

## Original Article

# (Very) high creatine kinase (CK) levels after Whole-Body Electromyostimulation. Are there implications for health?

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**Abstract:** Recently extreme increases in serum creatine-kinase (CK) concentration after initial whole-body electromyostimulation (WB-EMS) were reported that indicating a severe (exertional) rhabdomyolysis. Thus our aim was (1) to verify the reported WB-EMS induced CK-increases, (2) to determine the corresponding consequences for health and (3) to assess physiological CK-adaptation to frequent WB-EMS. Thirty-seven eligible WB-EMS novices and six marathon runners living in the Nürnberg-Erlangen area were included. Trial-I and trial-II determined the effect of one single WB-EMS session to exertion (20 min) on electrolytes, muscular and renal parameters; trial-III evaluated the effect of once a week WB-EMS application for 10 weeks on CK-kinetics. Blood samples of corresponding serum parameters were drawn before, immediately after and 24, 48, 72, and 96 h post WB-EMS exercise. After WB-EMS, serum CK-levels increased by the 96-fold (peak-CK:  $23.940 \pm 24.545$  U/L), 8.5-fold higher compared with CK-increases after a marathon run. However, we did not observe any relevant health consequences with respect to cardiac and renal burdens. Further, following the repeated bout effect, 10 weeks of WB-EMS resulted in a 21-fold reduction of CK-concentration ( $<1.000$  U/l) compared with the baseline test. We confirmed there were exceptionally high CK increases after initial WB-EMS when the intensity was (too) high, but this was ameliorated by a rapid and profound “repeated bout effect” after 10 weeks of WB-EMS application. Although we did not detect any negative consequences in this healthy, well-prepared and medically supervised cohort, initial WB-EMS application to exertion should be strictly avoided in order to prevent hepatic, renal and cardiac incidents.

**Keywords:** Whole-body electromyostimulation, creatine kinase, rhabdomyolysis, renal failure

## Introduction

During the last decade, whole-body electromyostimulation (WB-EMS) has experienced a rapid boom in Europe. Indeed, WB-EMS is a promising exercise technology which significantly affects body composition and strength parameters with low time effort [1-3]. However the mechanism of WB-EMS, i.e. the simultaneous stimulation of large muscular areas (up to  $2,800$  cm<sup>2</sup> [4]), combined with the application of too high current intensity causes severe muscle soreness and may induce rhabdomyolysis [5]. A broad discussion concerning a harmful effect of WB-EMS based on extremely high increases in serum creatine kinase (CK) activity

reported after WB-EMS application has recently emerged [6]. Corresponding observations [7, 8] reporting individual CK levels of up to a thousand-fold ( $240,000$  U/l) of the normal range ( $<180$  U/l) have further intensified this issue. Although the discussion on the clinical relevance of high CK levels was not uniform [9], the appearance of high CK levels in blood is nevertheless considered to be a marker of severe muscle damage [10, 11]. Extreme increases in CK concentration constitute a potential risk of renal damage [5]. Due to the high correlation of CK to myoglobin [12, 13], in the worst case there may even be acute renal failure (ARF) [14, 15], at least in persons with prevalent renal impairment. Besides ARF, rhabdomyolysis may

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**Table 1.** Implementation time and study endpoints of trial-I-III

	TRIAL-I	TRIAL-II	TRIAL-III
Implementation	Cross-sectional; May 2014 (EMS) June 2014 (Marathon)	Cross-sectional; July 2014	Longitudinal; May to July 2014 Participants of trial-I
Study Endpoints	Serum CK	Serum CK Myoglobin LDH (lactate dehydrogenase) Electrolyte balance Creatinine eGFR Urine parameter*	Serum CK

EMS: Electromyostimulation; eGFR: estimated glomerular filtration rate. \*urinary parameters: urinary pH values, leucocytes, blood and protein.

