

# Clinical Characteristics and Outcomes of Exertional Rhabdomyolysis after Indoor Spinning: A Systematic Review

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## Systematic Review

**Keywords:** rhabdomyolysis, spinning, indoor cycling, systematic review

**Posted Date:** October 21st, 2021

**DOI:** <https://doi.org/10.21203/rs.3.rs-959099/v1>

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**Version of Record:** A version of this preprint was published at The Physician and Sportsmedicine on March 7th, 2022. See the published version at <https://doi.org/10.1080/00913847.2022.2049645>.

# Abstract

## Objectives

More patients are being diagnosed with exertional rhabdomyolysis secondary to indoor spinning. We conducted a systematic review to characterize the clinical characteristics of this new clinical entity.

## Methods

We conducted a thorough literature search on PubMed, Embase, Web of Science, Scopus and The Cumulative Index to Nursing and Allied Health Literature (CINAHL). Articles published from inception till 23<sup>rd</sup> June 2021 were considered for inclusion. A two-stage article selection process was performed. Articles that reported clinical characteristics and outcomes for patients with SIER were included. Quality assessment was performed using the Joanna Briggs Institute checklists.

## Results

There was a total of 22 articles and 97 patients with SIER. Most patients were healthy females who had attended their first spinning session. The average time to clinical presentation was  $3.1 \pm 1.5$  days. The most common presenting symptoms were myalgia, dark urine and muscle weakness involving the thigh. Seven patients (7.2%) developed acute kidney injury, and two patients (2.1%) required temporary inpatient haemodialysis. Four patients (4.1%) developed thigh compartment syndrome and required fasciotomies. There were no long-term sequelae or mortality observed. The average length of stay was  $5.6 \pm 2.9$  days.

## Conclusions

Healthcare professionals must have a high index of suspicion of SIER if any patient presents with myalgia, dark urine or weakness after a recent episode of indoor spinning. Fitness centre owners, spinning instructors and participants should also be better educated about the clinical characteristics and manifestations of SIER.

## 1. Introduction

Indoor spinning is a high-intensity indoor physical activity offered in many fitness centres.<sup>1,2</sup> During each spin session, participants cycle on modified stationary bikes under the direction of an instructor with accompanying music. The intensity of each spin session is closely associated with changes in position, pedal resistance, music rhythm, and pedal cadence. Participants can adjust the pedal resistance to mimic either cycling on a flat road or against a positive gradient. Due to easy accessibility and purported health benefits<sup>2-4</sup>, spinning has gained significant traction amongst the general public and has emerged as a growing fitness trend, especially within the past decade.

Accompanying the rising popularity of spinning is the increasing number of people who develop injuries<sup>5,6</sup> from spinning. One of the most severe complications of spinning is the development of exertional

rhabdomyolysis (ER), termed as spinning-induced ER (SIER). A relatively new clinical entity, SIER is emerging as one of the top causes of ER at some hospitals.<sup>7</sup> Although ER has been typically associated with extreme or endurance sports such as marathon running, it is interesting to note that spinning has similarly led to occurrences of ER in young and healthy individuals.<sup>7-9</sup>

The recent surge in patients diagnosed with SIER is an interesting phenomenon that could be attributed to several reasons. Firstly, individuals with varying fitness levels can participate in spinning due to its accessibility and low barrier of entry. Secondly, the high-intensity and repetitive nature of spinning may predispose to the development of SIER.<sup>10,11</sup> Furthermore, the group-based nature of SIER may increase individual motivation during the activity, resulting in over-exertion.<sup>12</sup> Lastly, the environment that SIER is often conducted in, which usually involves loud rhythmic music, may also induce increased exertion and decrease the level of perceived exhaustion.<sup>13</sup>

Similar to other causes of ER, SIER can present as a classical triad of myalgia, dark-colored urine, and weakness.<sup>14</sup> However, only a tiny proportion of patients with SIER present with the classical triad of symptoms. In most patients, their presenting symptoms can be varied. If not diagnosed and treated in a timely fashion, SIER can result in serious sequelae such as compartment syndrome and acute kidney injury (AKI). Given the rising popularity of spinning, there is an urgent need to better characterize this new clinical entity. Hence, we conducted a systematic review to consolidate current literature and better characterize the clinical characteristics and outcomes of SIER.

## **2. Materials And Methods**

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>15</sup> and Meta-Analyses and Systematic Reviews of Observational Studies (MOOSE) guidelines.<sup>16</sup> This review is registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42021262637).<sup>17</sup>

### **2.1 Search strategy**

Our search strategy was developed in consultation with a medical information specialist. We utilized the MeSH term “rhabdomyolysis” and the non-MeSH terms “rhabdomyolysis, myoglobin, myoglobinemia, myoglobinuria, muscle breakdown, muscle death, spin, spinning, cycle, cycling, indoor cycle, indoor-cycle, indoor cycling, indoor-cycling”. We performed an exhaustive literature search without any language restrictions with these search terms in five bibliographic databases: PubMed, EMBASE, Web of Science, Scopus and The Cumulative Index to Nursing and Allied Health Literature (CINAHL). We ensured that we included all possible relevant literature by performing backward reference searching of included studies and published review articles. Our search strategy is available in the Appendix.

