Bilateral Changes in Forearm Oxygen Consumption at Rest and After Exercise in Patients With Unilateral Repetitive Strain Injury: A Case-Control Study

Repetitive strain injury (RSI) is considered a nonspecific neck, shoulder, elbow, forearm, wrist, and/or hand-related overuse pain syndrome caused by sustained low-level static and/or repetitive muscle activity. This type of prolonged, low-intensity, and repetitive muscle activity induces local changes in skeletal muscle morphology and circulation, such as changes in the amount and distribution of muscle type I and IIA fibers, mitochondrial alterations, reduced capillarization, lower local blood flow, inhibited local vascular responses, and an increase in anaerobic metabolism. These local changes have been found in muscles affected by RSI and are believed to contribute to the clinical presentation of RSI complaints.

Interestingly, RSI is also related to systemic problems such as reduced function of small and large sensory and sympathetic fibers. Moreover, a lower skin temperature was found in both arms of patients with unilateral RSI, which may be related to an underlying systemic change in the regulation of skin blood flow. Nonetheless, previous studies have typically examined muscular or vascular adaptations of the affected side only.

Recently, we found lower muscle oxygen consumption in forearm muscles affected by RSI. Whether changes in oxygen consumption are also present in the nonaffected arm of patients with unilateral RSI has not been investigated and may have important clinical implications. To date, treatment of RSI has often focused on local complaints only; however, if systemic changes are present in patients with RSI, optimal treatment may require a more systemic approach. For example, whole-body exercise training has well-established beneficial and systemic effects on the vasculature.

*STUDY DESIGN: Case-control study.

*OBJECTIVES: To investigate whether oxygen consumption and blood flow at rest and after exercise are lower in the affected arm of patients with repetitive strain injury (RSI) compared to controls, and lower in the healthy nonaffected forearm within patients with unilateral RSI.

*BACKGROUND: RSI is considered an upper extremity overuse injury. Despite the local presentation of complaints, RSI may be represented by systemic adaptations. Insight into the pathophysiology of RSI is important to better understand the development of RSI complaints and to develop effective treatment and prevention strategies.

*METHODS: Twenty patients with unilateral RSI and 20 gender-matched control subjects participated in this study. Forearm muscle blood flow and oxygen consumption were measured using near-infrared spectroscopy at baseline and immediately after isometric handgrip exercises at 10%, 20%, and 40% of the individual maximal voluntary contraction.

*RESULTS: Unilateral RSI resulted in a lower oxygen consumption and blood flow in the affected forearm at baseline and lower oxygen consumption after incremental handgrip exercises compared to controls (P<0.05). In addition, exercise-induced blood flow and oxygen consumption in the nonaffected forearm in patients with RSI were similarly reduced.


*KEY WORDS: overuse injuries, pain, upper extremity

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Therefore, the aim of the study was to examine the hypothesis that oxygen consumption and blood flow at rest and immediately after exercise would be lower in the affected arm of patients with RSI compared to controls and lower compared to the healthy nonaffected forearm in patients with unilateral RSI. RSI symptoms primarily occur on the dominant side. The comparison of the affected forearm versus the nonaffected forearm in patients with RSI may therefore be confounded by dominance of the forearm. To control for this, we have examined whether there is a systemic difference between the dominant and nondominant forearm in healthy controls.

METHODS

Subjects

A total of 20 patients with unilateral computer work-related pain in at least their elbow/forearm region for at least 6 months were included. All patients were diagnosed with RSI by their family physician. The recruitment of patients with RSI was performed through physicians or physical therapists treating patients with RSI. In addition, patients with RSI were recruited by advertisement through the Dutch RSI patients' organization. All patients reported unilateral pain symptoms in their elbow/forearm region, which were aggravated by computer-related work. Moreover, all subjects reported having pain when performing computer-related activities on the day of testing. Subjects performed computer work for at least 2 hours a day. Individuals with RSI were excluded if there was any evidence of vasospastic disease, occlusive atherosclerosis, diabetes mellitus, peripheral neuropathies, history of complex regional pain syndrome type 1, a diagnosed muscular disease other than RSI, or use of medications known to interfere with the vascular system. We also included a gender-matched control group of 20 healthy computer workers without a history of RSI symptoms. The control group was recruited from employees of the Radboud University Nijmegen Medical Centre. The study was approved by the Dutch Central Committee on Research Involving Human Subjects, in accordance with the Declaration of Helsinki (2000) of the World Medical Association. Prior to the study and after a detailed explanation of the study, all subjects gave their informed consent.

