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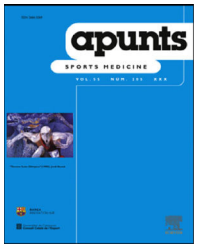

REVIEW

Beyond the intensity: A systematic review of rhabdomyolysis following high-intensity functional training

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Abstract
Objective: Rhabdomyolysis is a dangerous medical condition with potentially serious or fatal outcomes. It has been notably linked with high-intensity functional training (HIFT), a highly popular form of exercise.
Methods: This research aimed to analyze reported cases of exertional rhabdomyolysis (ER) resulting from HIFT through a systematic review following the PRISMA guidelines.
Results: A total of 26 studies encompassing 63 cases were included. Commonly observed symptoms include muscle pain, swelling, exceptionally high creatine kinase levels, and dark urine, with creatine kinase levels ranging from 7,816 to 232,579 U/L. The predominantly affected muscles were in the upper body, especially the arms. Elevated creatine kinase levels, severe muscle pain, and swelling emerged as the most reliable ER indicators. The patient age range was predominantly 20–40 years. Notably, over one-third of the cases analyzed were of low quality.
Conclusion: Our findings suggest HIFT may pose a higher risk for ER compared to most other common sporting activities.

Introduction

Rhabdomyolysis is a complex medical condition that occurs when damaged muscle tissue releases muscle cell contents (myocytes) into the bloodstream. Consequently, levels of myoglobin, potassium, and creatine kinase (CK) rise, which can cause arrhythmias or kidney failure.[1] Rhabdomyolysis can be related to physical exertion—exertional rhabdomyolysis (ER)—and in severe cases, it may result in death or necessitate surgical intervention due to compartment syndrome.[2] The incidence of ER has increased over the last decade and may be more prevalent than current literature suggests.[3] Comparable conclusions are drawn from military data, where 529 cases of ER were recorded between 2019 and 2023.[4,5]

The diagnosis of ER is often based on CK levels, which should be greater than five times the normal or exceed 1000 U/L.[6] At a level >6000 U/L, there is a risk of kidney

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failure.[7] Accompanying symptoms include myalgia, muscle weakness and/or swelling, and myoglobinuria, which causes urine to appear reddish-brown. Contributing factors may include metabolic myopathy, obesity, smoking, statin use, dehydration, exposure to heat, a history of heat-related illness, and sickle cell trait.[5,8]

High-intensity functional training (HIFT) has gained popularity over the past 15 years. It is ranked among the top 8 Global Fitness Trends for 2022[9] and is particularly appealing to the 20–50 age group. HIFT serves as an effective method for developing performance, endurance, and strength, as well as for weight management.[10,11] HIFT can be defined as a training style (or program) that incorporates a variety of functional movements, performed at high intensity, designed to improve general physical fitness and performance.[12] A mix of multimodal exercises—such as Olympic weightlifting, dumbbells, gymnastics, running, and rowing—can be combined in various sequences. HIFT also includes CrossFit©, its most prevalent form.

HIFT is associated with an increased heart rate and blood lactate concentration, typically after 5–20 min of activity.[13] It is rated as 'very hard', and according to the rate of perceived exertion (RPE), it is performed at a higher intensity than the recommendations of the American College of Sports Medicine (ACSM).[5] Executing numerous repetitions in a short span of time and employing weightlifting exercises can have detrimental effects on muscular and respiratory functions. Most importantly, due to the high intensity, significant physiological stress occurs, resulting in pronounced hormonal, metabolic, and inflammatory changes.[14]

CrossFit© has long been linked with ER, as noted by Glassman,[15] and its basic characteristics are outlined in the official manual for Level 1 CrossFit© trainers. Feito, Burrows et al. [16] reported a relatively low incidence of ER at 0.6%, while Drum et al. [5] reported only 1 case (out of 101 studied) in CrossFit© participants. Unfortunately, accurate information is scarce, and ER is not always included in injury statistics for CrossFit©.[17,18] HIFT is not solely a sport but is also employed in strength and conditioning training for athletes, with recorded cases of ER in football, swimming, and American football following HIFT.[19]

There have been several review studies on ER recently. Masuda et al.,[20] focused solely on indoor spinning, Dantas et al. [21] on military personnel, and Bäcker et al.[22] on athletes from all sports; however, they did not distinguish between HIFT and weightlifting, and case studies—a common information source—were not included in the review. Lastly, a review on athletes included cases of ER as a consequence of training and competition.[19] In no review study was HIFT investigated and reported cases of ER analyzed in detail.