### **2.2 Selection criteria**

We included all descriptive and comparative observational studies that had reported clinical characteristics and outcomes of patients presenting with SIER published from inception till 23 June 2021. We defined SIER as patients who developed ER after participating in an instructor-led group-based stationary cycling session, usually conducted in an indoor setting. We excluded studies that described patients presenting with ER from similar exercises such as outdoor cycling or individual indoor gym cycling. We also excluded conference abstracts, commentaries, review articles, and articles where full-text cannot be obtained after correspondence with the authors. We ensured that there was no overlapping or repeated data, and if so, we only included the study with the larger sample size. We used the web-based platform Rayyan QCR1<sup>18</sup> to perform article deduplication, screening and assessment for final eligibility. Two authors (YM and JJN) performed the literature search and evaluated the eligibility of studies in an independent fashion. Any disagreements during the study selection process were arbitrated after consensus with a third author (AMTLC).

## **2.3 Data extraction**

An author (JJN) extracted data from the included studies into a pre-specified data collection form. The data was cross-checked and validated by another author (YM) for any discrepancies. We extracted the following data - (i) study characteristics including first author details, year of publication, study origin, study design and sample size; (ii) patient characteristics including age, gender, body mass index, significant past medical history, spin class attendance history and spin class duration; (iii) clinical characteristics such as time to presentation, presenting symptoms, physical examination findings, and relevant laboratory values; and (iv) patient outcomes such as length of stay, complications and sequelae. If the data presented was unclear, we contacted the corresponding author by email for clarification.

## **2.4 Quality assessment**

The methodological quality of the included studies was assessed by two authors (YM and JJN) independently using the Joanna Briggs Institute (JBI) critical appraisal tool.<sup>19</sup> For individual case reports, we utilized the case reports critical appraisal checklist comprised of eight domains.<sup>20</sup> For case series and case-control studies, we utilized the case series critical appraisal checklist comprised of ten domains.<sup>19</sup> These domains serve to assess the internal validity and risk of bias of each included study. Case-control studies were assessed using the case series appraisal tool as only data from the SIER arm was relevant in this systematic review.

## **2.5 Statistical analysis**

Due to the small sample size of each study, we did not perform formal weighted pooling of data such as meta-analysis of proportions or means due to the risk of bias caused by sampling error. We only utilized simple statistical methods to report non-weighted combined proportions and means for relevant categorical and continuous outcomes. For categorical outcomes, we obtained the non-weighted combined proportions by simple arithmetic addition of each reported proportion. For continuous outcomes, we used the Cochrane's method<sup>21</sup> to combine and obtain the average mean values. If studies reported their data as median and interquartile range, we converted them to mean and standard deviation

using a validated statistical method.<sup>22</sup> We excluded studies that did not provide any data or had provided incomplete or inaccurate data from statistical analysis.

## 3. Results

### 3.1 Literature retrieval

Our initial search yielded a total of 9463 studies. After the removal of duplicates, 8475 articles were included for the initial title and abstract screening. After screening, 82 studies remained for full-text review. We were unable to obtain the full text of seven studies despite contacting the corresponding author. A total of 75 studies underwent full-text review, and eventually, 22 studies<sup>7-9, 23-41</sup> met our inclusion criteria and was included in our systematic review. We excluded 53 studies for the following reasons - 19 articles were conference abstracts, 22 studies reported on ER secondary to other etiologies, four articles were editorials, and eight studies did not report relevant clinical outcomes. Our study identification and selection process are illustrated in the PRISMA-P flowchart (Figure 1).

### 3.2 Study characteristics

Of the 22 studies included, nine studies were from the United States of America<sup>7-9, 28-30, 35, 36, 39</sup>, five studies were from South Korea<sup>32, 33, 37, 38, 40</sup> and two studies were from Italy<sup>23, 26</sup>. The remaining six articles were from Australia, Argentina, Israel, Singapore, Turkey and the United Kingdom, respectively.<sup>24, 25, 27, 31, 34, 41</sup> Sixteen studies were case reports<sup>8, 9, 23, 24, 26-31, 33-37, 39</sup>, whilst three studies were case series which included between five to eleven patients<sup>25, 32, 41</sup>. The remaining three studies were retrospective case-control studies which compared clinical characteristics and outcomes between patients with SIER and patients with ER from other aetiologies.<sup>7, 38, 40</sup> All included studies were published between 2003 and 2021, of which 19 studies<sup>7-9, 26-41</sup> were published within the last decade (2011 - present). A total of 97 patients were diagnosed and treated for SIER across the included studies. Individual patient data could be obtained in 20 out of 22 studies except for the studies by Cutler et al. and Shim et al. Characteristics of all included studies are demonstrated in Table 1, and where appropriate, individual patient data from the studies are summarized and presented.

### 3.3 Quality assessment

Sixteen studies were assessed using the JBI case report appraisal checklist<sup>8, 9, 23, 24, 26-31, 33-37, 39</sup>, whilst six studies were assessed using the JBI case series appraisal checklist<sup>7, 25, 32, 38, 40, 41</sup>. A summary of the quality assessment that was conducted for all included studies can be seen in the Appendix.