Experimental Procedures

After reporting to our laboratory, subjects completed a standard questionnaire to gain insight into localization, extent, and duration of the RSI symptoms. The affected RSI locations were recorded on a body diagram. All subjects in our study reported unilateral RSI symptoms present around the elbow region. Therefore, location of RSI symptoms matched the location of the near-infrared spectroscopy (NIRS) assessment of blood flow and oxygen uptake. The daily level of pain was measured on a 10-cm visual analog scale (a 0-to-10 scale, with 0 as no pain and 10 as maximum pain) and was scored by the patient after an experienced researcher provided verbal information. In addition, age, hours of work per week, and daily computer use were recorded. Forearm circumference and adipose tissue thickness were measured at the same location as placement of the NIRS optodes. Adipose tissue thickness was measured using a skinfold caliper (Holtain Ltd, Crymmych, UK). Hemoglobin concentration was determined from a capillary blood sample from the fingertip (HemoCue AB, Angelholm, Sweden). Maximal voluntary muscle contraction (MVC) was measured using a handgrip dynamometer (J00105 JAMAR Hydraulic Hand Dynamometer; Lafayette Instrument Company, Lafayette, IN). Subjects were requested to perform a maximal contraction for 3 seconds, repeated 3 times, with a 1-minute interval between each, using the highest score as MVC.

Subjects refrained from smoking or drinking coffee for at least 5 hours prior to the experiment to avoid the possible influence of caffeine or nicotine on the local vascular bed. For testing, all subjects were seated in a comfortable chair. A pneumatic cuff was placed distally around the upper arm. The hand rested on a handgrip dynamometer, with the upper arm at the level of the heart, and the forearm in an upward angle of 30° on an inclined platform.

Our protocol is described in detail elsewhere. Briefly, we started with a 5-minute rest, followed by 5 venous occlusions (15 seconds, 50 mmHg), separated by a 45-second rest to obtain the average local muscle blood flow at rest. Subsequently, arterial occlusion (60 seconds, 250 mmHg) was applied to determine baseline local muscle oxygen consumption. After a rest of 120 to 240 seconds, subjects performed 60 seconds of rhythmic handgrip exercises on a dynamometer (1-second contraction, 1-second relaxation), assisted by a metronome in a consecutive order of 10%, 20%, and 40% of MVC. For visual feedback, the level of workload was indicated on a computer. Immediately after each exercise period, an arterial occlusion was applied (30 seconds, 250 mmHg) to assess the muscle oxygen consumption after exercise. Between exercise sessions, rest periods (120-240 seconds) were used to allow blood flow to return to baseline. Finally, 45 seconds after the test at 40% MVC, a venous occlusion was applied (15 seconds, 50 mmHg) to determine postexercise muscle blood flow.

Measuring Hemoglobin Oxygenation

NIRS was used to assess regional concentration changes in oxyhemoglobin and deoxyhemoglobin, using a continuous-wave near-infrared spectrophotometer (OXYMON; Artinis Medical Systems, Zetten, The Netherlands). This technique is described in detail elsewhere. Briefly, this technique is based on the relative transparency of tissue for light in the near-infrared region and on the oxygen-dependent absorption changes of hemoglobin and myoglobin. As one cannot distinguish between myoglobin and hemoglobin, the combined effect of these 2 substances is studied. For convenience, we refer in this article only to he-
moglobin. These changes are converted into concentration changes of oxyhemoglobin and deoxyhemoglobin. NIRS measurements in the forearm were obtained by positioning the NIRS optodes over the extensor carpi radialis brevis muscles, 50 mm distal to the lateral epicondyle. This area corresponded with localization of the RSI symptoms in all subjects. The distance between the 2 optodes was fixed at 35 mm to allow sufficient penetration of the near-infrared light and to assess the underlying muscle tissue.

