

Clinical outcomes of hospitalised individuals with spin-induced exertional rhabdomyolysis

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ABSTRACT

Introduction: Exertional rhabdomyolysis (ER) is caused by myocyte breakdown after strenuous physical activity. In recent years, the incidence of spin-induced ER (SER) has been increasing. We describe the clinical characteristics, management and outcomes of patients admitted for SER.

Method: A review was conducted for all patients admitted to Singapore General Hospital for SER from 1 March 2021 to 31 March 2022. All patients with the admission diagnosis of “rhabdomyolysis”, “raised creatine kinase (CK) level”, or “elevated CK level” with a preceding history of spin-related physical exertion were included. Patients without a history of exertion, with a history of non-spin related exertion, or with a peak serum CK <1000 U/L were excluded.

Results: There were 93 patients in our final analysis; mean age was 28.6±5.6 years and 66 (71.0%) were female patients. Mean body mass index was 25.0±5.7 kg/m²; 81 (87.1%) patients were first-time spin participants. All patients had muscle pain, 68 (73.1%) had dark urine, 16 (17.2%) muscle swelling and 14 (15.1%) muscle weakness. There were 80 (86.0%) patients with admission CK of >20,000 U/L. Mean admission creatinine was 59.6±15.6 µmol/L. Mean intravenous (IV) hydration received was 2201±496 mL/day, oral hydration 1217±634 mL/day and total hydration 3417±854 mL/day. There was 1 (1.1%) patient with acute kidney injury, which resolved the next day with IV hydration.

Conclusion: Inpatient management of SER includes laboratory investigations, analgesia and hydration. Risk of complications is low in SER patients. SER patients without risk factors for complications can be considered for hospital-at-home management with bed rest, aggressive hydration and early outpatient review.

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INTRODUCTION

Rhabdomyolysis is a clinical and biochemical syndrome caused by the breakdown of myocytes and release of intracellular components into the bloodstream.¹ A subset of rhabdomyolysis is exertional rhabdomyolysis (ER), which is caused by strenuous physical activity. Risk factors for ER include lack of physical endurance, increased duration and intensity of exercise, raised environmental temperature, male sex, genetically inherited metabolic diseases such as sickle cell trait or myopathies, concomitant infection, and consumption of medications or performance enhancing drugs (e.g. non-steroidal anti-inflammatory drugs [NSAIDs], statins, creatine and anabolic steroids).²⁻⁴ ER most commonly presents as muscle pain, swelling, weakness

and myoglobinuria.⁵ There is no defined creatine kinase (CK) level diagnostic of ER, but a commonly used cut-off is CK >1,000 U/L or 5 times the upper limit of normal in the presence of symptoms.⁶⁻⁹ Complications of ER include acute kidney injury (AKI), metabolic acidosis, electrolyte abnormalities, arrhythmias, compartment syndrome, disseminated intravascular coagulation and rarely, death.⁶

Spin is a form of high intensity interval training (HIIT) that has garnered widespread popularity worldwide due to its celebrity following, use of loud and fast-paced music, dim lighting with spotlights to encourage participants to exercise as hard as possible, for as long as possible. In the last decade, spin-induced exertional rhabdomyolysis (SER) emerged as a subset

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CLINICAL IMPACT

What is New

- First-time spin participants are more prone to developing spin-induced exertional rhabdomyolysis (SER).
- SER has a low risk of complications.

Clinical Implications

- Spin can lead to rhabdomyolysis.
- Low-risk patients with SER can be considered for hospital-at-home care.

of ER.¹⁰⁻¹⁵ Young and healthy individuals without pre-existing conditions have very low risk of developing complications of ER.¹⁶ The mainstays of treatment for ER are aggressive hydration, correcting electrolyte imbalances and preventing further muscular injury.¹⁷⁻¹⁹ Traditionally, most patients are treated as inpatients with intravenous (IV) hydration and monitoring. This imposes a strain on limited hospital resources.²⁰

There is a move in recent years towards delivering hospital care for patients at home for various conditions, including ER.^{21,22} Patients receiving hospital-at-home care are reviewed regularly by doctors and other healthcare professionals, who can perform blood tests and administer IV therapy. Ko et al. reported 108 patients who participated in a hospital-at-home programme, among whom 5 had rhabdomyolysis.²² However, as the intensity of monitoring and access to treatment are limited in a hospital-at-home setting, it is unclear if all SER patients are suitable for hospital-at-home care. Furthermore, apart from a guideline for military recruits,²³ guidance on safely managing ER patients as inpatients or outpatients is lacking.