### 3.4 Patient characteristics

The ages of the included patients ranged from 15 to 49 years with a combined mean of  $26.7 \pm 6.6$  years. From the 19 studies<sup>8, 9, 23, 24, 26-39, 41</sup> which provided individual patient data, nine (17.6%) patients were between 15 to 19 years of age, 33 (64.7%) patients were between 20 to 29 years of age, and nine (17.6%)

patients were 30 years of age and above. All studies provided gender data, and 74 out of 97 (76.3%) patients were female. Seven studies<sup>9, 28, 32, 33, 37, 38, 40</sup> reported patient body mass index which ranged from 18.5 kg/m<sup>2</sup> to 33.4 kg/m<sup>2</sup>, with a combined mean of 24.4 ± 3.9 kg/m<sup>2</sup>. The large majority of patients were healthy and had no reported comorbidities. Six patients were reported to have the following comorbidities – hereditary neuropathy with liability to pressure palsy, lower extremity congenital bony anomalies, Gilbert's syndrome, juvenile myoclonic epilepsy, sickle cell trait and hyperlipidemia, respectively. Nineteen studies<sup>7-9, 23-34, 36, 39-41</sup> provided data about spinning class participation. Amongst 80 patients, 67 patients (83.8%) had never participated in a spinning session before and developed SIER after their first spinning session. Meanwhile, data from 12 studies<sup>8, 23, 26, 27, 30, 31, 35-38, 40, 41</sup> reported the duration of the spinning session to range from 15 to 100 minutes, with a combined mean of 53.4 ± 15.7 minutes.

### 3.5 Clinical presentation

The time interval between the spinning session and initial symptom development ranged from 0 to 2 days, with a combined mean of 0.8 ± 0.5 days. On the other hand, the time interval between spinning session to clinical presentation to a healthcare facility ranged from 0 to 5 days, with a combined mean of 3.1 ± 1.5 days. Out of 18 studies<sup>7-9, 23, 24, 27-31, 34-41</sup> with individual patient data, 17 (34%) patients presented 48 hours or less after the spinning session, whereas 33 (66%) patients presented after 48 hours. The most commonly reported presenting symptoms were myalgia and dark urine. Among relevant studies, 69.1% of patients reported myalgia and 56.7% had reported dark urine. Only 16.5% of patients reported muscle weakness on initial presentation. Consequently, the most common findings on clinical examination were muscle tenderness, muscle swelling and reduced power. On clinical examination, 27.8% of patients had muscle tenderness, 33% had muscle swelling, 25.8% had reduced power, and 17.5% had reduced range of motion. The most commonly involved muscle group was the thigh (97.7%). A summary of the study and patient characteristics can be seen in Table 1.

### 3.6 Laboratory results

Aside from the study by Mong et al., 21 studies<sup>7-9, 23-40</sup> had reported serum creatine kinase (CK) levels on initial presentation. CK levels ranged from more than 11000 to 261177 U/L and had a combined mean of 80627.8 ± 64774.4 U/L. Six studies<sup>9, 26, 31-33, 40</sup> had reported serum myoglobin levels on initial presentation ranging from 1000 to more than 20000 ng/ml, with a combined mean of 11154.5 ± 5575.5 ng/ml. Nine studies<sup>23, 25-27, 31-33, 37, 38</sup> had reported serum lactate dehydrogenase (LDH) levels on initial presentation, ranging from 1446 to 62970 U/L, with a combined mean of 5246 ± 10063 U/L. Fourteen studies<sup>9, 24, 26-29, 31-35, 37, 38, 40</sup> had reported serum aspartate aminotransferase (AST) levels on initial presentation. AST levels ranged from 249 to 3380 U/L with a combined mean of 1121.1 ± 639.9 U/L. Meanwhile, 12 studies<sup>9, 24, 27, 28, 31-35, 37, 38, 40</sup> had reported serum alanine aminotransferase (ALT) levels on initial presentation, ranging from 64 to 656 U/L with a combined mean of 318.2 ± 169.8 U/L. Five studies<sup>28, 32, 37, 38, 40</sup> provided serum blood urea nitrogen (BUN) levels on initial presentation ranging from 7.2 to 61.4 mg/dL with a combined mean of 11.5 ± 7.8 mg/dL. Lastly, ten studies<sup>9, 23, 28, 29, 32, 35, 37-40</sup>

had reported serum creatinine levels on initial presentation. Creatinine levels ranged from 0.5 to 7.4 mg/dL with a combined mean of  $0.9 \pm 1$  mg/dL. A summary of laboratory investigations on the initial presentation can be seen in Table 2.