Given the dangerous and even fatal consequences of ER, it is crucial to obtain as much evidence-based information as possible. To our knowledge, no similar study has been conducted on this research topic. The aim of this research is to analyze relevant cases of ER due to HIFT and, on this basis, describe the clinical manifestations, risks, and causes.

Methods

The authors of this review conducted the research following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[23]

Identification and screening

The authors conducted a systematic review of research studies written in English and published in peer-reviewed journals accessed through the Web of Science, Scopus, and PubMed databases. The processes of identification, screening, and eligibility assessment were carried out from April 2023 to July 2023 to incorporate the most recent findings related to this research topic.

The selection of research studies was based on topics including 'Rhabdomyolysis,' 'creatine kinase,' 'muscle soreness,' 'muscle damage,' 'exercise,' 'exertion,' 'high-intensity functional training,' 'functional fitness,' and 'CrossFit.' Search terms were combined using 'AND' to connect the keywords and 'OR' to minimize duplication in the search results where feasible. Additionally, a backward search was performed, meaning the references of the identified studies were examined for any relevant research that may have been missed in the initial search. A Google search was also conducted to identify unpublished or 'gray' literature.

Eligibility

The authors independently evaluated titles, abstracts, and full-text articles. Consensus was mandatory for the decision on whether to include or exclude a study in the review. The search targeted descriptive studies, case series, and individual case reports.

Participants consisted of patients who received hospital treatment for ER. These patients were required to be free from other serious health issues and to have no personal history of prior treatment related to ER occurrence. ER must have been induced by HIFT — an activity acknowledged as HIFT. The training in question had to encompass multimodal compound movements and conditioning, distinguishing it from 'traditional' strength training. Studies involving patients over the age of 14 were included, as HIFT is practiced by teenagers and may be incorporated into their training programs. The criteria did not weigh the methods or duration of treatment.

All case studies had to adhere to the CARE guidelines, as suggested by Gagnier et al. [24] Studies ($n = 40$) that failed to fulfil the case report requirements or did not conclusively diagnose ER in patients were omitted from the review. Additionally, studies describing cases of rhabdomyolysis not induced by HIFT (such as those caused by bodybuilding/strength training, endurance activities, or other activities) were also excluded. A study by Glassman [15] was excluded from this review, despite describing five cases of ER triggered by CrossFit©, for the following reasons: it was published in a non-peer-reviewed journal, the case descriptions lacked adequate medical examination details, and they did not meet the case study criteria. From five case series,[25–29] only select cases were accepted.

Inclusion

The authors concentrated on gathering critical information regarding the etiology of ER, as well as the clinical examinations and diagnoses. The data collected were synthesized and critically discussed, while the methodological quality of the included studies was concurrently evaluated. Studies of

lower quality were also included in the analysis due to their significant information content; this was taken into consideration during interpretation.

Quality assessment

The methodological quality of the studies was evaluated according to the criteria set forth by Murad et al.[30] which includes four domains and employs an eight-point scale to determine quality (8—7 points signifies high quality, 6—5 points moderate quality, and 4—1 points low quality). Quality assessment and its results are presented in Table 1.

Results

Initially, 1368 studies were identified. After the exclusion of irrelevant studies, duplicates, reviews, meta-analyses, and observational studies, 66 studies remained for inclusion. In the end, the analysis encompassed 26 case studies (Fig. 1).

The studies identified were either case studies or case series.[26,28,29,31—34] There were 63 recorded ER cases diagnosed. Patients were aged 15—46 and 26 of them (41%) were women. In total, 12 studies were assessed as low quality.

Biochemical markers, including creatine kinase (CK), aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea nitrogen, and lactate dehydrogenase (LDH), were selected due to their relevance to the sequelae of ER. The reference ranges [29,35] are as follows: CK 26—192 U/L, AST 0—31 U/L, ALT 0—32 U/L, urea nitrogen 6—20 mg/dL, and LDH 110—220 U/L.