In this study, we aimed to describe the clinical characteristics, inpatient management and clinical outcomes of patients admitted for SER. We also aim to identify SER patients who may be suitable for hospital-at-home care.

METHOD

Data source and study population

We performed a case note review for all patients admitted to the Department of Internal Medicine, Singapore General Hospital (DIM, SGH) between 1 March 2021 and 31 March 2022. SGH is the largest tertiary hospital in Singapore

with a bed capacity of 1750. All patients with the admission diagnosis of “rhabdomyolysis”, “raised CK level” or “elevated CK level” with a preceding history of spin-related physical exertion were included. Patients without a history of exertion, or with a history of non-spin related exertion, or with a peak serum CK value of less than 1000 U/L were excluded per CK cut-off for diagnosis of rhabdomyolysis.⁶⁻⁹

The following data were collected from patients’ electronic medical records: baseline demographics, date and type of physical exertion, past medical history, clinical presentation, serum levels of CK, creatinine, electrolytes, alanine transaminase (ALT), aspartate transaminase (AST), hydration (both IV and oral) received, and analgesia prescribed. For patients who had multiple episodes of physical exertion prior to admission, the date of the first episode of physical exertion was taken as the date of exertion. Due to institutional laboratory limitations, CK values above 20,000 U/L were reported as >20,000 U/L. Other data collected include complications of rhabdomyolysis, length of stay (LOS) and readmissions within 30 days.

Our study was reviewed, and ethical approval was waived by the SingHealth Centralised Institutional Review Board (Reference Number: 2022/2486).

Institutional practice

In our institution, the Emergency Physician decides on the initial diagnostic tests, management, and whether admission is required. In general, all cases of rhabdomyolysis with or without AKI are admitted to the DIM. Treatment with IV fluids and analgesia is started in the Emergency Department (ED). Inpatient management varies as there are no treatment guidelines. Blood tests such as CK levels, creatinine, ALT, AST are performed every 1 to 2 days based on physician discretion. Volume of IV hydration and type of analgesia also varies depending on the managing physician, and is based on clinical findings such as hydration status and symptom improvement.

Statistical analysis

All statistical analysis was conducted using R version 4.1.3 (R Foundation, Vienna, Austria). Descriptive statistics were used for the demographic information and clinical characteristics. Results were presented either as a number and percentage for categorical variables or mean±standard deviation for continuous variables. Pearson’s correlation was used to calculate the correlations between ALT/AST and creatinine/LOS. A *P* value of <0.05 was taken to be statistically significant.

RESULTS

There was a total of 101 patients admitted with exertional rhabdomyolysis from 1 March 2021 to 31 March 2022. There were 8 patients who had non-spin-induced exertion prior to presentation and were excluded from statistical analysis (2 induced by gym, 2 running, 1 CrossFit, 1 cycling/weights, 1 sit-ups/weights and 1 push-ups). There were 93 patients who had attended spin class prior to hospital presentation for ER and were included in the final analysis (Fig. 1).