Table 2  
Laboratory results on initial presentation

Author	N	Creatine kinase (U/L)	Myoglobin (ng/mL)	LDH (U/L)	AST (U/L)	ALT (U/L)	BUN (mg/dL)	Creatinine (mg/dL)
Bertoldo et al. <sup>23</sup>	1	185600	NR	8840	NR	NR	NR	1.5
Young et al. <sup>24</sup>	1	24540	NR	NR	3380	511	NR	NR
Montero et al. <sup>25</sup>	9	70933.8 ± 57810 (1650 – 165000) <sup>†</sup>	NR	1750.7 ± 1529.1 (646 – 5175) <sup>†</sup>	NR	NR	NR	NR
Boni et al. <sup>26</sup>	1	124688	18488	62970	1219	NR	NR	NR
Benish et al. <sup>27</sup>	1	132170	NR	6995	1256	280	NR	NR
Parmar et al. <sup>28</sup>	2	118288.5 ± 44825.6 (86592 – 149985) <sup>†</sup>	NR	NR	1808.5 ± 601.7 (1383 – 2234) <sup>†</sup>	468 ± 144.2 (366 – 570) <sup>†</sup>	14 ± 4.2 (11 – 17) <sup>†</sup>	0.9 ± 0.1 (0.8 – 1.0) <sup>†</sup>
DeFilippis et al. <sup>29</sup>	2	88255 ± 103654.8 (14960 – 161550) <sup>†</sup>	NR	NR	1117.5 ± 1224 (252 – 1983) <sup>†</sup>	NR	NR	0.9 (0.87 – 0.93) <sup>†</sup>
Cutler et al. <sup>7</sup>	14	73000*	NR	NR	NR	NR	NR	NR

LDH lactate dehydrogenase, AST aspartate transaminase, ALT alanine transaminase, BUN blood urea nitrogen, NR not reported

\*Only median value provided.

§No definite value provided.

<sup>†</sup>Continuous individual patient data is summarized to mean ± standard deviation with minimum and maximum values in parentheses, where applicable.

<sup>‡</sup>Data reported as median (range) or median (interquartile range) but converted to mean ± standard deviation (not shown) for pooling using a validated statistical method.



Author	N	Creatine kinase (U/L)	Myoglobin (ng/mL)	LDH (U/L)	AST (U/L)	ALT (U/L)	BUN (mg/dL)	Creatinine (mg/dL)
Eichner et al. <sup>30</sup>	1	80000	NR	NR	NR	NR	NR	NR
Fidan et al. <sup>31</sup>	1	55235	3984	1508	974	314	NR	NR
Kim et al. <sup>32</sup>	11	>11,000 (11) <sup>§</sup>	12081.2 ± 3125.8 (8472 – 16849) <sup>†</sup> >20000 (3) <sup>§</sup> , NR (2)	3698.4 ± 1917 (1446 – 7350) <sup>†</sup> NR (2)	1073.5 ± 487.4 (415 – 2020) <sup>†</sup>	323.2 ± 153.0 (127 – 550) <sup>†</sup>	10.4 ± 2.1 (8.1 – 14.3) <sup>†</sup>	0.8 ± 0.1 (0.6 – 0.9) <sup>†</sup>
Ryu et al. <sup>33</sup>	1	25010	15510.4	7370	1728	364	NR	NR
Beavis et al. <sup>34</sup>	1	261177	NR	NR	2575	551	NR	NR
Brogan et al. <sup>35</sup>	3	14493 NR (2)	NR	NR	1116 ± 33.9 (1092 – 1140) <sup>†</sup> NR (1)	276 ± 8.5 (270 – 282) <sup>†</sup> NR (1)	NR	0.7 ± 0.2 (0.5 – 0.8) <sup>†</sup> NR (1)
Gould et al. <sup>36</sup>	1	53000	NR	NR	NR	NR	NR	NR
Jeong et al. <sup>37</sup>	1	16370	NR	2310	537	160	8	0.5

LDH lactate dehydrogenase, AST aspartate transaminase, ALT alanine transaminase, BUN blood urea nitrogen, NR not reported

\*Only median value provided.

§No definite value provided.

<sup>†</sup>Continuous individual patient data is summarized to mean ± standard deviation with minimum and maximum values in parentheses, where applicable.

<sup>‡</sup>Data reported as median (range) or median (interquartile range) but converted to mean ± standard deviation (not shown) for pooling using a validated statistical method.

Author	N	Creatine kinase (U/L)	Myoglobin (ng/mL)	LDH (U/L)	AST (U/L)	ALT (U/L)	BUN (mg/dL)	Creatinine (mg/dL)
Kim et al. <sup>38</sup>	13	14035 (1) >15000 (12) <sup>§</sup>	NR	4236 ± 2541.4 (1459 – 9381) <sup>†</sup> NR (1)	1158.9 ± 627.4 (249 – 2080) <sup>†</sup>	365.1 ± 187.9 (64 – 656) <sup>†</sup>	14.6 ± 14.3 (7.2 – 61.4) <sup>†</sup>	1.4 ± 2.1 (0.51 – 7.39) <sup>†</sup>
Ramme et al. <sup>9</sup>	3	95949.3 ± 49769.6 (59651 – 152684) <sup>†</sup>	1075 (1) NR (2)	NR	662 NR (2)	121 NR (2)	NR	0.7 ± 0.2 <sup>†</sup> (0.6 – 0.9)
Hamilton et al. <sup>39</sup>	1	18200	NR	NR	NR	NR	NR	0.9
Shim et al. <sup>40</sup>	23	>15000 (23) <sup>§</sup>	>1000 (23) <sup>§</sup>	NR	869 (632.5 – 1250.5) <sup>‡</sup>	298 (154 – 378) <sup>‡</sup>	10.6 (8 – 12.2) <sup>‡</sup>	0.6 (0.5 – 0.6) <sup>‡</sup>
Longo et al. <sup>8</sup>	1	74978	NR	NR	NR	NR	NR	NR
Mong et al. <sup>41</sup>	5	NR	NR	NR	NR	NR	NR	NR
Combined values	<b>97</b>	<b>80627.8 ± 64774.4</b>	<b>11154.5 ± 5575.5</b>	<b>5246 ± 10063</b>	<b>1121.1 ± 636.9</b>	<b>318.2 ± 169.8</b>	<b>11.5 ± 7.8</b>	<b>0.9 ± 1</b>
LDH lactate dehydrogenase, AST aspartate transaminase, ALT alanine transaminase, BUN blood urea nitrogen, NR not reported								
*Only median value provided.								
§No definite value provided.								
†Continuous individual patient data is summarized to mean ± standard deviation with minimum and maximum values in parentheses, where applicable.								
‡Data reported as median (range) or median (interquartile range) but converted to mean ± standard deviation (not shown) for pooling using a validated statistical method.								