Outcomes
Local muscle blood flow was determined at baseline and at the end of the protocol, 45 seconds after release of an arterial cuff that followed the exercise at 40% MVC. The blood flow was measured by inflating a blood pressure cuff to 50 mmHg. This results in a blockage of the venous outflow, without affecting the arterial inflow. The muscle blood flow was then measured by analyzing the slope of the total hemoglobin signal, being the sum of the oxyhemoglobin and deoxyhemoglobin (in mL/min/100 ml).26,27

Local muscle oxygen consumption was determined at baseline and at 10%, 20%, and 40% of MVC. The oxygen consumption was measured by inflating the blood pressure cuff to 250 mmHg. This blocks the arterial inflow, whereby the forearm fully depends on the available oxygen. The decrease over time of the oxygen concentration signal represents the local muscle oxygen consumption (in mL/O2/min/100 g).29,31

The coefficients of variation for measuring forearm blood flow and oxygen consumption are 22.4% and 16.2%, respectively.29 Therefore, this procedure is considered a reliable and reproducible method for determining blood flow and oxygen consumption at rest, as well as after a broad range of exercise intensities.29-31

Statistical Analysis
Statistical analyses were performed using SPSS Version 16.0 (SPSS Inc, Chicago, IL). All data are reported as mean ± SD and statistical significance was set at P<.05. Based on our previous study that found differences of 0.26 mL/O2/min/100 g between individuals with RSI and controls in muscle oxygen consumption at 10% MVC, with a standard deviation of 0.30 mL/O2/min/100 g, we included 18 subjects per group, based on an alpha of .05 and a power of 80%. Repeated-measures 2-way analyses of variance (ANOVAs) were used to detect changes in forearm muscle blood flow and oxygen consumption across the various exercise intensities (baseline, 10%, 20%, and 40% MVC) within groups (affected versus nonaffected and dominant versus nondominant arm). Another 2-way mixed-model ANOVA was used to detect changes between groups (affected versus dominant control and nonaffected versus nondominant arm). Because the dominant arm was most often the affected arm in patients with RSI, the comparisons between controls and RSI were performed between the dominant and affected forearm, as well as the nondominant and nonaffected forearm, respectively. In addition, this comparison was done to correct for the potential influence of arm dominance.

A Pearson 2-tailed correlation analysis identified adipose tissue thickness as a potential confounding variable. Therefore, we included adipose tissue thickness as a covariate in the repeated-measures ANOVA. Because both smoking and age have an impact upon vascular function, these variables were also added as covariates in the analyses. Student t tests were used to calculate differences in adipose tissue thickness, MVC, and forearm circumference between both arms (paired) or between groups (unpaired).

RESULTS

No differences were found between the patients with unilateral RSI and their gender-matched con-
trols for daily computer use, hemoglobin concentration, and working hours per week. Comparison between the dominant and nondominant arm of controls showed a higher MVC on the dominant side ($P = .002$). Comparison within subjects showed a larger circumference of the forearm for both the dominant control and affected RSI arm ($P = .002$ and $P = .001$, respectively). Comparison between subjects showed no differences in forearm circumference, adipose tissue thickness, or MVC ($P > .05$). The average duration of the RSI symptoms was 2 years and 5 months. The mean ± SD pain level in the RSI group was $3.6 ± 1.7$ cm on the visual analog scale (TABLE 1).

Local Muscle Oxygen Consumption
At baseline, muscle oxygen consumption in the affected arm of the individuals with RSI was significantly lower compared to the dominant arm of controls ($P < .01$). We found a significant exercise-by-group interaction effect ($P < .001$) for increase in oxygen consumption during the 3 stages of incremental handgrip, indicating a lower increase in oxygen consumption after exercise in patients with RSI compared to their gender-matched controls (FIGURE 1). No difference in baseline oxygen consumption was observed between the affected and nonaffected arm of patients with unilateral RSI (TABLE 2). We found no significant exercise-by-arm interaction effect ($P = .68$) for oxygen consumption after incremental exercise between the affected and nonaffected forearm in patients with unilateral RSI. There was also no main effect for arm ($P = .99$), indicating a similar increase in oxygen consumption after exercise in both arms. Similarly, for the healthy controls, no differences in oxygen consumption were found at baseline and during the incremental exercise protocol between forearms (ANOVA, exercise by arm, $P = .44$; arm main effect, $P = .80$).