Majority of patients (81, 87.1%) were first-time participants in a spin class. Mean age was 28.6 ± 5.6 years and there were 66 (71.0%) female patients. Mean BMI was 25.0 ± 5.7 kg/m². Eleven (11.8%) patients had chronic medical comorbidities (2 patients had hypertension and the other 9 patients had any of the following comorbidities: hyperlipidaemia/asthma/allergic rhinitis/bronchiectasis/epilepsy/mitral valve prolapse/polycystic ovarian syndrome/Sjögren's syndrome/obsessive compulsive disorder/obstructive sleep apnea/gastroesophageal reflux disease/chronic spontaneous urticarial/eczema). Only 1 patient had a history of statin use for hyperlipidaemia. There were no patients with genetically-inherited metabolic diseases, such as sickle cell trait or myopathies. With regard to symptoms, all patients had muscle pain, 68 (73.1%) had dark urine, 16 (17.2%) had muscle swelling and 14 (15.1%) had muscle weakness. Mean days of exertion to presentation to hospital was 3.5 ± 1.2 days (Table 1).

Table 1. Baseline characteristics and clinical presentation of patients admitted for spin-induced exertional rhabdomyolysis.

	Spin-induced ER n=93
Sex, no. (%)	
Male	27 (29.0)
Female	66 (71.0)
Age, mean (SD), years	28.6 (5.6)
BMI, mean (SD), kg/m ²	25.0 (5.7) ^a
Risk factors for ER, no. (%)	
First episode spin	81 (87.1)
Statin use	1 (1.1)
Myopathy	0 (0)
Symptoms, no. (%)	
Muscle pain	93 (100)
Muscle swelling	16 (17.2)
Muscle weakness	14 (15.1)
Dark urine	68 (73.1)
Number of days from exertion to presentation, mean (SD)	3.5 (1.2)

BMI: body mass index; ER: exertional rhabdomyolysis;

SD: standard deviation

^a Data were available for 66 patients for BMI.