### 3.7 Sequelae and length of stay

All included studies had provided relevant information regarding the complications of SIER. The incidence of acute kidney injury secondary to SIER was 7.8% (7 out of 97 patients). Two of the seven patients with acute kidney injury required temporary inpatient hemodialysis. No patients developed chronic kidney disease or required long-term renal replacement therapy. On the other hand, the incidence of lower extremity compartment syndrome secondary to SIER was 4.1% (4 out of 97 patients). All four patients who developed lower extremity compartment syndrome required emergency fasciotomies. Seventeen studies<sup>7, 23-29, 31, 32, 34, 36-41</sup> had reported the hospital length of stay (LOS), ranging from 1 to 16 days. The combined mean length of stay was  $5.6 \pm 2.9$  days. A summary of sequelae and length of stay can be seen in Table 3.

Table 3  
Sequelae and length of stay

Author	N	Acute kidney injury	Temporary hemodialysis	Compartment syndrome	Fasciotomy	Length of stay (days)
Bertoldo et al. <sup>23</sup>	1	1/1	0/1	1/1	1/1	16
Young et al. <sup>24</sup>	1	0/1	0/1	0/1	0/1	4
Montero et al. <sup>25</sup>	9	1/9	0/9	0/9	0/9	2.1 (1 – 3)*
Boni et al. <sup>26</sup>	1	0/1	0/1	0/1	0/1	7
Benish et al. <sup>27</sup>	1	0/1	0/1	0/1	0/1	6
Parmar et al. <sup>28</sup>	2	0/2	0/2	0/2	0/2	4
DeFilippis et al. <sup>29</sup>	2	1/2	0/2	1/2	1/2	6.5 ± 2.1 <sup>†</sup> (5 – 8)
Cutler et al. <sup>7</sup>	14	1/14	0/14	1/14	1/14	4 (1 – 7) <sup>‡</sup>
Eichner et al. <sup>30</sup>	1	0/1	0/1	0/1	0/1	NR
Fidan et al. <sup>31</sup>	1	0/1	0/1	0/1	0/1	3
Kim et al. <sup>32</sup>	11	0/11	0/11	0/11	0/11	7.6 ± 1.9 <sup>†</sup> (6 – 12)
Ryu et al. <sup>33</sup>	1	0/1	0/1	0/1	0/1	NR

NR not reported

\*Data represented as mean (range).

<sup>†</sup>Continuous individual patient data is summarized to mean ± standard deviation with minimum and maximum values in parentheses, where applicable.

<sup>‡</sup>Data reported as median (range) or median (interquartile range) but converted to mean ± standard deviation (not shown) for pooling using a validated statistical method.

Author	N	Acute kidney injury	Temporary hemodialysis	Compartment syndrome	Fasciotomy	Length of stay (days)
Beavis et al. <sup>34</sup>	1	0/1	0/1	0/1	0/1	4
Brogan et al. <sup>35</sup>	3	1/3	1/3	0/3	0/3	NR
Gould et al. <sup>36</sup>	1	0/1	0/1	1/1	1/1	14
Jeong et al. <sup>37</sup>	1	0/1	0/1	0/1	0/1	10
Kim et al. <sup>38</sup>	13	2/13	1/13	0/13	0/13	7.5 ± 2.2
Ramme et al. <sup>9</sup>	3	0/3	0/3	0/3	0/3	NR
Hamilton et al. <sup>39</sup>	1	0/1	0/1	0/1	0/1	4
Shim et al. <sup>40</sup>	23	0/23	0/23	0/23	0/23	6 (4.5 – 7) <sup>‡</sup>
Longo et al. <sup>8</sup>	1	0/1	0/1	0/1	0/1	NR
Mong et al. <sup>41</sup>	5	0/5	0/5	0/5	0/5	2.4 ± 1.5 <sup>†</sup> (1 – 4)
Combined values	<b>97</b>	<b>7/97 (7.2%)</b>	<b>2/97 (2.1%)</b>	<b>4/97 (4.1%)</b>	<b>4/97 (4.1%)</b>	<b>5.6 ± 2.9</b>
NR not reported						
*Data represented as mean (range).						
†Continuous individual patient data is summarized to mean ± standard deviation with minimum and maximum values in parentheses, where applicable.						
‡Data reported as median (range) or median (interquartile range) but converted to mean ± standard deviation (not shown) for pooling using a validated statistical method.						

