Efficacy of laser therapy for exercise-induced fatigue
A meta-analysis

Dongmei Wang, MS∗, Xingtong Wang, MS

Abstract
Background: Laser therapy is widely used for exercise-induced fatigue, while the effect among different studies remains controversial. The present study was to summary available randomized controlled trials (RCTs) to evaluate the effect of laser therapy in subjects with exercise-induced fatigue.

Methods: PubMed, Embase, and Cochrane Library were searched to identify the potential RCTs from inception to October 2017. The weighted mean difference (WMD) with 95% confidence intervals (CIs) was calculated using a random-effects model.

Results: Twenty RCTs involving a total of 394 individuals were included in final analysis. No significant differences were observed between the laser therapy and control for the outcomes of lactate (WMD: −0.19; 95%CI: −0.52 to 0.13; P = .244), repetitions (WMD: 4.44; 95%CI: −1.43 to 10.32; P = .138), work load (WMD: 3.38; 95%CI: −1.15 to 7.91; P = .144), time taken to perform the exercise tests (WMD: 4.42; 95%CI: −2.33 to 11.17; P = .199), creatine kinase (WMD: −41.80; 95%CI: −168.78 to 85.17; P = .519), maximum voluntary contraction (WMD: 23.63; 95%CI: −7.41 to 65.07; P = .135), mean peak forces (WMD: 2.87; 95%CI: −1.01 to 6.76; P = .147), and visual analog scale (VAS) (WMD: −1.91; 95%CI: −42.89 to 39.08; P = .927). The results of sensitivity analysis suggested that laser therapy might play an important role on the levels of lactate (WMD: −0.50; 95%CI: −0.59 to −0.01; P = .037), maximum voluntary contraction (WMD: 33.54; 95%CI: 1.95 to 65.12; P = .037), and VAS (WMD: −2.10; 95%CI: −40.78 to −1.22; P = .037). The results of subgroup analyses indicated no significant differences between the laser therapy and placebo for lactate and repetitions when stratified by study design, mean age, gender, and study quality.

Conclusions: The findings of this meta-analysis did not indicate any significant differences between the laser therapy and placebo.

Abbreviations: CI = confidence interval, CIs = confidence intervals, RCTs= randomized controlled trials, VAS = visual analog scale, WMD = weighted mean difference.

Keywords: exercise-induced fatigue, laser therapy, meta-analysis

1. Introduction
A continuous decrease in muscle strength was associated with the progression of skeletal muscle fatigue.[11] Although the mechanisms of muscle fatigue are not yet elucidated, the most common manifestations include the inability of spontaneous generation and maintenance of strength in a synchronized and efficient manner for a specific period.[12] Several factors including the types, duration, the intensity of exercise, the muscle groups involved, and the local physical and biochemical environment were correlated with progressive fatigue.[3] Furthermore, age, gender, motivation, and adaptation to contract the skeletal muscle withstand the development of fatigue.[4,5] As stated above, the progression of muscle fatigue involved physiological, biomechanical, and psychological elements.[3,5–9]

A previous study illustrated that low power laser radiation exerted physiological therapeutic effects with an increase in cellular metabolism for the synthesis of protein, which could prevent fatigue and improve the recovery of skeletal muscle.[10] In addition, the radiation treatment on skeletal muscle could affect energy metabolism including the mitochondrial level, oxidation-reduction of the cells, and transport of electrons in the respiratory chain. Another previous study demonstrated that subjects, who underwent pre- or post-exercise radiation treatment exhibited diverse effects. The pre-exercise phototherapy could enhance strength gains by reducing fatigue and catabolic effect, while the post-exercise phototherapy could prevent an exaggerated inflammatory response caused by muscle damage.[11–13]

In the previous meta-analysis, the date of included trials was through 2012, which was deemed as an early date, nowadays, more and more studies shown that laser therapy might play a critical role in the regulation of the levels of lactate and VAS. Moreover, the prospective retrieved data were limited to the
number of repetitions and time until exhaustion with respect to muscle performance and creatine kinase of low-level laser therapy.\textsuperscript{[14]} Therefore, we conducted an update of the previous study in order to evaluate the effect of laser therapy in the treatment of exercise-induced fatigue.