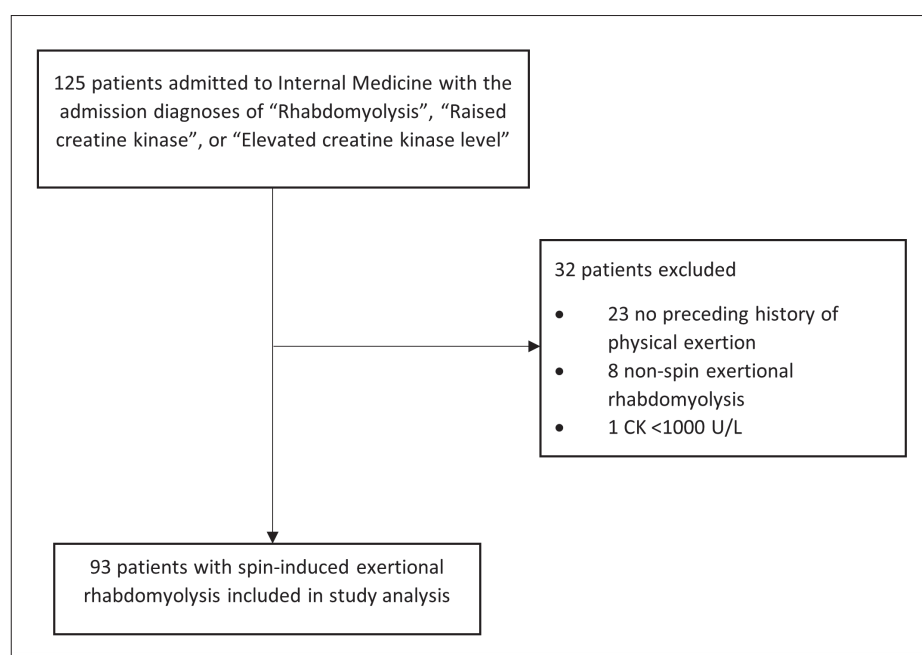


Fig. 1. Flowchart of study design.
CK: creatine kinase

There were 80 (86.0%) patients with an admission CK of >20,000 U/L. Patients with admission CK >20,000 U/L required a mean of 7.9 ± 1.3 days after exertion for CK values to decrease to <20,000 U/L. For patients who had a quantifiable CK <20,000 U/L on admission, a mean of 2.3 ± 1.1 days was needed to achieve a downward trend. There were 83 (89.2%) patients with peak CK >20,000 U/L. With regard to discharge CK, 17 (18.3%) patients discharged with CK >20,000 U/L, without a measurable downtrend of CK due to laboratory limitations (Table 2). Among them, 13 (76.5%) presented for follow-up appointments and all showed a downtrend in CK. Overall mean LOS was 5.5 ± 1.8 days (Table 2). Mean LOS was longer for patients with admission CK >20k (5.74 ± 1.71 vs 4.15 ± 1.77 days, $P=0.01$). Patients who were discharged with CK >20,000 U/L had a shorter LOS (4.12 ± 1.17 days) than those who were discharged with CK <20,000 U/L (5.83 ± 1.77 days, $P<0.01$). There was no significant difference in the incidence of complications like AKI ($P=1$) and electrolyte abnormalities ($P=0.40$) in those were discharged with CK >20,000 U/L and <20,000 U/L. No patient was discharged with a documented uptrend in CK.

Mean initial creatinine was 59.6 ± 15.6 $\mu\text{mol/L}$, mean peak creatinine was 60.5 ± 15.8 $\mu\text{mol/L}$, and mean discharge creatinine was 51.8 ± 14.1 $\mu\text{mol/L}$. Liver function test was done for 88 (94.6%) patients. Mean initial ALT and AST were 191.3 ± 128.2 U/L and 806.6 ± 608.5 U/L, respectively. Mean peak ALT and AST were 270.0 ± 164.2 U/L and 1002.1 ± 680.5 U/L, respectively. Mean ALT and AST on discharge were 219.5 ± 138.2 U/L and 444.9 ± 406.2 U/L, respectively (Table 2). Hepatitis and human immunodeficiency virus (HIV) screens were performed for 4 patients with raised liver enzymes and were negative. Abdominal ultrasound scans were performed for 2 patients, of which 1 scan was normal and the other showed hepatic steatosis. Neither admission ALT nor AST were significantly correlated to admission creatinine and LOS (admission ALT vs LOS: $r=-0.02$, $P=0.85$, 95% confidence interval (CI) -0.23 – 0.19; admission ALT vs LOS: $r=0.06$, $P=0.57$, 95% CI -0.15 – 0.27; admission AST vs admission creatinine: $r=0.00$, $P=1.00$, 95% CI -0.21 – 0.21; admission AST vs LOS: $r=0.13$, $P=0.23$, 95% CI -0.08 – 0.33).

Mean IV hydration received was 2201 ± 496 mL/day, mean oral hydration achieved by patients was 1217 ± 634 mL/day, and mean total hydration was 3417 ± 854 mL/day. The maximum volume of IV hydration received per day was 4250 mL. All patients received IV hydration up until at least the day before discharge.

Table 2. Laboratory investigations of patients admitted for spin-induced exertional rhabdomyolysis.

	Spin-induced ER n=93
Creatine kinase (CK)	
Admission CK >20,000 U/L, no. (%)	80 (86.0)
Peak CK >20,000 U/L, no. (%)	83 (89.2)
Discharge CK >20,000 U/L, no. (%)	17 (18.3)
No. of days from exertion to CK <20,000 U/L, mean (SD) ^a	7.9 (1.3)
Creatinine, mean (SD), $\mu\text{mol/L}$	
Admission	59.6 (15.6)
Peak	60.5 (15.8)
Discharge	51.8 (14.1)
ALT, mean (SD), U/L	
Admission	191.3 (128.2)
Peak	270.0 (164.2)
Discharge	219.5 (138.2)
AST, mean (SD), U/L	
Admission	806.6 (608.5)
Peak	1002.1 (680.5)
Discharge	444.9 (406.2)
Length of stay, mean (SD), days	5.5 (1.8)

ALT: alanine transaminase; AST: aspartate transaminase; ER: exertional rhabdomyolysis; SD: standard deviation

^a For patients with admission CK >20,000 U/L and discharge CK <20,000 U/L.