## 4. Discussion

An increasing number of patients are being diagnosed with SIER. While there have been systematic reviews evaluating other types of ER<sup>42, 43</sup>, there has been no systematic review of SIER to date. In our systematic review, we describe the clinical characteristics and outcomes of 97 patients with SIER. We also report several significant findings that might have potential implications in the regulation and conduct of spinning classes.

In this systematic review, we elucidated several key findings. First, data from our systematic review suggests that SIER is a relatively new clinical phenomenon. The majority of articles (19 out of 21) relevant to SIER were published within the last decade. The recent surge in the number of patients diagnosed with SIER can be correlated to the increasing popularity of spinning classes. Ever since spinning classes first started in the 1980s, the number of spinning venues and participants has surged exponentially. According to the UK Group Exercise National Survey Report, 745,000 individuals participated in spinning classes in 2018. Similarly, survey data from the ukactive Research Institute revealed that spinning classes were the most popular amongst various group workouts.<sup>44</sup> A similar trend was reflected in data from the American College of Sports Medicine, where group training activities such as spinning classes was the third-ranked worldwide fitness trend of 2020. The reasons why spinning classes have soared in popularity over the last decade can be attributed to several reasons, such as easy accessibility and a low barrier of entry. The number of dedicated spinning studios or fitness facilities that offer spinning classes is increasing, possibly fueled by lucrative margins and good participation rates.<sup>45</sup> Approximately 7000 businesses in the United States offer spinning classes, according to the latest market research reports.<sup>46</sup> Similarly, more than 70% of fitness centers tracked by the International Health, Racquet and Sportsclub Association (IHRSA) provide spinning classes.<sup>47</sup> Moreover, in a 400 spinning participants and instructors survey, 50% of respondents report a commute time of fewer than 10 minutes to their spinning class.<sup>48</sup> Undoubtedly, the commonality, easy accessibility, and convenience of participating in a spinning session have contributed to spinning classes' popularity. Spinning classes also generally have a low barrier of entry, and individuals of varying fitness levels can sign up and participate.

Second, we found that the predominant demographic profile of patients diagnosed with SIER were young adult females with no significant comorbidities. This preponderance can be explained by the fact that the same young female demographic profile generally attends group exercises such as spinning classes. Data from the UK Group Exercise National Survey Report revealed that almost 80% of group exercise participants were female. This trend is also corroborated by survey data from Australia, where 76% of individuals who were willing to spend money on exercises classes such as spinning were female.<sup>49</sup> A plausible explanation for the stark female preponderance in spinning class participation may explain the difference in exercise motivators between males and females. Several studies have demonstrated that females were more likely to engage in exercise conducted in a group setting for social reasons such as meeting friends or creating social bonds.<sup>50-52</sup>

Third, we found that most patients who develop SIER are participating in their first spinning session. This is unsurprising as several studies have shown that ER tends to affect individuals who are untrained or unconditioned to the causative activity.<sup>53</sup> However, several factors are inherent to spinning classes that may further predispose individuals to develop ER. Spinning classes are usually high-intensity in nature and conducted in an indoor group setting with rhythmic music accompaniment. The Köhler effect is a well-documented phenomenon that describes increased motivational gain in individuals when executing a task in a group setting.<sup>54</sup> Hence, spinning in a group setting may spur weaker participants to be more motivated and push themselves harder, increasing the risk of developing SIER. The Köhler effect has been demonstrated in several studies involving different physical activities, such as stationary bike exercise.<sup>55</sup> Next, dissociative attentional stimuli such as music has also been shown to reduce perceived exertion during strenuous physical activity. A clinical trial showed that listening to music resulted in lower perceived exertion in adults undergoing high-intensity exercises using a cycling ergometer.<sup>56</sup> A recent meta-analysis also found that listening to music during physical activity improved performance and reduced perceived exertion.<sup>57</sup> These positive effects were further enhanced by listening to fast tempo music. Therefore, it is highly plausible that the environment and setting of spinning classes may reduce perceived exertion in first-time participants, putting them at increased risk of developing SIER.

The classical triad of symptoms associated with ER is myalgia, weakness and dark urine.<sup>58</sup> However, only a handful of patients present with the classical triad of symptoms in our study.<sup>59</sup> We found that 69.1% of patients diagnosed with SIER had reported presenting symptoms of myalgia, whilst 56.7% reported dark urine and only 16.5% reported weakness. More importantly, we also found that patients with SIER typically present in a delayed fashion, with a mean time to presentation to a healthcare facility of  $3.1 \pm 1.5$  days, despite developing symptoms much earlier. Healthcare professionals should be cognizant of the variability of symptoms and the potential for delayed presentation in patients with SIER. If in doubt, patients who present with suspicious clinical history or symptoms should be referred to the emergency department for diagnostic work-up.<sup>59</sup> The absence of dark-colored urine or myoglobinuria also does not preclude the diagnosis of ER, or more specifically, SIER.<sup>60</sup>

During the clinical examination of patients with SIER, the most commonly reported signs were muscle tenderness, swelling, reduced power and reduced range of motion. In 97.7% of patients, the signs and symptoms reported during the clinical presentation were predominantly in the thigh. This preponderance can be attributed to the muscle groups that are involved in indoor cycling. In general, the cycling pedal stroke can be divided into the downstroke and the upstroke. During the downstroke, the quadriceps, hamstrings, and gluteus maximus work together to generate the power required to push the pedal downwards.<sup>61</sup> Interesting, a study has found that the use of the gluteus maximum is significantly lower in indoor cycling than outdoor cycling.<sup>62</sup> This phenomenon may be due to steeper seat tube angles in indoor cycling, leading to more quadriceps and hamstring activation.