Except for the study by Routman et al.,[34] all authors reported CK levels. Owing to varying laboratory conditions, not all CK measurements were precise; the highest recorded level was reported. CK levels varied between 7816 and 232,579 U/L. Table 1 presents the values measured upon patient admission. For instance, Oh et al. [28] noted an increase in CK levels in subsequent measurements for some patients..

Severe muscle pain was a common initial complaint in all cases, except in the report by Huynh et al. [23] which does not mention this symptom. In 40 cases (63%), patients reported pain during arm movement, pain upon palpation, or swelling of the upper arm muscles. Lower limb pain was noted by only 5 patients (8%), while the location of pain was not specified in 7 subjects (11%). Dark urine, a common symptom, was reported in 25 cases (40%); however, several studies did not report urine examination.

Most accounts provided detailed descriptions of the training protocols, commonly highlighting the performance of numerous repetitions. Specific training durations were not always known. Of the participants, 43% indicated they specifically engaged in CrossFit©. A coach supervised the training of 32 patients (51%), while the remaining sessions were either unsupervised or part of a competition. Experience with HIFT was reported by 35% of subjects, although for 37% of them, this information was not available.

Discussion

The objective of this systematic review was to scrutinize the mechanisms by which HIFT induces ER. Compared with other sports, our investigation into 63 cases reveals that ER associated with HIFT is marked by symptoms such as muscle soreness, swelling, significantly elevated CK levels, and dark urine. Upper body muscles, particularly arm muscles, appear more susceptible. Training regimens that are unfamiliar to the athlete or involve an exceptionally high volume and/or intensity appear to pose the greatest risk of ER. Although the exact average age of affected individuals could not be determined, it is estimated to be around 30 years.

Based on the data available, it is difficult to determine the incidence of ER due to HIFT. Research by Feito, Burrows, et al. [16] and Drum et al. [5] suggests a relatively low risk (0.6% of reported injuries), but the prevalence may be higher.[3] However, the number of reported cases suggests that HIFT may be a more dangerous activity compared to other sports such as weight training, swimming, American football, wrestling, and spinning.[7,25,51—54] A notably higher incidence has been observed in ultramarathon runs or extensive endurance activities, with 345 cases recorded between 2009 and 2020.[55]

Lima et al.[56] conducted a direct comparison of the incidence of ER across running, strength training, and CrossFit©, with the number of CrossFit-induced cases being lower than those caused by strength training (24% versus 57% of all cases) and comparable to running. However, their differentiation between CrossFit© and other training types is not clarified. Additionally, it must be acknowledged that their data collection spanned from 1998 to 2015, which predates the cases in our current analysis. Contemporary research on this subject would be invaluable.

Improperly structured training, often featuring numerous repetitions of push-ups and pull-ups, is a likely cause of ER, with a higher incidence noted in upper body or arm muscles (63%). This might suggest that lower limb muscles better tolerate high loads or that activities involving large muscle groups may prompt an earlier cessation of activity due to a 'central governor' mechanism, thereby preventing systemic organ failure.[57] The training programs, often self-devised and executed without professional supervision, can lead to ER even when monitored by trainers, as shown in the studies.[35,46,50] However, identifying the exact causes of ER is complex, as genetic predisposition, environmental factors, and medication can also play significant roles.[5,58]

CK levels stand as the most reliable objective indicator of ER,[6] with cases of myoglobinuria also frequently reported. Elevated levels of AST (76—3185 U/L) and ALT (33—722 U/L) were observed, but these alone are insufficient for an ER diagnosis.[1,8] None of the reviewed studies showed blood urea nitrogen levels exceeding the normal range. Additionally, glomerular filtration rate was monitored, with elevated levels noted in some cases.[29]

Teenagers have also been identified as at risk for ER,[25,27] though the most vulnerable group appears to be physically active individuals aged 20—40. This demographic is the most engaged in fitness activities, where high exertion and muscle soreness are often erroneously equated with a successful workout.

ER affects not only beginners but experienced and professional athletes as well.[19] HIFT's popularity for strength and conditioning in various sports is due to its efficacy in developing strength, power, and endurance.[11] Increased risk occurs in the off-season or preparatory camps, which tend

Table 1 An overview of studies on exercise-induced rhabdomyolysis due to HIFT.