Types of IV fluids prescribed for hydration included sodium chloride solution, Plasma-Lyte-A (Baxter International), and Hartmann's solution. None of the patients were given sodium bicarbonate to alkalinise the urine. With regard to analgesia, 80 (86.0%) patients received paracetamol or paracetamol-orphenadrine, 11 (11.8%) patients received systemic NSAIDs, 31 (33.3%) patients received topical NSAIDs (ketoprofen patch) and 36 (38.7%) patients received weak opioids (codeine or tramadol) (Table 3).

With regard to complications, 1 (1.1%) patient had a disease-related complication and developed AKI. The patient with AKI was a 21-year-old man with an admission creatinine of 127 mmol/L and received IV hydration of 2400 mL within 24 hours of admission. Repeat creatinine the next day was normal at 100 mmol/L . One (1.1%) patient had a treatment-related complication and developed thrombophlebitis (Table 3).

Table 3. Treatment and complications of spin-induced exertional rhabdomyolysis patients.

	Spin-induced ER n=93
Hydration, mean (SD), mL/day	
Intravenous	2201 (496)
Oral	1217 (634)
Total	3417 (854)
Analgesia, no. (%)	
Paracetamol/paracetamol-orphenadrine	80 (86.0)
Topical NSAIDs	31 (33.3)
Systemic NSAIDs	11 (11.8)
Weak opioids	36 (38.7)
Complications, no. (%)	
Acute kidney injury	1 (1.1)
Electrolyte abnormalities ^a	32 (34.4)

ER: exertional rhabdomyolysis; NSAIDs: non-steroidal anti-inflammatory drugs; SD: standard deviation

^a Metabolic acidosis (bicarbonate <19 mmol/L): 3 patients, metabolic alkalosis (bicarbonate >29 mmol/L): 15 patients, hypokalaemia: 4 patients, hyperkalaemia: 1 patient, hypomagnesaemia: 2 patients, hypermagnesaemia: 1 patient, hyperphosphataemia: 2 patients, metabolic alkalosis and hypokalaemia: 3 patients, metabolic alkalosis and hyperphosphataemia: 1 patient.

Electrolyte levels for calcium, magnesium and phosphate were tested for 41 (44.1%) patients. Electrolyte and metabolic abnormalities were detected: 3 (3.2%) patients with metabolic acidosis (bicarbonate <19 mmol/L), 15 (16.1%) with metabolic alkalosis (bicarbonate >29 mmol/L), 4 (4.3%) with hypokalaemia, 1 (1.1%) with hyperkalaemia, 2 (2.2%) with hypomagnesaemia, 1 (1.0%) with hypermagnesaemia, 2 (2.2%) with hyperphosphataemia, 3 (3.2%) with metabolic alkalosis and hypokalaemia, and 1 (1.1%) with metabolic alkalosis and hyperphosphataemia. A total of 7 (18.1%) patients received oral treatment and no patients required IV therapy to correct electrolyte abnormalities. There were no other complications, such as the need for renal replacement therapy, disseminated intravascular coagulopathy or compartment syndrome. There were no readmissions to our group of healthcare institutions within 30 days (Table 3).

DISCUSSION

The majority of patients in our study were young adult women. There were no patients with pre-existing myopathies or sickle cell disease, which reflects the low incidence of these conditions in Singapore. The majority

of SER (81, 87.1%) developed in patients who attended their first spin class. Common presenting symptoms were muscle pain (93, 100%), dark urine (68, 73.1%), muscle swelling (16, 17.2%) and muscle weakness (14, 15.1%). There were 80 (86.0%) patients with an admission CK of >20,000 U/L and mean LOS was 5.5±1.8 days. Only 1 patient had mild AKI which resolved with IV hydration. There were few complications, no patients required dialysis, no inpatient referrals made to other specialties for reasons related to ER and no readmissions within 30 days. Increased awareness of SER in spin participants and instructors is important so that they can recognise symptoms and seek treatment early. First-time spin participants should attend a beginner class and start at a lower intensity to reduce the risk of SER.