The diagnosis of ER is usually based on the clinical history and is supported by biochemical investigations. There must be a preceding or inciting exercise activity, followed by the onset of muscle-

related symptoms. In terms of biochemical investigations, the diagnosis of ER is typically based on serum CK levels. Serum CK is a reliable diagnostic marker of ER as it gradually rises to its peak 24-36 hours after the inciting exercise activity and then slowly declines back to baseline over the next few days.<sup>63</sup> There, however, has not been a consensus regarding the diagnostic cut-off level of serum CK for ER. Some authors have suggested a level of more than five times the upper limit of normal, while others have proposed using a level of more than fifty times the upper limit of normal.<sup>64-66</sup> In our systematic review, we found that most studies had performed and reported CK levels on presentation. On the other hand, serum myoglobin levels were only reported in five studies. This paucity of serum myoglobin data likely reflects real-world clinical practice where myoglobin may not be performed routinely in the diagnosis of ER. Serum myoglobin, however, has been shown to have some predictive value in the development of acute kidney injury and should be performed if available in the laboratory.<sup>67</sup> In our systematic review, we also found that liver enzymes were commonly performed and reported. Abnormal liver enzymes are frequently observed in patients with severe rhabdomyolysis and they seem to have a predictive role in mortality for critically ill patients with rhabdomyolysis.<sup>68</sup> However, more specific to ER and SIER, the role of abnormal liver enzymes has not been well established.

The main goal of management for patients with ER is to prevent complications such as acute renal failure. In our systematic review, all patients received intravenous hydration, which is the primary supportive treatment of ER. Patients with ER can be severely hypovolemia due to water sequestration by the injured muscle and must be rehydrated aggressively.<sup>69</sup> In addition to intravenous hydration, one-third of patients with SIER received intravenous sodium bicarbonate. The administration of sodium bicarbonate for alkalinization of the urine is routinely performed. For instance, some authors propose a fluid regimen consisting of half isotonic saline and sodium bicarbonate.<sup>70</sup> Urine alkalinization with sodium bicarbonate may reduce the precipitation of Tamm-Horsfall protein complexes and the formation of brown granular casts.<sup>71</sup> Moreover, urine alkalization has been demonstrated to help diminish redox cycling and lipid peroxidation, thus preventing oxidative stress, tubular damage, renal vasoconstriction and eventual renal impairment.<sup>72</sup> However, there is limited high-quality evidence that alkaline diuresis has a proven clinical benefit over standard saline resuscitation.<sup>73, 74</sup> More trials are thus needed to ascertain if bicarbonate therapy should be part of the mainstay treatment for SIER.

While we did not observe any long-term sequelae of SIER, a small proportion of patients developed acute kidney injury.<sup>7, 23, 25, 29, 35, 38</sup> Although two out of the seven patients who developed acute kidney injury required temporary inpatient hemodialysis, no patients developed long-term renal sequelae.<sup>35, 38</sup> This finding is consistent with current literature, where a generally favorable renal prognosis is observed following acute kidney injury related to exertional rhabdomyolysis. Several studies have reported the risk of renal failure in healthy young individuals with ER to be from 0-8%.<sup>75, 76</sup> In our systematic review, aside from transient renal dysfunction, four patients with SIER developed compartment syndrome of the thigh requiring fasciotomies. Compartment syndrome in the setting of ER is a rare complication. As most patients with SIER may present with typical symptoms of muscle pain, tenderness and swelling, we need to have a high index of suspicion for compartment syndrome if the pain does not improve or subside with



medical management.<sup>77</sup> As the clinical diagnosis of compartment syndrome in patients with SIER can be challenging due to overlapping signs and symptoms; we should consider using a handheld pressure monitor to evaluate the intercompartmental pressures of the lower extremities if compartment syndrome is suspected.<sup>78</sup> An intercompartmental pressure of more than 30 mmHg is suggestive of compartment syndrome.<sup>79</sup> If in doubt, consider an urgent orthopedic surgery or vascular surgery consult. Expedient diagnosis and treatment are vital to prevent sequelae such as irreversible muscle damage, nerve injury or limb ischemia.

With the increasing popularity of spinning, there is an urgent need to exercise greater caution to prevent SIER. Guidelines that recommend safe ways to start indoor spinning should be established for the public. First and foremost, participants of spinning classes, especially first-timers, should be adequately informed about the risks of SIER and taught how to prevent over-exertion. Second, spinning classes should take precautions by reducing the intensity of exercise for first-time spinners by prescribing a graded program. Third, spinning instructors should be taught how to identify participants at higher risk of developing SIER. Next, there should be greater public awareness of the signs and symptoms of SIER such that patients can seek medical attention earlier. Lastly, medical professionals should be aware of the clinical signs and symptoms of SIER and possess a high index of suspicion to diagnose SIER. Early intervention is vital to prevent short and long-term sequelae of SIER.