2. Methods

2.1. Experimental approach to the problem

This review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement issued in 2009.\textsuperscript{[13]} The studies with randomized controlled design and evaluation of the effect of laser therapy in subjects with exercise-induced fatigue were eligible for the current study. Herein, we systematically searched PubMed, Embase, and the Cochrane Library up to October 2017 for potential studies with the terms “laser” and “fatigue.” Furthermore, the reference lists of all the retrieved studies and relevant reviews were searched manually to identify additional eligible articles. Variables such as the study design, subjects' status, intervention, control, and desirable outcome were employed to select the included studies for analysis.

The literature search was independently undertaken by 2 investigators using a standardized approach, and any discrepancies were settled by a group discussion to achieve a consensus. A study was eligible for inclusion if the following criteria were fulfilled:

1. the study was a randomized controlled design (parallel or crossover);
2. the study investigated the effect of laser therapy in subjects with exercise-induced fatigue;
3. the study report at least 1 of following outcomes: lactate, repetitions, workload, time taken to perform the exercise tests, creatine kinase, maximum voluntary contraction, mean peak forces, and visual analog scale (VAS).

All the observational studies were excluded as the various confounding factors could bias the results.

2.2. Procedures

The following data from each study were extracted by 2 investigators independently: first author's name, publication year, country, study design, sample size, mean age, percentage of males, intervention, control, and reported outcomes. Any disagreement was resolved by discussion until a consensus was reached. The Jadad scale was used to assess the methodological quality, which is comprehensive and has been partially validated for evaluating the quality of randomized controlled trials (RCTs) in a meta-analysis.\textsuperscript{[16]} The Jadad scale is based on the following 5 subscales: randomization (1 or 0), concealment of the treatment allocation (1 or 0), blinding (1 or 0), completeness of follow-up (1 or 0), and the use of intention-to-treat analysis (1 or 0). Thus, we developed a scoring system ranging from 0 to 5 for quality assessment. In the current study, we considered the study with a score 4 or 3 as high quality. The quality was assessed by the 2 investigators independently.

2.3. Statistical analyses

Weighted mean difference (WMD) was used as a summary statistic for all the investigated outcomes based on the mean, standard deviation, and sample size in each group. A random-effects model was employed to calculate the summary effects, and the WMD was significant if the 95% confidence interval (CI) did not include 0.\textsuperscript{[17,18]} The potential heterogeneity across studies was examined via Cochrane Q-statistic and $I^2$ statistic test.\textsuperscript{[19,20]} The $P$ value for heterogeneity $< .05$ or $I^2 > 50\%$ indicated that the heterogeneity was statistically significant. A sensitivity analysis was conducted by removing each trial from the meta-analysis sequentially.\textsuperscript{[21]} The subgroup analysis for lactate and repetitions was performed according to the study design, mean age, gender, and study quality. The funnel plots for lactate and repetitions were qualitatively assessed the publication bias, and the Egger\textsuperscript{[22]} and Begg tests\textsuperscript{[23]} quantitatively evaluated the publication bias for lactate and repetitions. All the reported $P$ values were two-sided and values $< .05$ were considered as significant for all the included trials. Statistical analyses were performed using STATA software (version 10.0 StataCorp, Texas, USA).

3. Results

The study selection process is illustrated in Figure 1. A total of 769 potentially relevant articles were identified after a systematic search of electronic databases. After reviewing the title or abstract, 739 articles were excluded, and 30 articles were subjected to full-text review. Ten articles were discarded at the stage of full-text review, and 20 studies were finally identified and included in the analysis of the efficacy of laser therapy in adult patients with exercise-induced fatigue.\textsuperscript{[24-43]} Studies were excluded for the following reasons: if the subjects received other therapies, the outcome of interest was unavailable, and the study reported same populations. A manual search of the reference lists of these trials did not yield any new eligible trials. The general characteristics of the included studies are presented in Table 1. Of the 20 included trials, 11 studies were crossover design and the remaining 9 trials were parallel design. The sample sizes of each trial varied from 7 to 39 subjects, and the mean age of the subjects ranged from 18 to 63.8 years. Furthermore, 13 included trials comprised of males, 4 trials included female, and the remaining 3 trials included both males and females. Of these 20 trials, the study quality was evaluated using the Jadad scale. Overall, 3 trials presented a score of 5,\textsuperscript{[25,33,39]} 8 trials had a score of 4,\textsuperscript{[24,26,29,32,34,37,41,42]} and the remaining 9 trials had a score of 3.\textsuperscript{[27,28,30,31,35,36,38,40,43]}