Several studies have suggested CK >20,000 U/L as the cut-off for inpatient management.^{23,24} There were 86.0% of patients in our study who had CK >20,000 U/L at presentation, and did not develop complications after adequate IV hydration. There were 89.2% of patients who had a mean peak CK >20,000 U/L. Quantifying the exact value of CK would allow more research to be done to adjust the thresholds for admission and increased risk of developing complications. In addition, when assessing the necessity for inpatient management, the number of days to presentation needs to be taken into consideration as CK levels may take up to 7 days to peak depending on the type of exercise.²⁵⁻²⁷ The mean number of days required for CK to fall below 20,000 U/L was 7.9±1.3 days post-exertion; 17 (18.3%) patients were discharged with CK >20,000 U/L and all were given up a follow-up appointment within 1 month. Of the 13 patients who attended their follow-up appointment, all had a downward trend in CK. CK and myoglobin levels individually have been shown to have no correlation with AKI or mortality,^{28,29} although higher admission CK levels are associated with a longer LOS ($P<0.01$).³⁰

Hence, persistently high CK levels should not be a contraindication to patients' discharge as long as the patient has improved symptomatically and does not have any complications. Test for CK levels are often repeated daily and this practice should be reevaluated with consideration given to the time taken for levels to fall. However, CK levels should not be the main factor determining the patient's suitability for discharge. In this study, other criteria used for discharge included improvement of symptoms, ambulatory status and absence of complications. Other factors that may be considered include severity of symptoms, ability to tolerate oral hydration, the availability of a caregiver (if necessary) and the accessibility of medical care.

Among the 41 patients whose additional electrolytes such as serum calcium, magnesium and phosphate were checked, 6 patients were found to have mild electrolyte abnormalities and 2 with hypomagnesaemia were treated with oral therapy. For patients with liver function tests performed, there was no correlation with outcomes (either creatinine levels or LOS). Average peak ALT and AST were 270.0 ± 164.2 U/L and 1002.1 ± 680.5 U/L, respectively. Some patients were subjected to additional investigations in the absence of abdominal signs or symptoms, such as hepatitis/HIV screens (4 patients), and abdominal ultrasound scans (2 patients) which returned negative. Furthermore, the mean discharge ALT (219.5 ± 138.2 U/L) was higher than admission ALT (191.3 ± 128.2 U/L). The utility of performing tests for electrolytes levels (such as calcium, magnesium, phosphate) and liver function is unclear. Any abnormalities should be treated conservatively and further tests are only indicated if the clinical or biochemical picture suggests concomitant pathologies. Further investigation for metabolic myopathies should be considered in patients with recurrent ER, persistently high CK beyond 8 weeks, positive family history of rhabdomyolysis, exertion-induced muscle cramps or intolerance to exercise.³¹

Mean IV hydration received by patients was 2201 ± 496 mL/day and mean oral hydration 1217 ± 634 mL/day. All patients were kept on IV hydration at least until the day before discharge. Studies report fluid hydration for ER commencing at rates of 200–1000 mL/h, and subsequently reduced to a maintenance rate of 120–300 mL/h guided by a urine output target of 300 mL/h.^{18,23,32} Type of fluid and addition of electrolytes or mannitol has not been shown to affect LOS or demonstrate clear utility, respectively.^{18,23,32} While the SER patients in our study received a lower volume of hydration than suggested in literature, no patient developed AKI during admission, and the creatinine levels of the only patient with AKI normalised within 24 hours. More studies are needed to determine if SER patients at low risk of complications and who can tolerate large volumes of oral hydration are able to be managed with oral hydration alone.