**Table 2.** Subjects characteristics at baseline (MV  $\pm$  SD). WB-EMS: Whole-Body Electromyostimulation

Variable	TRIAL-I		TRIAL-II	TRIAL-III
	WB-EMS (n=25)	Marathon (n=6)*	WB-EMS (n=12)	WB-EMS (n=13)
Age [years]	32.0 $\pm$ 7.9	41.7 $\pm$ 8.1	31.1 $\pm$ 8.4	32.9 $\pm$ 7.7
Body mass [kg]	78.4 $\pm$ 11.2	74.5 $\pm$ 4.1	71.8 $\pm$ 8.6	85.5 $\pm$ 9.1
Body height [cm]	181.1 $\pm$ 6.0	179.7 $\pm$ 5.5	178.3 $\pm$ 4.1	183.6 $\pm$ 6.4
BMI [kg/m <sup>2</sup> ]	23.6 $\pm$ 2.3	22.9 $\pm$ 1.0	22.5 $\pm$ 2.2	24.9 $\pm$ 1.8
LBM [kg]	66.0 $\pm$ 9.4	-----*	60.8 $\pm$ 8.8	71.7 $\pm$ 6.3
Body-fat [%]	15.7 $\pm$ 4.8	-----*	15.5 $\pm$ 4.5	15.9 $\pm$ 5.2
Exercise volume [min/week]	327 $\pm$ 128	277 $\pm$ 118	374 $\pm$ 193	293 $\pm$ 105

\*BIA analysis of the marathon runners was not possible due to the logistics required.

trigger more acute effects (e.g. hyperkalemia and hypocalcemia) with corresponding problems for muscle and heart [16, 17].

In the present study, we aimed to answer three research questions: (1) Are the CK concentrations after exertional initial WB-EMS application actually that high? (2) If so, what is the clinical implication of those high CK concentrations? (3) Is there a pronounced "repeated bout effect" after frequent WB-EMS application?

Our hypotheses were: (1) Serum CK concentrations after exertional initial WB-EMS application are exceptionally high and are 4 times greater than the CK levels induced by a marathon run. (2) Exertional WB-EMS application in WB-EMS novices may have serious health implications. (3) Following a repeated bout effect, CK levels are significantly reduced after 10 weeks of once a week WB-EMS training session and may reach uncritical levels that are comparable to resistance training protocols.

### Materials and methods

The study was designed and realized by the Institute of Medical Physics in close cooperation with the Institute of Nephrology and Medical Department III of the University of Erlangen-Nürnberg (FAU), Germany. All parts of the project were conducted between May and October 2014 and complied with the Helsinki Declaration "Ethical Principles for Medical Research Involving Human Subjects". The ethics committee of the FAU (Ethikantrag 183\_14B) approved this study. All participants gave their written informed consent.

#### Study design

The project was structured into three parts (**Table 1**): The aim of trial-I was to determine the effects of an initial WB-EMS application on serum CK concentration in subjects without previous WB-EMS experience (n=25). In order to appraise the significance of WB-EMS-induced changes, data were compared with a marathon run (42.2 km) run by male runners

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**Figure 1.** miha bodytec WB-EMS equipment. Electrodes for trunk and extremities (left side), WB-EMS-device (central) and control panel (right side).

(n=6). Trial-II focused on the clinical relevance of high CK concentration after WB-EMS application in untrained subjects (n=12). In this project, we sampled relevant serum parameters to decide if exertional WB-EMS creates critical physiological changes related to rhabdomyolysis. Finally, in trial-III we conducted a longitudinal trial to observe whether frequently conducted WB-EMS sessions trigger relevant physiological adaptations in serum CK peaks (“repeated bout effect”).

### Subjects

**WB-EMS:** We included 25 eligible subjects recruited by personal approach (23 men, 2 women) with no previous WB-EMS experience. WB-EMS participants were eligible if they met the inclusion criteria: (a) healthy and 20-50 years old, (b) unfamiliar with WB-EMS (no WB-EMS application during the last 12 months), (c) experienced in resistance exercise training ( $\geq 2$  sessions/week) for longer than 5 years and satisfied the corresponding exclusion criteria of (d) medication/diseases affecting muscle metabolism or kidneys, (e) conditions that prevent WB-EMS (e.g. epilepsy, cardiac pacemaker) as listed by the manufacturer (miha bodytec®, Gersthofen, Germany).

**Marathon:** Competitors of the 2014 Fürth marathon were contacted by personal letters to their addresses provided by the organizers a few weeks before the event. Applying comparable eligibility criteria six experienced male marathon runners exercising more than three sessions/week for  $\geq 5$  years (instead of  $\geq 2$  resistance exercise sessions/week) agreed to participate and accepted the 5-day test schedule. **Table 2** gives the baseline characteristics of the subjects of all groups.