A total of 6 trials displayed data for the effect of laser therapy on the level of lactate. The pooled WMD showed a 0.19 mmol/L reduction in lactate level, while this reduction was not statistically significant (WMD: $-0.19$; 95% CI: $-0.52$ to $-0.13$; $P = .244$; Fig. 2). In addition, significant heterogeneity was evident across the included trials ($I^2$ = 54.7%; $P = .050$). According to the sensitivity analysis, we concluded the study by Marchi et al.\textsuperscript{[10]} and concluded that subjects received laser therapy were associated with a significantly reduced lactate level (WMD: $-0.30$; 95% CI: $-0.59$ to $-0.01$; $P = .040$; Table 2). In addition, a subgroup analysis was conducted for analyzing the lactate level according to the study design, mean age, gender, and study quality in order to evaluate the effect of laser therapy in specific subsets. We noted laser therapy did not yield a significant effect on lactate level in all the subsets (Table 3).

The data for the effect of laser therapy were available from the number of repetitions from 5 trials. However, no significant difference was observed between laser therapy and placebo for the number of repetitions (WMD: 4.44; 95% CI: $-1.43$ to $10.32$;
and substantial heterogeneity was observed ($I^2: 65.8\%; P = .020$). Next, we then conducted sensitivity analysis and found that the conclusion was not affected by the exclusion of any individual trial (Table 2). Similarly, subgroup analysis suggested no significant differences between the laser therapy and placebo in all the subsets (Table 3).

Three trials reported the effect of laser therapy on workload; however, no significant effect of laser therapy was observed (WMD: 3.38; 95% CI: −1.15 to 7.91; $P = .144$; no evidence of heterogeneity; Fig. 4). The results of sensitivity analysis indicated the conclusion was not altered by excluding any individual trial (Table 2). Subsequently, 4 trials reported the effect of laser therapy on the duration required to perform the exercise tests and did not find any significant effect (WMD: 4.42; 95% CI: −2.33 to 11.17; $P = .199$; Fig. 5). Substantial heterogeneity was detected among the included trials. Next, we conducted sensitivity analysis and found that the conclusion was not affected by the exclusion of any individual trial (Table 2). Third, 4 trials reported the effect of laser therapy on the level of creatine kinase and indicated no significant effect of laser therapy (WMD: −41.80; 95% CI: −168.78 to 85.17; $P = .519$; Fig. 6). Moreover, substantial heterogeneity was observed, and the results of sensitivity analysis remained unaltered (Table 2). Finally, no significant differences were observed between laser therapy and placebo regarding the outcomes of maximum voluntary contraction (WMD: 23.83; 95% CI: −7.41 to 55.07; $P = .135$; substantial heterogeneity; Fig. 7), mean peak forces (WMD: 2.87; 95% CI: −1.01 to 6.76; $P = .147$; no evidence of heterogeneity; Fig. 8), and VAS (WMD: −1.91; 95% CI: −42.89 to 39.08; $P = .927$; substantial heterogeneity; Fig. 9). The conclusion of sensitivity analysis was not altered for mean peak forces (Table 2). In addition, the sensitivity analysis for maximum voluntary contraction and VAS indicated the conclusions were changed after sequentially excluding individual trials (Table 2).

The review of funnel plots did not reveal any significant publication bias for lactate level and the number of repetitions (Fig. 10). Also, the Egger and Begg tests did not present any evidence of publication bias for lactate level ($P$ value for Egger: 0.102; $P$-value for Begg: 0.452) and the number of repetitions ($P$ value for Egger: 0.182; $P$ value for Begg: 0.221).