The use of NSAIDs for pain control is not recommended in the management of ER due to the risk of AKI.³³ Despite this, 11 (11.8%) of patients were prescribed NSAIDs. More should be done to increase awareness among physicians regarding the preferred class of analgesia to avoid medication-related AKI. While the patients prescribed NSAIDs in our study did not develop AKI, several case reports have shown such patients developing AKI.^{34–36}

Our patient who had AKI showed rapid resolution by the second day of admission after receiving IV hydration and did not require renal replacement therapy. Among SER patients, a systematic review found that 7.2% and 4.1% of patients developed AKI and compartment syndrome, respectively.³⁷ Patients with AKI were older, had elevated creatinine on arrival, presented later to the hospital or had a history of NSAID use.^{34,38,39} The ER-related complication rate found in our study is much lower at 1.1%. The higher complication rate in previous studies may be contributed by publication bias, where the more severe cases of SER or SER with complications are more likely to be reported. Singapore studies have also found few cases of AKI in patients with SER, which is similar to our results.^{10,14,40} Due to the increased incidence of SER, there have also been news articles and online educational materials to increase public awareness of SER in Singapore. Increased awareness of SER is important to allow for timely intervention and prevention of complications. Hence, patients with normal creatinine on admission, or mildly elevated creatinine that normalises, all remain potential candidates for hospital-at-home care.

Our institution is running a pilot hospital-at-home care programme as an alternative to in-hospital management. In this programme, selected patients are discharged from the inpatient ward but continue to receive hospital care at home. These patients would be reviewed daily by a doctor and nurse, either physically or via teleconsultation, depending on clinical condition. During physical visits, IV medications and IV hydration can be given, and multiple visits per day can be arranged. Blood tests can be done daily, and results are obtained within a few hours of sample collection. In the event that complications occur during hospital-at-home care, there are channels for patients to contact the healthcare team for assessment and transfer to hospital if required.

ER patients have been treated under hospital-at-home programmes and as outpatients in small case series and did not develop any complications.^{22,24} The low complication rate in our study further supports that SER patients who require admission can be considered for hospital-at-home management. They should be able to ambulate, do not have severe AKI or have worsening AKI despite initial hydration, do not have severe electrolyte abnormalities, and have not developed complications related to ER. Patients with underlying medical comorbidities, such as congestive cardiac failure, liver or renal impairment, or syndrome of inappropriate secretion of anti-diuretic hormone, which limit their hydration should be excluded from hospital-at-home management and admitted for in-hospital management instead.

Our study has a few limitations. First this is a single-centre study and our study population is limited to patients who were admitted to the DIM service. It does not capture patients who were either discharged directly from the ED or admitted to another service. These numbers are likely to be small as the current practice in our institution is for rhabdomyolysis patients to be admitted to DIM. Second our institution's laboratory did not routinely quantify CK levels above 20,000 U/L unless specifically requested by the patient's managing physician. Hence, the exact CK values on admission and at peak for majority of our patients are unknown, and the mean peak CK values reported in our study are underestimations. In addition, charting of the volumes of IV and oral hydration commences after patients are admitted to an inpatient ward. Data on hydration received while patients are still in the ED waiting for an inpatient bed were not captured, leading to an underestimation of hydration volumes on day 1 of admission. Readmissions to healthcare institutions outside of our healthcare cluster were not captured in our data. Data collection coincided with the period of COVID-19 pandemic where indoor gyms were closed or operated at a lower capacity due to Singapore's prevailing social distancing measures, likely resulting in fewer people attending spin class than usual. Thus, the reported incidence of SER is likely to be an underestimate.

There are several potential areas for future research, such as the admission criteria for inpatient care of SER, relative CK value for which discharge is safe, and optimal amount of intravenous and/or oral hydration. More prospective studies are also required to determine patient suitability, and feasibility, safety and outcomes of the management of SER patients in the hospital-at-home setting.

CONCLUSION

Inpatient care of SER patients consists mainly of basic laboratory investigations, oral analgesia and hydration. As the risk of complications is low, majority of SER patients without risk factors for complications can be considered for hospital-at-home care. More can be done to increase public awareness of SER to reduce the incidence and healthcare burden of this preventable condition.

Disclosure

The authors report no conflict of interest or relationships with industry.

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