### Measurements & testing

Height was determined with a Harpenden stadiometer (Holtain Ltd., Crymmych, Wales). Body mass, lean body mass and body fat were tested via segmental multi-frequency bioelectrical impedance analysis (DSM-BIA, Inbody230, Biospace, Seoul, Korea). A standardized questionnaire was used to evaluate the level of physical activity and sports as well as the exertion during the WB-EMS test sessions (i.e. initial session of trial-I and -II, initial and last session of trial-III) on a scale from 1 (no pain) to 7 (extreme pain) over 5 days.

Blood was sampled under non-fasting condition from an antecubital vein before, immediately after, 24 h, 48 h, 72 h, and 96 h post exercise (i.e. WB-EMS or marathon run). The same researchers consistently conducted procedures of blood sampling and analysis. In summary, CK, myoglobin, LDH, creatinine, potassium, calcium and sodium were analyzed using the Beckmann Coulter Inc. device (Brea, USA).

Urinary analysis (Multistix 10SG; Siemens Healthcare Diagnostics, Frimley, Great Britain) was conducted to determine urinary pH values, leucocytes, blood and protein. Urine was sampled over the same period just a few minutes before or after the blood samples.

### WB-EMS application

The WB-EMS equipment (miha bodytec GmbH, Gersthofen, Germany) used in this project consisted of an electrode vest and various, hip, leg and arm cuffs that allows simultaneous stimulation of up to 10 muscle groups with a stimulation area of 2.800 cm<sup>2</sup> [4]. The device permits a dedicated current intensity setup for each single muscle group (**Figure 1**).

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**Table 3.** Mean value and standard deviation for baseline data and differences within groups, mean differences between groups with 95% confidence interval (95%-CI), significance (P) and effect size (D')

	WB-EMS (n=25) (MV ± SD)	Marathon (n=6) (MV ± SD)	Difference MV (95%-CI)	P	D'
Creatine kinase (CK) [U/l]					
Baseline (pre)	249	130	---	0.06	--
All-time peak (post)	23940	2795	---	<0.01	--
Difference	23691 ± 24521 (P<0.01)	2665 ± 2166 (P=0.030)	21026; (10.772-31.279)	0.01	.94

All trials followed a bipolar training protocol. As per the literature and use in a commercial environment, the impulse frequency was set at 85 Hz with an impulse width of 350  $\mu$ s [1] and an impulse raise time of 1 s. Also similar to commercial usage we applied a duration of 20 minutes with a protocol of 6 s under current intermitted by a 4 s break. During the 6 s current phase slight movements were performed. To standardize movements we used a synchronized animated video. The participants completed 1-3 sets with 6-8 reps of 7-10 easy movements in a minor range of motion (ROM) to keep the effect of the movement itself as low as possible. The exercises performed consisted of dynamic squatting and additional movement pattern for the upper limbs, such as biceps curl, shoulder press, butterfly or chest-press.

During the WB-EMS test session strong emphasis was placed on generating maximum effort of the participants, i.e. close to an inability to move due to the EMS-induced muscle tetanus. Certified instructors supervised participants, monitored the proper WB-EMS implementation and encouraged participants to work to maximum effort. In close cooperation with the participants, (current) intensity was increased every 3-5 minutes to maintain maximum or near-maximum load. In parallel, participants of the longitudinal 10-week WB-EMS trial were requested to exercise at a rate of perceived exertion of "6-7" ("hard" to "very hard") on the BORG CR-10 Scale. Apart from the lower intensity, the WB-EMS protocol for the weekly WB-EMS trainings session (trial-III) was identical to the protocol described above. To ensure the safe implementation, all WB-EMS sessions were supervised by medical staff.

### Statistical procedures

We conducted a formal sample size analysis based on the primary endpoint of trial-I and -II.