4. Discussion

The present meta-analysis determined the effect of laser therapy in adults with exercise-induced fatigue. A total of 20 trials were identified that encompassed 394 individuals. The findings of this study indicated no significant differences between laser therapy and placebo for the outcomes of lactate, repetitions, workload, time taken to perform the exercise tests, creatine kinase, maximum voluntary contraction, mean peak forces, and VAS. In addition, the sensitivity analyses showed that laser therapy played a major role in lactate, maximum voluntary contraction and VAS. However, no significant difference was observed for lactate and repetitions when stratified by study design, mean age,
| Study       | Publication year | Country | Study design | Sample size | Mean age (y) | Percentage male (%) | Intervention                                                                 | Control | Reported outcomes                                                                 | Jadad score |
|------------|------------------|---------|--------------|-------------|--------------|---------------------|----------------------------------------------------------------------------|---------|--------------------------------------------------------------------------------|-------------|
| Alves[24]  | 2014             | Brazil  | Cross-over design | 18          | 22.0         | 50.0                | 850 nm wavelength, 100 mW/diode, 14 J/site Placebo | Placebo | Work load, lactate                                                             | 4           |
| Toma[25]   | 2013             | Brazil  | Cross-over design | 24          | 63.8         | 0.0                 | 808 nm wavelength, 100 mW/diode, 7 J/site Placebo | Placebo | Repetitions                                                                  | 5           |
| Junior[26] | 2009             | Brazil  | Cross-over design | 10          | 22.3         | 100.0               | 830 nm wavelength, 100 mW/diode, 5 J/site Placebo | Placebo | Repetitions, time taken to perform the exercise tests, lactate | 4           |
| Junior[27] | 2008             | Brazil  | Parallel design  | 12          | 22.0         | 100.0               | 650 nm wavelength, 50 mW/diode, 5 J/site Placebo | Placebo | Time taken to perform the exercise tests                                    | 3           |
| Reis[28]   | 2014             | Brazil  | Parallel design  | 27          | 15.0–30.0    | 100.0               | 830 nm wavelength, 60 mW/diode, 0.6 J/site Placebo | Placebo | Repetitions, time taken to perform the exercise tests, work load            | 3           |
| Toma[29]   | 2016             | Brazil  | Parallel design  | 38          | 63.7         | 0.0                 | 808 nm wavelength, 100 mW/diode, 7 J/site Placebo | Placebo | Work load                                                                   | 4           |
| Marchi[30] | 2012             | Brazil  | Cross-over design | 22          | 22.0         | 100.0               | 810 nm wavelength, 200 mW/diode, 6 J/site Placebo | Placebo | Creatine kinase, lactate                                                      | 3           |
| Vanin[31]  | 2016             | Brazil  | Parallel design  | 28          | 18.0–35.0    | 100.0               | 810 nm wavelength, 200 mW/diode, 10, 30, 50 J/site Placebo | Placebo | Visual analog scale, maximum voluntary contraction                           | 3           |
| Baron[32]  | 2010             | Brazil  | Parallel design  | 36          | 24.8         | 100.0               | 810 nm wavelength, 200 mW/diode, 6 J/site Placebo | Placebo | Visual analog scale, lactate, creatine kinase, maximum voluntary contraction | 4           |
| Junior[33] | 2010             | Brazil  | Cross-over design | 9           | 18.6         | 100.0               | 810 nm wavelength, 200 mW/diode, 6 J/site Placebo | Placebo | Time taken to perform the exercise tests                                    | 5           |
| Almeida[34] | 2012           | Brazil  | Cross-over design | 10          | 22.3         | 100.0               | 830 nm wavelength, 100 mW/diode, 5 J/site Placebo | Placebo | Mean peak forces                                                             | 4           |
| Vieira[35] | 2014             | Brazil  | Cross-over design | 7           | 21.0         | 100.0               | 808 nm wavelength, 100 mW/diode, 4 J/site Placebo | Placebo | Repetitions                                                                  | 3           |
| Higash[36] | 2013             | Brazil  | Cross-over design | 20          | 21.9         | 0.0                 | 808 nm wavelength, 100 mW/diode, 4 J/site Placebo | Placebo | Repetitions                                                                  | 3           |
| Larkin-Kaiser[37] | 2015       | Canada  | Cross-over design | 39          | 20.0         | 53.8                | 800–970 nm wavelength, 100 mW/diode, 15 J/site Placebo | Placebo | Maximum voluntary contraction                                                | 4           |
| Bublitz[38] | 2016            | Brazil  | Parallel design  | 20          | 53.2         | 55.0                | 808 nm wavelength, 100 mW/diode, 7 J/site Placebo | Placebo | Lactate                                                                      | 3           |
| Junior[39] | 2009             | Brazil  | Cross-over design | 8           | 18.5         | 100.0               | 810 nm wavelength, 200 mW/diode, 6 J/site Placebo | Placebo | Creatine kinase, lactate                                                      | 5           |
| Paolillo[40] | 2011           | Brazil  | Parallel design  | 20          | 55.0         | 0.0                 | 850 nm wavelength, 31 mW/cm², 55.8 J/cm² Placebo | Placebo | Mean peak forces                                                             | 3           |
| Fritsch[41] | 2016            | Brazil  | Parallel design  | 24          | 25.0         | 100.0               | 810 nm wavelength, 200 mW/diode, 30 J/site Placebo | Placebo | Maximum voluntary contraction                                                | 4           |
| Rosatto[42] | 2016            | Brazil  | Cross-over design | 10          | 18.0–35.0    | 100.0               | 808 nm wavelength, 100 mW/diode, 7 J/site Placebo | Placebo | Mean peak forces                                                             | 4           |
| Ferraresi[43] | 2015           | Brazil  | Parallel design  | 12          | 25.5         | 100.0               | 850, 630 nm wavelength, 130, 80 mW/diode, 7, 8, 48 J/site Placebo | Placebo | Creatine kinase                                                              | 3           |
Figure 2. Effect of the laser therapy on lactate.