Study	Sex	Age	Biochemistry	Time from training to medical examination	Health conditions	Training protocol	QA
Adhikari et al. (2021)[36]	Male	22	CK of 132,540 U/L; AST 136 U/L; ALT 722 U/L	2 days	generalized body ache; dark-colored urine for one day	CrossFit© exercise which included three hours of abdominal crunches, sit-ups, and weightlifting	7
Ávila-Reyes et al. (2022)[37]	Male	32	CK 189,000 U/L, BUN 12.6 mg/dL, GRF 57.9 mL/min/1.73m2, AST 3185 U/L, ALT 589 U/L	2 days	abdominal, lumbar, and thigh region pain; changes in color in the urine of several hours of evolution; mild pain on palpation of the abdominal flanks	intense work on the lower limbs	7
Aynardi & Jones (2016)[2]	Female	43	CK of >64,000 U/L, BUN 9 mg/dL	72 h	upper arms were equally swollen, elbows were held in a 30° flexed posture; anterior compartments were tense and painful to palpation; passive extension beyond 30° was too painful to tolerate; myoglobinuria	3 sets of chin-ups that were performed until "failure," lasting approximately 20 min	8
Cohen (2018)[38]	Female	26	CK of 73,044 U/L, AST 770 U/L, ALT 189 U/L, BUN 14 mg/dL	on day 3 after workout	muscle soreness/pain, increasing weakness, marked swelling of her arms, unable to raise her arms above chest level	21 week program: 125 push-ups and 85 pull-ups within a 12-minute period	7
	Female	27	CK of >8000 U/L, urine showed trace blood and protein, AST 709 U/L, ALT 271 U/L, BUN 10 mg/dL	on day 4 after workout	muscle soreness/pain, increasing weakness, marked swelling of her arms	21 week program: 125 push-ups and 85 pull-ups within a 12-minute period	7
	Female	27	CK of 10,971 U/L, urine showed trace blood and protein, AST 414 U/L, ALT 66 U/L, BUN 12 mg/dL	on day 4 after workout	muscle soreness/pain, increasing weakness, marked swelling of her arms	21 week program: 125 push-ups and 85 pull-ups within a 12-minute period	7
Doarn & Carlson (2020)[39]	Male	37	CK of 89,527 U/L, myoglobin of 8548	24 h	severe bilateral upper arm pain, swelling, and decreased motion of the elbows as well as hematuria; bilateral median nerve paresthesia that were worse with elbow extension	CrossFit© workout "Murph": 1 mile run, 100 pull-ups, 200 push-ups, 300 squats, 1 mile run.	8
Doughty (2017)[40]	Male	31	CK of 6794 U/L, AST 513 U/L, ALT 205 U/L, normal renal function	2 days	bilateral arm/upper back pain as well as stiffness and mild swelling	CrossFit© workout "Murph": 1 mile run, 100 pull-ups, 200 push-ups, 300 squats, 1 mile run. With a 20-pound vest.	7

Table 1 (*Continued*)