With respect to trial-I, we expect a 12-fold increase of CK after a marathon run. In order to prove our hypothesis of a 4-fold higher CK increase after WB-EMS (compared with marathon; i.e.  $\approx$ 50-fold increase from baseline), 13 subjects had to be included to generate a power of 80% ( $\alpha=0.05$ ). The 13 subjects recruited for trial-I who went on to participate in trial-III generated a power of  $\geq$ 80% ( $\alpha=0.05$ ) based on a 5-fold CK reduction after the 10-week conditioning period. For trial-II, expecting a 40-fold increase in myoglobin 12 persons had to participate to generate 80% power ( $\alpha=0.05$ ). However, in this article we combined the CK data after initial exertional WB-EMS application generated by trial I and III and thus generated a power of 95% to address hypothesis (1).

We conducted a per-protocol analysis. Due to relevant alcohol abuse during the test period of trial-I we had to exclude one subject from the analysis. Data were consistently reported as means and standard deviations (MV  $\pm$  SD). Depending to the distribution of the data, changes within groups were analyzed using Student t-tests or Wilcoxon rank-tests. Differences between WB-EMS versus marathon run as well as CK increases during the initial versus 10 week FU-test of trial-III were determined via Welch-t-tests. Significance was accepted at P<0.05. Effect size (ES) was calculated by using Cohen d'. SPSS 22 (IBM, Chicago USA) was used for all statistical procedure.

### Results

Baseline characteristics of the participants are shown in **Table 2**. All of the subjects participating in trial-III attended at least 9 of the 10 prescribed WB-EMS sessions. Further, all subjects said that they had maintained their lifestyle, nutrition and physical activity/exercise habits during this period.

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**Table 4.** Changes (MV  $\pm$  SD) of parameters monitored during trial-II

	Pre-	Post-exercise	24 h	48 h	72 h	96 h	Overall Peak
CK [U/l]	235 $\pm$ 211	263 $\pm$ 199	3156 $\pm$ 3845*	12538 $\pm$ 14487*	30558 $\pm$ 31002**	31080 $\pm$ 26980**	32272 $\pm$ 30881**
Myoglobin [ug/l]	68.2 $\pm$ 440.	257.5 $\pm$ 277.4	649.0 $\pm$ 757.1*	2100.0 $\pm$ 2027.7**	2296.9 $\pm$ 2116.1**	896.2 $\pm$ 6310.**	2705.8 $\pm$ 2193.9**
LDH [U/l]	187.6 $\pm$ 43.2	212.9 $\pm$ 31.9*	229.4 $\pm$ 73.3	428.6 $\pm$ 258.1**	787.6 $\pm$ 576.9**	687.0 $\pm$ 371.8**	814.4 $\pm$ 565.8**
Potassium [mmol/l]	4.3 $\pm$ 0.4	4.3 $\pm$ 0.3	4.6 $\pm$ 0.3*	4.7 $\pm$ 0.4**	4.7 $\pm$ 0.3*	4.6 $\pm$ 0.3	5.0 $\pm$ 0.2***
Calcium [mmol/l]	2.35 $\pm$ 0.15	2.36 $\pm$ 0.10	2.38 $\pm$ 0.06	2.38 $\pm$ 0.08	2.32 $\pm$ 0.10	2.41 $\pm$ 0.08	2.43 $\pm$ 0.06
Sodium [mmol/l]	140.9 $\pm$ 1.5	139.8 $\pm$ 1.6**	138.8 $\pm$ 0.6***	139.1 $\pm$ 1.3***	138.7 $\pm$ 1.2**	139.7 $\pm$ 1.4	141.4 $\pm$ 1.2*
Creatinine [mg/dl]	0.86 $\pm$ 0.12	0.93 $\pm$ 0.16*	0.92 $\pm$ 0.18	0.93 $\pm$ 0.15**	0.89 $\pm$ 0.15	0.84 $\pm$ 0.15	0.99 $\pm$ 0.19**
Urea [mg/dl]	34.0 $\pm$ 7.9	35.5 $\pm$ 7.8*	29.0 $\pm$ 12.4	30.8 $\pm$ 7.4	30.4 $\pm$ 8.9	31.7 $\pm$ 7.5	39.1 $\pm$ 8.9**

*p*-values: \* $<$ 0.05; \*\* $<$ 0.01; \*\*\* $<$ 0.001 (compared with baseline).