Table 2
Sensitivity analysis.

| Outcomes                          | Excluding study | WMD and 95% CI       | P value | Heterogeneity (%) | P value for heterogeneity |
|-----------------------------------|-----------------|----------------------|---------|-------------------|--------------------------|
| Lactate                           |                 |                      |         |                   |                          |
| Alves                             | −0.19 (−0.54 to 0.16) | .279                 | 62.9    | .029              |                          |
| Junior                            | −0.18 (−0.54 to 0.18) | .335                 | 61.4    | .035              |                          |
| Marchi                            | −0.30 (−0.59 to −0.01) | .040                 | 12.5    | .334              |                          |
| Baroni                            | −0.05 (−0.28 to 0.18) | .662                 | 23.1    | .267              |                          |
| Bublitz                           | −0.24 (−0.70 to 0.22) | .300                 | 58.8    | .046              |                          |
| Junior                            | −0.26 (−0.68 to 0.17) | .235                 | 63.6    | .027              |                          |
| Toma                              | 7.07 (−2.84 to 16.98) | .162                 | 73.5    | .010              |                          |
| Junior                            | 5.33 (−3.08 to 13.73) | .214                 | 73.8    | .009              |                          |
| Repetitions                        |                 |                      |         |                   |                          |
| Reis                              | 5.11 (−1.49 to 11.70) | .129                 | 74.1    | .009              |                          |
| Vieira                            | 2.71 (−0.02 to 5.44) | .051                 | 0.0     | .932              |                          |
| Higashi                           | 6.47 (−2.63 to 15.57) | .164                 | 74.2    | .009              |                          |
| Alvsa                             | 3.51 (−1.07 to 8.08) | .133                 | 0.0     | .341              |                          |
| Workload                          |                 |                      |         |                   |                          |
| Reis                              | 4.91 (−0.70 to 10.51) | .086                 | 0.0     | .627              |                          |
| Toma                              | 0.31 (−7.18 to 7.80) | .935                 | 0.0     | .837              |                          |
| Junior                            | 4.73 (−4.60 to 14.02) | .320                 | 85.7    | .001              |                          |
| Junior                            | 1.63 (−1.92 to 5.17) | .368                 | 0.0     | .723              |                          |
| Time taken to perform the exercise tests |                 |                      |         |                   |                          |
| Reis                              | 5.79 (−1.63 to 13.20) | .126                 | 85.0    | .001              |                          |
| Junior                            | 5.38 (−3.42 to 14.18) | .231                 | 81.0    | .005              |                          |
| Marchi                            | −185.87 (−537.91 to 166.18) | .301             | 87.1    | <.001             |                          |
| Baroni                            | 2.56 (−23.47 to 26.59) | .847                 | 0.0     | .717              |                          |
| Creatine kinase                   |                 |                      |         |                   |                          |
| Junior                            | −177.51 (−513.89 to 158.87) | .301             | 87.2    | <.001             |                          |
| Ferraresi                         | −79.54 (−228.97 to 69.89) | .297             | 86.6    | .001              |                          |
| Baroni                            | 14.64 (−17.07 to 46.35) | .365             | 82.1    | .004              |                          |
| Vanin                             | 15.61 (−19.86 to 50.18) | .376             | 91.8    | <.001             |                          |
| Maximum voluntary contraction     |                 |                      |         |                   |                          |
| Larkin-Kaiser                     | 33.54 (1.95 to 65.12) | .037               | 74.9    | .019              |                          |
| Fritsch                           | 32.48 (−5.66 to 70.63) | .095             | 94.2    | <.001             |                          |
| Almeida                           | 2.36 (−7.89 to 12.61) | .652             | 14.6    | .279              |                          |
| Mean peak forces                  |                 |                      |         |                   |                          |
| Paolillo                          | 2.50 (−1.48 to 6.48) | .219             | 0.0     | .483              |                          |
| Rossiolo                          | 2.48 (−0.70 to 7.60) | .103             | 0.0     | .431              |                          |
| Visual analog scale               |                 |                      |         |                   |                          |
| Vanin                             | −21.00 (−40.78 to −1.22) | .037             | 74.6    |         |                          |
| Baroni                            | 21.00 (−10.72 to 52.72) | .194             | 91.8    | .001              |                          |
Table 3
Subgroup analysis for lactate and repetitions.