Study	Sex	Age	Biochemistry	Time from training to medical examination	Health conditions	Training protocol	QA
Hadeed et al. (2011)[41]	Male	33	CK of 26,000 U/L	3 days	fatigue, muscle soreness and swelling, shortness of breath, muscular weakness, and sleep disturbance; muscle tenderness to light palpation, bicep/triceps compartment swelling and pectoralis major muscle swelling	high intensity crossfit exercise workout	3
Honda et al. (2017)[35]	Male	37	CK of 95,100 U/L, LHD 4750 U/L, AST 999 U/L, ALT 443 U/L, myoglobin 160,000 ng/mL	4 days	myalgia and dark urine; Muscle tenderness in the chest and upper limbs	100 pushups,100 exercises using a 20-kg dumbbell, 50 lifts using a 10-kg weight	8
Hopkins et al. (2019)[31]	9 male/ 2 female	34.9 ± 9.7	average CK - 39,195 U/L	2.9 ± 1.5 days	10 - Dark urine 2 - Fever 1 -Swelling 2 - Thigh and lower extremity pain 6 - Upper extremity pain 2 - Back pain	not specified	7
Hummel et al. (2016)[25]	male	15	CK of 154,000 U/L	3 days	swelling of latissimus dorsi and proximal arms	intense CrossFit© workout	3
Huynh et al. (2016)[26]	male	19	CK of 130,930 U/L	3 days	N/A	CrossFit©; deadlifts 5 sets and 22 repetitions of deadlifts, pullups, burpees, skipping	3
	male	29	CK of 194,320 U/L	4 days	N/A	CrossFit©; 20 min, 150 repetitions abdominal workout	
	male	36	CK of 80,724 U/L	3 days	past history of ER 12 months prior	CrossFit©; 15 min of sit-ups and chin-ups exercise	
	male	29	CK of 44,185 U/L	N/A	N/A	CrossFit©; 70 chin-ups	
	female	32	CK of 27,574 U/L	6 days	N/A	CrossFit©; 60 chin-ups	
	male	35	CK of 65,433 U/L	2 days	N/A	Heavy Hauler workout for 45 min of single dumbbells and fast repetitive arm lifts and squats	
Junior et al. (2021)[42]	female	35	CK of 42,040 U/L	1 day	great abdominal distension; bilateral areas of hemorrhage and rupture in the rectus abdominis and all its extension, with signs of inflammation in the adjacent subcutaneous planes	Reebok CrossFit© Games	8
Larsen & Jansen (2014)[43]	female	35	CK of > 20,000 U/L, myoglobin level 4437 ng/mL, ALT 258 U/L, LDH 1314 U/L	3 days	edema, loss of strength, severe restriction of motion, pain in both upper limbs	crossfit workout with many pull-ups	4

Table 1 (*Continued*)

Study	Sex	Age	Biochemistry	Time from training to medical examination	Health conditions	Training protocol	QA
Lawrensia et al. (2021)[44]	male	27	CK of 54,240 U/L, LDH 1670 U/L	3 days	tea-colored urine, soreness in both lower extremity muscles, lower extremities tenderness with light palpation without any bruises or swelling	12 repetitions of 60 times overhead squats (720 repetitions in total), five repetitions of a one-minute duration of battle rope, wall ball, and kettlebell overhead, respectively, with a brief interval of rest in between	4
Lozowska et al. (2015)[32]	1 male/ 5 female	30−43	CK of 11,000−60,000	1 day	muscle pain in body regions where the most vigorous exercises were performed, none of the patients reported noticeable urine discoloration	3 patients first encounter with CrossFit©	3
Meyer et al. (2018)[45]	female	31	CK of 18,441 U/L, AST 462 U/L, ALT 155 U/L	2 days	bilateral biceps pain and soreness, upper extremity swelling and bilateral biceps tenderness to deep palpation, not darkened urine	variety of high- intensity exercises such as pushups, plyometrics, and weightlifting	4
Mitchell et al. (2018)[27]	female	24	CK of 9482 U/L, AST 240 U/L, ALT 109 U/L	5 days	pain of arms including scapulae and, to a lesser extent thighs, brown urine, tender on palpation of biceps and over scapulae, unable to fully flex arms	45 min strength/ interval training-type class using kettlebells and included sit-ups, press-ups from knees, kneeling plank, isometric kettlebell front raise with hold or 30 s, triceps extensions, burpees to step and squats	4
	female	18	CK of 47,120 U/L, AST 524 U/L, ALT 126 U/L.	N/A	pain and swelling in arms (similar episode 4 months previously)	band-assisted chin-ups and triceps dips, squat jumps off a step and box jumps	
Nadaf et al. (2017)[46]	male	33	CK of 85,868 U/L, LDH 4750 U/L, AST 632 U/L, ALT 485 U/L, myoglobin level of 150,000 ng/mL	N/A	severe myalgia on shoulder and upper arm, dark colored urine	three sets of 100 pushups or 3 sets of shoulder exercises, which comprise 20 alternated biceps curls, 20 shoulder presses, 20 triceps kickbacks, 20 lateral raises, and 20 lying flies, with a 20- kg dumbbell. Each set is usually completed within few minutes with a 1-minute rest interval between sets	7

Table 1 (*Continued*)