The findings of this review should be interpreted in the context of known limitations. Due to our included studies' small sample sizes and methodology, we were unable to conduct formal weighted statistical analysis. Thus, we could not draw any statistical associations for the various outcomes of interest in our article. The majority of articles included in our systematic review were case reports or case series that may be associated with significant publication bias, in which only positive or interesting findings are published.

## 5. Conclusions

In conclusion, our article provides a comprehensive review of the demographics, patient characteristics and outcomes of SIER. SIER is a condition that the medical community will encounter more frequently due to the popularity of spinning classes. As medical professionals, we must be aware of the risk factors and clinical presentation of SIER. To mitigate the risk of developing SIER, formal guidelines regulating the participation of spinning classes should be developed.

## Declarations

**Funding Declaration: None**

**Conflict of Information Declaration: None**

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## Table 1

Table 1 is available in the Supplementary Files section.

## Appendix

An appendix is not available with this version.

## Figures

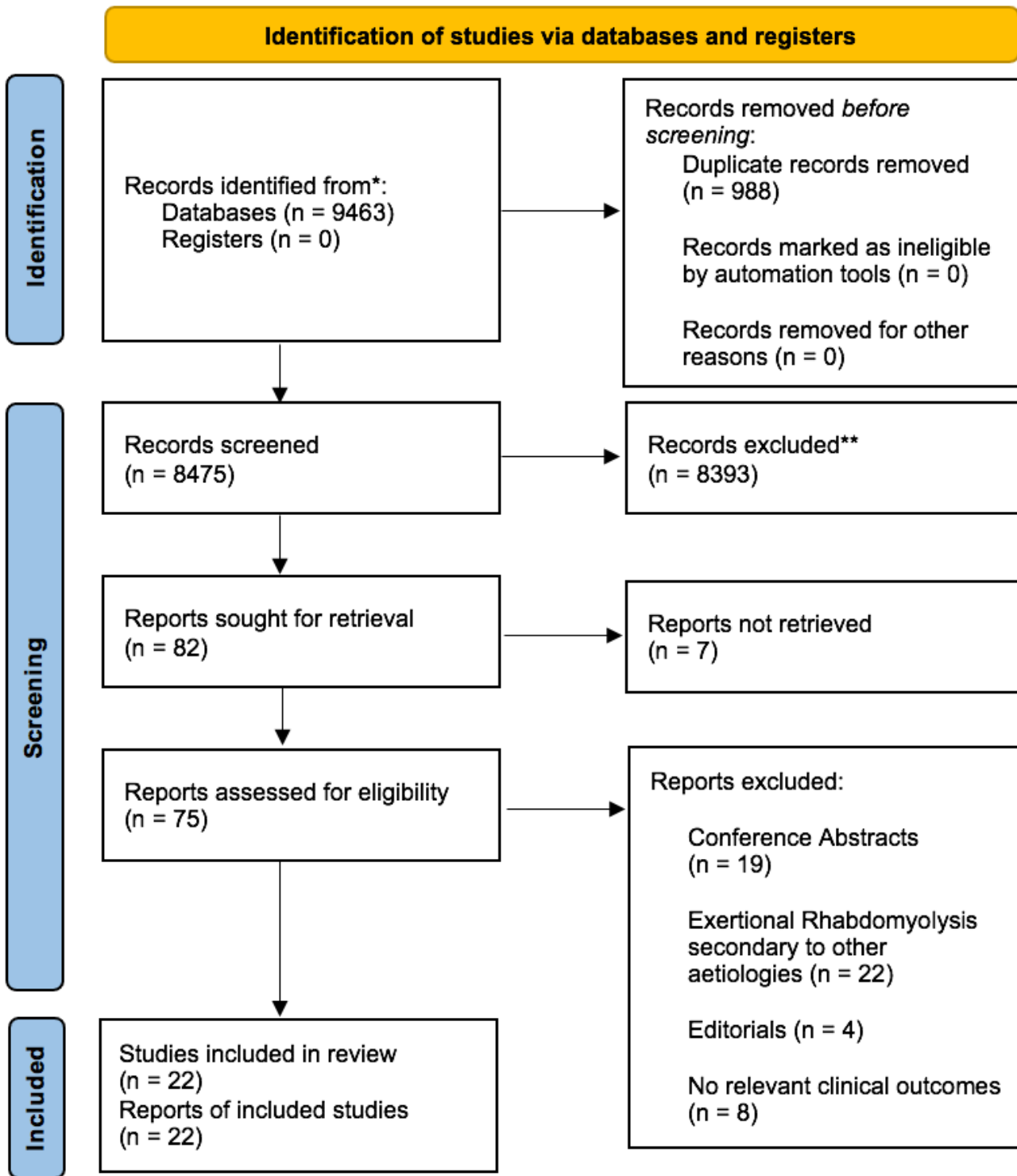


Figure 1

PRISMA-P flowchart of study identification and selection process

## Supplementary Files

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