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**Table 5.** Changes of CK-concentration after WB-EMS before and after 10 weeks of WB-EMS exercise training

CK [IE/l]	Before 10 weeks of WB-EMS (n=11)	After 10 weeks of WB-EMS (n=11)	Difference (95% KI)	P
Baseline	278 ± 155	287 ± 173	10 (-81 to 100)	.818
Peak	17575 ± 14717	906 ± 500	16669 (6810 to 26528)	.004

### *Trial-I: Maximum CK-levels after exertional WB-EMS versus marathon run*

In summary, altogether 25 WB-EMS novices and 6 marathon runners were included in the analysis (Table 2). Based on high initial values (249 ± 177 U/l) serum CK significantly increased (P<0.01) in the WB-EMS group 96-fold with a CK peak after 3-4 days. Absolute CK changes of the WB-EMS were significantly (P<0.01) higher compared with the marathon group, which demonstrated significantly lower baseline CK values (Table 3). No relevant differences were detected between male and female WB-EMS applicants. Thus, hypothesis (1) was confirmed that “serum CK concentrations after exertional WB-EMS initial application were exceptionally high” (i.e. 4-fold higher compared with marathon).

### *Trial-II: Clinical relevance of WB-EMS initial application to a voluntary maximum*

With respect to the participants of trial-II (n=12) peaks of CK, myoglobin and LDH concentration induced by WB-EMS averaged 137-fold for CK (P=0.04), 40-fold for myoglobin (P=0.02) and 4.3-fold for LDH (P=0.03) respectively compared with the baseline data (Table 4). All values consistently peaked after 3-4 days post WB-EMS application. Particularly, CK and myoglobin levels showed a close correlation with respect to the peak (r=0.92, P=0.01) and relative increase (r=0.67, P=0.02).

With one exception (57 ml/min after 24 hours only) estimated glomerular filtration rate (eGFR) consistently remained in the normal range of data (>60 ml/min). In parallel, the same male participant demonstrated slightly increased creatinine level (1.32 mg/dl after 24 hours only; normal range: 0.80 to 1.25 mg/dl). However, although average creatinine levels (P=0.01) rose significantly by 15.1 ± 9.3% with a peak after 48 hours, peak concentrations were well within the normal range.

Concerning electrolyte balance and corresponding potential muscular, neuronal and cardiac risks, sodium (P=0.026) and potassium (P≤0.01) significantly changed with a slight trend to hypernatremia or hyperkalemia. However, none of

the participants reached the cut-off for hypernatremia (>145 mmol/l) and only three participants showed potassium peak values slightly over 5.0 mmol/l, which is considered to be the upper border of normal serum potassium concentration. Calcium did not vary relevantly during the observational period (P=0.75) and no participant showed reduced calcium concentrations or hypocalcaemia (<2.2 mmol/l).

Overall, the analysis of the urinary parameters glucose, bilirubin, specific weight and leucocytes did not show any deviation. For three persons (for two after 24 hours; one after 48 h) we found traces of erythrocytes (<10 µl); one person demonstrated a slight increase after 72 h (≤80 µl) another two persons showed a moderate raise of 80-200 µl after 48 to 72 h. Further, we found traces of protein (consistently <30 mg/dl) in seven persons.

Both, the increase in myoglobin as well as traces of erythrocytes can cause myoglobinuria, indicated by reddish-brown cola- or tea-colored urine. However, no change in urinary color was observed.

Addressing hypothesis (2): although high CK and myoglobin levels indicate a severe exertional rhabdomyolysis, we were unable to determine serious health implications after initial WB-EMS application to a voluntary maximum.

### *Trial-III: Adaptations of CK after 10-week of WB-EMS training*

Table 5 gives changes of CK levels after WB-EMS to exhaustion before and after a 10-week training period of once a week 20 min WB-EMS. With respect to the participants of trial-III, levels during initial WB-EMS application increased significantly 63-fold (P=0.01) from 278 ± 155 U/l before, to a maximum time peak of 17575 ± 14717 U/l, 3-4 day after the WB-EMS session (Table 5). After 10 weeks, the CK response to exertional WB-EMS was less

pronounced, increasing only 3-fold ( $287 \pm 173$  to a peak of  $906 \pm 500$  U/l;  $P=0.02$ ). While baseline (pre-) CK concentrations were comparable, differences for peak CK levels before and after the 10-week conditioning period were significant ( $P=0.04$ ) and demonstrated a high effect size ( $d'=-1.48$ ). Thus, hypothesis (3), that CK levels fall significantly after 10 weeks of once a week WB-EMS training sessions, was confirmed.

