XW,LZ collected initial clinical data. HL,CW completed patient follow-up. YL Completed statistical analysis of the data. All authors read and approved the final manuscript.

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