Study	Sex	Age	Biochemistry	Time from training to medical examination	Health conditions	Training protocol	QA
Noren & Sriram (2018)[47]	female	29	CK of 70,400 U/L	2 days	severe arm pain, stiffness and weakness, nausea, loose stools and generalized back pain, pronounced swelling and tenderness to palpation over both upper extremities	dozens of body-weight pull-ups, bicep curls with 15- pound dumbbells and rope climbing over the course of 1 h	4
Oh et al. (2015)[28]	male	25	CK of 60,436 U/L, BUN 14 mg/dL	N/A	arms muscle pain	CrossFit©	4
	male	29	CK of >32,000 U/L, BUN 16 mg/dL	N/A	bilateral biceps muscle pain	CrossFit©	
	male	22	CK of 111,622 U/L, BUN 18 mg/dL	N/A	thighs pain	P90X	
	male	25	CK of >32,000 U/L, BUN 11 mg/dL	N/A	upper extremity pain	CrossFit©	
	male	23	Ck of 144,046 U/L, BUN 13 mg/dL	N/A	arms muscle pain	Body Composition Program; pull-ups and jump-ups	
	male	30	Ck of 232,579 U/L, BUN 23 mg/dL	N/A	thighs pain	CrossFit© (first time)	
	male	25	CK of 60,145 U/L, BUN 11 mg/dL	N/A	arms muscle pain	physical training and strenuous activity	
Pearsey et al. (2013)[48]	male	31	CK of 59,159 U/L, AST 776 U/L, ALT of 226 U/L	2 days	"cola colored" urine, intense (arm) pain	48 alternating sets (60 s duration) of push-up and pull-up variations. The subject performed the maximum number of repetitions possible of push-ups or pull-ups in each set. The total exercise duration was 48 min. The subject performed approximately 400 push-ups and approximately 200 pull-ups in 48 min	8
Rathi (2014)[33]	male	33	CK of 98,559 U/L	3 days	muscle pain, soreness and stiffness in biceps and across chest, diarrhea with very dark colored urine, nausea	100 plus push-ups, pull-ups, squats and sit-ups all in the span of thirty minutes	4
	male	37	CK of 148,182 U/L, AST 1997 U/L, ALT 638 U/L	3 days	upper extremity and abdominal pain, dark colored urine	100 plus push-ups, pull-ups, squats and sit-ups all in the span of thirty minutes	

Table 1 (*Continued*)

Study	Sex	Age	Biochemistry	Time from training to medical examination	Health conditions	Training protocol	QA
Routman et al. (2018)[34]	female	27	N/A	2 days	severe (right shoulder) pain over the posterior aspect of the right scapula, difficulty utilizing the right upper extremity, palpable tenderness over the belly of the infraspinatus muscle with moderate swelling and warmth in the area; MRI demonstrated marked edema in the infraspinatus fossa	20−19..1 burpees 1−2. . .19−20 kettlebell swing	7
	female	26	CK of 20,144 U/L	1 day	pain over the posterior aspect of both shoulders, unable to lift the right arm secondary to pain; MRI demonstrated isolated infraspinatus myositis with extension of the exuded fluid into the subacromial and subdeltoid spaces	20−19..1 burpees 1−2. . .19−20 kettlebell swing	
Stanfa et al. (2017)[29]	female	20	CK of 4326 U/L, ALT 33 U/L, AST 76 U/L, BUN 11 mg/dL	3−4 days	sever arm muscle pain, swelling, and dark colored urine	arm competition workout of completing a maximum number of pull-ups, rows, and bench presses for 2 complete cycles	8
	female	19	CK of 15,499 U/L, ALT 139 U/L, AST 414 U/L, BUN 19 mg/dL	3−4 days	sever arm muscle pain, swelling, and dark colored urine	arm competition workout of completing a maximum number of pull-ups, rows, and bench presses for 2 complete cycles	
	female	21	CK of >20,000 U/L, ALT 416 U/L, AST 1365 U/L, BUN 15 mg/dL	3−4 days	sever arm muscle pain, swelling, and dark colored urine	arm competition workout of completing a maximum number of pull-ups, rows, and bench presses for 2 complete cycles	
	male	19	CK of >20,000 U/L, ALT 383 U/L, AST 901 U/L, BUN 17 mg/dL	3−4 days	sever arm muscle pain, swelling, and dark colored urine	arm competition workout of completing a maximum number of pull-ups, rows, and bench presses for 2 complete cycles	
	male	21	CK of >20,000 U/L, ALT 150 U/L, AST 392 U/L, BUN 16 mg/dL	3−4 days	sever arm muscle pain, swelling, and dark colored urine	arm competition workout of completing a maximum number of pull-ups, rows, and bench presses for 2 complete cycles	
	male	19	CK of >20,000 U/L, ALT 487 U/L, AST 1459 U/L, BUN 11 mg/dL	3−4 days	sever arm muscle pain, swelling, and dark colored urine	arm competition workout of completing a maximum number of pull-ups, rows, and bench presses for 2 complete cycles	