### Discussion

In this project, we determined the consequences of exertional WB-EMS with respect to rhabdomyolysis and corresponding health consequences in active subjects with no previous experience in WB-EMS. Although common sense should rule out exertional WB-EMS application during the first sessions, athletes and other highly motivated groups regularly demand (too) high intensities during their initial, often familiarization, WB-EMS sessions. As a result, dramatic CK increases after exertional WB-EMS ( $240.000$  U/l; [8]) falling within the range of severe trauma have been reported. However, in the light of such data based on observations in individuals, trial-I was designed to evaluate changes of serum CK activity after an initial WB-EMS session to exertion in a group of skilled sportspersons with no previous WB-EMS experience. In order to estimate the impact of potential CK changes we compared the data of this group with the CK results after a marathon run completed by well-trained runners. As hypothesized, exertional initial application of WB-EMS resulted in extensive increases in CK that exceeded the CK peak concentration after a marathon 8.5-fold. However, the data of the marathon group actually ranged at the upper end of the data spectrum reported for CK increases after a marathon, which ranged from  $1.104$  U/l to  $3.322$  U/l [18-21]. Reviewing the literature, only a few studies were found that reported higher CK peaks after "voluntary" exercise. While a 48-hour run induced similar average CK values ( $20,600$  U/l, 48 h post-race,  $n=7$ ) [22] compared with the present study, Skenderi et al. reported a CK peak of  $43,763$  U/l ( $n=39$ ) following 48 hours after a 246-km run [23]. Addressing individual CK peaks, the exertional WB-induced peak value of  $240.000$  U/l reported for a young soccer player [7, 8] is only

exceeded by an individual CK peak of  $264.300$  U/l determined immediately after a mountainous 100-mile run [24].

Revisiting the underlying mechanism of excessive CK response to exertional WB-EMS, most criteria of high CK increases reported after exhaustive exercise perfectly match with WB-EMS application [10, 25]. However, the most prominent feature of WB-EMS that affects CK concentration is definitely the high volume of simultaneously stimulated muscle area (up to  $2,800$  cm<sup>2</sup>) [4] associated with a supra-maximal intensity which is able to generate complete tetanus of the muscle.

Considering that 26% of our cohort demonstrated a mild, and 70% a severe exertional rhabdomyolysis (defined as an 11- to 49-fold or  $\geq 50$ -fold increase of resting CK concentration [26]) we correspondingly expected the negative health consequences reported by the literature [5]. Overall, however, we failed to clearly determine relevant negative consequences of exertion on parameters reported to be affected by (severe) rhabdomyolysis.

Acute renal failure might be the most prominent clinical complication of severe rhabdomyolysis. The combination of high serum CK and high release and subsequent deposition of myoglobin can cause intrarenal vasoconstriction, direct toxic and isochemic tubule injury and obstruction followed by acute tubular necrosis with the result of ARF [5, 14]. As described above, myoglobin concentration rose 40-fold ( $P=0.02$ ) based on normal resting values ( $\leq 70$   $\mu\text{g/l}$ ; [27]). The corresponding myoglobin peak of  $2.706$   $\mu\text{g/l}$ , however, was within the very wide range observed after acute traumas ( $107$ - $8340$   $\mu\text{g/l}$ ; [28]) which are regularly accompanied by ARF. Indeed, high serum CK with corresponding high myoglobin values are strongly correlated with the onset of ARF, even though the risk seems to be low for  $\text{CK} \leq 15.000$ - $20.000$  U/l [14, 29] and myoglobin  $< 4.000$   $\mu\text{g/l}$  [30]. However, we failed to determine relevant renal consequences (i.e. ARF according to the RIFLE criteria [31]) including myoglobinuria [5] with its appearance of dark, reddish-brown (tea-colored) urine [14]. This result could be partially referred to the relative low peak myoglobin concentration. Indeed, despite the parallel increases in CK and myoglobin reported in the literature [32], myoglobin shows a considerable (3.5-fold) lower factorial manifestation.