| Outcomes | Factor          | Groups | Number of studies | WMD and 95% CI                  | P value | P value between subgroups |
|----------|-----------------|--------|-------------------|---------------------------------|---------|--------------------------|
| Lactate  | Study design    | Crossover | 4 | 0.07 (−0.16 to 0.30) | .556    | .041                     |
|          |                 | Parallel  | 2 | −0.63 (−1.61 to 0.36) | .213    | .248                     |
|          | Mean age (y)    | >40.0  | 1 | −0.22 (−0.54 to 0.10) | .181    | .288                     |
|          |                 | <40.0  | 5 | −0.24 (−0.70 to 0.22) | .300    | .061                     |
|          | Gender          | Male    | 4 | −0.24 (−0.74 to 0.26) | .349    | .205                     |
|          |                 | Both    | 2 | −0.23 (−0.55 to 0.08) | .153    | .391                     |
|          | Study quality   | High    | 4 | −0.45 (−0.96 to 0.06) | .083    | .081                     |
|          |                 | Low     | 2 | −0.00 (−0.41 to 0.40) | .984    | .734                     |
| Repetitions | Study design  | Crossover | 4 | 5.11 (−1.49 to 11.70) | .129    | .744                     |
|          |                 | Parallel | 1 | 0.40 (−16.05 to 16.85) | .962    | .962                     |
|          | Mean age (y)    | >40.0  | 1 | 2.30 (−1.42 to 6.02) | .226    | .538                     |
|          |                 | <40.0  | 4 | 7.07 (−2.84 to 16.98) | .162    | .312                     |
|          | Gender          | Male    | 3 | 15.08 (−6.71 to 36.87) | .175    | .318                     |
|          |                 | Female  | 2 | 2.36 (−0.71 to 5.44) | .132    | .318                     |
|          | Study quality   | High    | 2 | 2.87 (−0.33 to 6.08) | .079    | .792                     |
|          |                 | Low     | 3 | 14.31 (−7.73 to 36.35) | .203    | .318                     |

Figure 3. Effect of the laser therapy on repetitions.

Figure 4. Effect of the laser therapy on workload.
gender, and study quality. These observations might better define the effect of laser therapy in adults with exercise-induced fatigue. A previous meta-analysis included 13 RCTs and suggested that the laser therapy was associated with high levels of exhaustion (WMD: 4.12; 95% CI: 1.21–7.02; \( P < .005 \)) and the number of repetitions (WMD: 5.47; 95% CI: 2.35–8.59; \( P < .001 \)). Also, the study pointed out that laser therapy improved the muscle performance and accelerated the recovery if used before exercise.\[14\] However, the effects on other outcomes were not investigated, and the analysis was not further stratified by factors that could affect the treatment effects of laser therapy. In the present study, the overall analyses were inconsistent, and subgroup analysis yielded similar conclusions as compared to a previous meta-analysis; this phenomenon might be attributed to the need for updated data from additional trials.