Table 1 (*Continued*)

Study	Sex	Age	Biochemistry	Time from training to medical examination	Health conditions	Training protocol	QA
Tibana et al. (2018)[49]	female	35	CK of 43,322 U/L, AST 477 U/L, 74 U/L	1 day	abdominal pain	2 days competition (5 events) 21 chest-to-bar pull-ups, 21 thrusters (40 kg), 9 chest-to-bar pull-ups, 9 thrusters (40 kg); 60 GHD sit ups (unaccustomed exercise), 15 toes-to-bar; AMRAP during 5 min of strict handstand push-ups; 40 deadlifts (45 kg), 20 kettlebells clean and jerks (24 kg), 5 bar muscle ups	8
Wagner et al. (2015)[50]	female	21	CK of 7816 U/L	2 days	significant edema of elbow areas of both arms, extreme fatigue and muscle soreness, visually observing and palpating a "bump" on the posterior aspect at the elbow	5 pushups in the first minute, 10 in the second, and adding 5 push-ups each minute until participants can no longer continue. She recalls completing 6 rounds of increasing repetitions in each minute, thereby performing 105 pushups in 6 min	4
			CK of 21,948 U/L	N/A	after 4,5 months extreme fatigue and muscle soreness	for approximately 7−8 min: maximum number of pushups completed on the ground alternating with a maximal amount of pull ups completed on a weight assisted pull up machine	
	female	26	CK of >32,000 U/L, 14 mg/dL	N/A	arms, abdomen and thighs pain	physical training and strenuous activity	

QA − Quality assessment, CK - creatin kinase; ALT - alanine transaminase; AST - aspartate transaminase; BUN - blood urea nitrogen; LHD - lactate dehydrogenase.