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Although CK may be the more reliable marker in assessing the intensity of muscle damage due to its slower overall degradation and removal, (serum) myoglobin was a much more effective predictor of acute kidney injury [32]. Therefore, in combination with non-parallel 'not-as-high-as-expected' enhancement without even approaching the stated limit for serum myoglobin, all such clinical concerns proved to be unfounded, despite rhabdomyolysis, in reference to organ failure. Another key factor that differs between trauma and exercise-induced rhabdomyolysis relates to the inherent consequences of a trauma. Unlike an obstruction due to a large amount of proteins, acute trauma can lead to a reduction of circulating bloodstream with subsequent insufficient perfusion of the kidneys. Consequently, permeability drops and thus promotes ARF [33].

Thus, the "blunted" myoglobin rise with its correspondingly low risk of renal obstruction, sufficient perfusion of the kidney and the detailed preparation, briefing and supervision might explain why we failed to find harmful renal effects in this trial.

Besides ARF, rhabdomyolysis can also cause acute clinical complications such as hypernatremia, hyperkalemia, hypocalcemia [5, 14]. Concerning electrolyte balance and corresponding potential muscular, neuronal and cardiac risks, our results show a significant increase in sodium (peak: 141.4 mmol/l;  $P=0.026$ ) which is, however, still below the upper range of the norm ( $\geq 145$  mmol/l) [34, 35]. Although not fulfilling the criteria of hypernatremia, this increase may affect intracellular permeability and cause diffusion of different enzymes and proteins into the bloodstream. We also determined a significant increase in potassium (peak: 5.0 mmol/l;  $P=0.001$ ), but the individual peak values did not exceed the upper limit of the normal range ( $\geq 5.5$  mmol/l) [14]. In parallel, no participant fell below the criterion for hypocalcemia ( $< 2.2$  mmol/l) as a third parameter for possible cardiac disturbances, arrhythmia or cardiac arrest [5]. Thus in summary, no relevant WB-EMS induced clinical abnormalities could be observed for electrolyte balance.

In summary, although we found a definite "exertional rhabdomyolysis", we did not determine any relevant rhabdomyolysis-induced complica-

tion in this healthy, fit, well-prepared and supervised cohort.

Although we did not determine negative side effects of a single exertional session, frequently triggered WB-EMS induced rhabdomyolyses, might induce harmful effects for users in the long term. However, in brief we determined a "repeated bout effect" [25] for WB-EMS-induced CK increases with a more than 20-fold reduced CK increase after the 10-week WB-EMS conditioning period. This result was supported by data summarized by Nosaka et al. who reported significant reductions of CK increases ( $\approx 10$ -fold) already after the second EMS bout [36]. Addressing the peak values after the 10-week WB-EMS conditioning period, we rank the average CK concentration of  $906 \pm 501$  U/l in the lower range of (eccentric) resistance exercise (review in [25]).

However, some limitations weaken the evidence generated by the present study. (1) With respect to trial-I, the cohort of WB-EMS novices was significantly younger compared with the marathon group. There is no evidence that this variation relevantly explains the corresponding CK difference. (2) With respect to trial-II, hepatic parameters or metabolic acidosis that might also be affected by rhabdomyolysis were not determined or observed. (3) With respect to trial-III we are unable to present a detailed kinetic of CK changes. Thus, it is possible that the CK response to WB-EMS predominately decreases at an earlier stage of conditioning. (4) We focus on healthy, active and highly motivated people, optimally prepared, briefed and supervised. Divergent, commercial settings may not be that rigorous, thus WB-EMS-induced rhabdomyolysis can lead to more unfavorable side effects compared with the present study.

Not a limitation of the present study, but a general problem of WB-EMS has been that until recently there were no mandatory recommendations for safe and effective WB-EMS application [6]. However, this gap has now been closed by a corresponding guideline [37].

Summing up, we determined extremely high CK increases after an exertional initial WB-EMS application that were significantly reduced after 10 weeks of WB-EMS once a week for 20 min. Further, we were unable to detect relevant negative health consequences although the CK

concentration of most participants indicated a severe rhabdomyolysis. However, in less fit and healthy subjects not optimally prepared and supervised, initial WB-EMS to exertion may have more far-reaching consequences. Thus, although some groups of highly motivated WB-EMS novices may request an exertional initial WB-EMS application, this approach should be strictly avoided.

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### Disclosure of conflict of interest

None.

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