The current findings did not reveal any significant difference in the investigated outcomes among all groups. However, several studies reported inconsistent results. Baroni et al indicated that laser therapy before exercise significantly attenuated the increased muscle proteins and decreased the muscle force, which in turn, could reduce the levels of lactate, creatine kinase, and VAS and increase the maximum voluntary contraction.\[32\] Vieira et al suggested that laser therapy increased the number of repetitions, with a small electromyography fatigue index in vastus medialis (\( P = .004 \)) and rectus femoris.\[35\] Junior et al suggested that the laser therapy delayed the onset of muscle fatigue and exhaustion.\[27\] Vanin et al demonstrated that laser therapy significantly increased the maximum voluntary contraction immediately after exercise up to 24 hours.\[31\] These observations could be attributed to the interaction between laser
therapy and biological tissues, especially in mitochondria and blood flow.\textsuperscript{[44]} The effects of laser therapy were similar to aerobic training on muscle cells, thereby positively affecting the fatigue and exercise capacity.\textsuperscript{[30,45]}

Although no significant differences were noted in all the investigated outcomes, the results of sensitivity analysis indicated that laser therapy might play a critical role on the lactate level, maximum voluntary contraction and VAS. This might be effectuated based on the numerous studies designed with other outcomes as a primary endpoint, and their sample sizes were not sufficient to detect the potential clinical differences among the investigated outcomes. In addition, the differences between the laser therapy and placebo for lactate and repetitions were not observed in all the subsets, while these results were variable due to a small number of studies included.

Nevertheless, the present meta-analysis has 3 highlighted. First, only RCTs were included, which should eliminate the bias of confounders as compared to other observational studies. Second, the summary results suggested that laser therapy could improve the lactate level and VAS. Third, a large sample size was included, which strengthened the result of the present study than any individual trial. The limitations of the present meta-analysis stated that substantial heterogeneity was not addressed using sensitivity and subgroup analysis. The data and the consequently introduced potential bias might be attributed to the difference in subjects’ characteristics, intervention, and study design of the

| Study          | Mean difference (95% CI) | % Weight |
|----------------|--------------------------|----------|
| Vanin          | 48.71 (30.33, 67.09)     | 26.6     |
| Baroni         | 50.95 (22.04, 79.86)     | 23.4     |
| Larkin–Kaiser  | 2.18 (–0.79, 5.15)       | 29.2     |
| Fritsch        | –8.01 (–44.73, 28.71)    | 20.8     |
| Overall        | 23.83 (–7.41, 55.07); P=0.135 (I-square: 91.4%; P<0.001) | 100.0    |

Figure 7. Effect of the laser therapy on maximum voluntary contraction.

| Study          | Mean difference (95% CI) | % Weight |
|----------------|--------------------------|----------|
| Almeida        | 3.08 (–1.22, 7.38)       | 81.8     |
| Paolillo       | 10.50 (–7.46, 28.46)     | 4.7      |
| Rossato        | –1.00 (–11.55, 9.55)     | 13.6     |
| Overall        | 2.87 (–1.01, 6.76); P=0.147 (I-square: 0.0%; P=0.544) | 100.0    |

Figure 8. Effect of the laser therapy on mean peak forces.
included trials. Finally, the findings of subgroup analyses might be unreliable and variable due to the small number of studies included. Despite the limitations, our findings exhibit significant clinical implications since systematic reviews and meta-analyses are the most powerful tools for evaluating inconsistencies. The findings of this meta-analysis did not indicate any significant differences between the laser therapy and placebo for lactate, repetitions, workload, the time taken to perform the exercise tests, creatine kinase, maximum voluntary contraction, mean peak forces, and VAS. Thus, the treatment effect between laser therapy and placebo requires further investigations in large-scale RCTs.

**Author contributions**

**Conceptualization:** Dongmei Wang, Xingtong Wang.  
**Data curation:** Dongmei Wang, Xingtong Wang.  
**Formal analysis:** Dongmei Wang.  
**Investigation:** Dongmei Wang, Xingtong Wang.  
**Methodology:** Xingtong Wang.  
**Resources:** Dongmei Wang.  
**Software:** Dongmei Wang, Xingtong Wang.  
**Validation:** Xingtong Wang.  
**Visualization:** Xingtong Wang.  
**Writing – original draft:** Dongmei Wang.  
**Writing – review & editing:** Xingtong Wang.

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