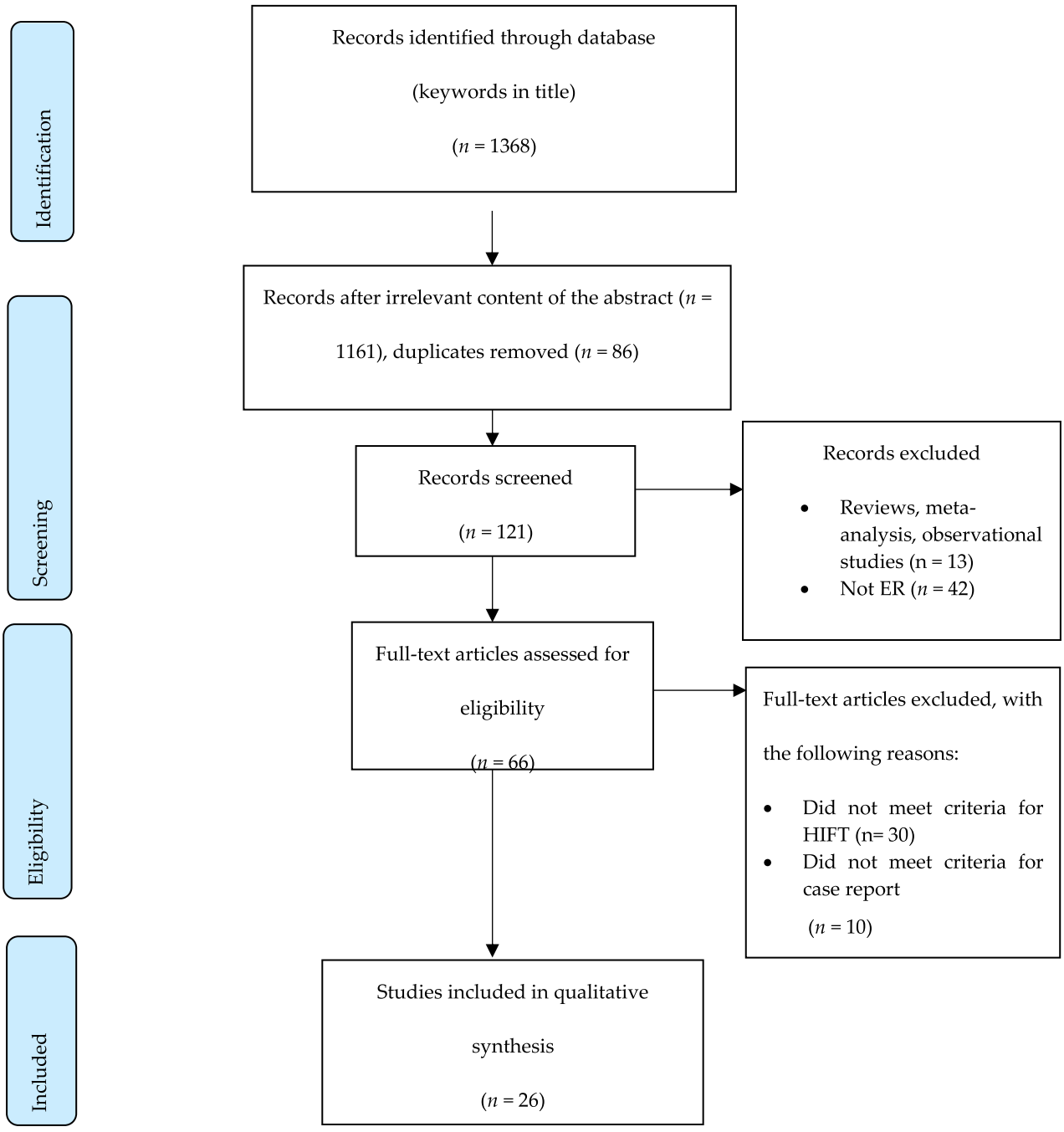

Fig. 1 An overview of the selection procedure.

to be more demanding.[29] Another domain where HIFT is prevalent is the military, which demands high levels of physical readiness from soldiers. Its effectiveness aligns with the principles of military training.[59] Records from the military hospital from the years 2010–2012 report a total of 30 ER cases caused by a strenuous physical program and/or HIFT.[28] Even though soldiers need to be physically and mentally resilient, it would be advisable to consider the risks and consequences associated with ER.

Although ER is a serious and sometimes life-threatening condition, it should be noted that severe cases involving renal failure are less frequent compared to other types of rhabdomyolysis.[60] These severe cases are quite uncommon and typically arise in situations of extreme stress and fatigue, such as military actions or intense exercise. In the context of HIFT, the risks should not be underestimated, given the potential for serious health outcomes. Monitoring symptoms, ensuring proper hydration, and gradually increasing training intensity can help mitigate the risk.[8] Coaches and athletes should also implement structured rest periods and recovery strategies to reduce the likelihood of ER occurring.

This review is not without limitations. Case series typically provided less information than individual case reports. For example, Huynh et al. [26] omitted initial examination details regarding patient symptoms. Furthermore, not all

studies provide comprehensive details on the health status of participants or their HIFT experience,[31] and training protocols are sometimes inadequately described.[28,32] Additionally, 12 studies were deemed to be of low quality.

Conclusions

HIFT is a widely practiced form of exercise characterized by participants pushing themselves to fatigue, exhaustion, or muscle soreness. The high effort coupled with frequent repetitions at submaximal or maximal intensities renders HIFT a potentially hazardous activity for the development of ER. Our results suggest that the incidence of ER from HIFT is likely higher than that associated with other physical activities, with the upper body and arms being particularly vulnerable. The most reliable indicators for diagnosing ER are intense muscle pain, muscle swelling, elevated CK levels, and myoglobinuria. Given the serious and sometimes fatal consequences of ER, there is a critical need for education among coaches, professional athletes, and the general physically active population.

Conflicts of interest

No potential conflict of interest was reported by the authors.

Author contributions

Conceptualization, Methodology, Quality assessment, Writing, Supervision — PS

Data analysis, Quality assessment, Writing - TP

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