Local Muscle Blood Flow
At baseline, muscle blood flow in the affected arm of the individuals with RSI was significantly lower compared to that in the dominant arm of the individuals in the control group ($P = .03$). A significant time-by-group interaction ($P = .04$) revealed that the increase in blood flow after the 3 levels of incremental exercise was significantly lower in patients with RSI compared to controls (FIGURE 2). No differences in baseline blood flow were observed between the affected and nonaffected arm of patients with unilateral RSI (TABLE 2). No significant time-by-arm interaction ($P = .47$) was found for the increase in blood flow after exercise between the affected and nonaffected forearm in patients with unilateral RSI. There was also no significant main effect for arm ($P = .82$). Also, in healthy controls, there was no significant time-by-arm interaction ($P = .59$) between the dominant and nondominant forearm in controls for the increase in blood flow after exercise. There was also no significant main effect for arm ($P = .44$).

DISCUSSION

The results of our study indicate that patients with unilateral RSI demonstrate a lower oxygen consumption and blood flow at baseline, as well as after incremental handgrip exercise in the affected forearm, compared to healthy controls. The most innovative finding of this study, however, is that the nonaffected forearm, where no symptoms of RSI were experienced, showed a similarly decreased oxygen consumption and blood flow after exercise compared with
**TABLE 2**

<table>
<thead>
<tr>
<th>Muscle Blood Flow and Oxygen Consumption</th>
<th>RSI Affected</th>
<th>RSI Nonaffected</th>
<th>Control Dominant</th>
<th>Control Nondominant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Muscle blood flow, mL/min/100 mL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>0.83 ± 0.39</td>
<td>0.96 ± 0.53</td>
<td>1.38 ± 0.89</td>
<td>1.22 ± 0.63</td>
</tr>
<tr>
<td>After exercise</td>
<td>1.64 ± 0.80</td>
<td>1.62 ± 0.80</td>
<td>3.04 ± 2.24</td>
<td>2.58 ± 1.27</td>
</tr>
<tr>
<td><strong>Muscle oxygen consumption, mL/min/100 g</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>0.08 ± 0.04</td>
<td>0.08 ± 0.03</td>
<td>0.15 ± 0.07</td>
<td>0.09 ± 0.04</td>
</tr>
<tr>
<td>After exercise at 10% MVC</td>
<td>0.27 ± 0.22</td>
<td>0.31 ± 0.20</td>
<td>0.60 ± 0.37</td>
<td>0.59 ± 0.46</td>
</tr>
<tr>
<td>After exercise at 20% MVC</td>
<td>0.37 ± 0.27</td>
<td>0.37 ± 0.27</td>
<td>0.74 ± 0.57</td>
<td>0.81 ± 0.57</td>
</tr>
<tr>
<td>After exercise at 40% MVC</td>
<td>0.95 ± 0.28</td>
<td>0.50 ± 0.38</td>
<td>1.34 ± 0.91</td>
<td>1.11 ± 0.93</td>
</tr>
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</table>

Abbreviations: MVC, maximal voluntary muscle contraction of the forearm; RSI, repetitive strain injury.
*Values are mean ± SD.
+P < 0.05 for comparisons between the side affected by RSI and the dominant side of control subjects.
+P < 0.01 for comparisons between the side not affected by RSI and the nondominant arm of the control subjects.
+P < 0.01 for comparisons between the side affected by RSI and the dominant side of control subjects.
+P < 0.05 for comparisons between the side not affected by RSI and the nondominant arm of the control subjects.

In the forearm of patients with RSI, such impaired exercise-induced forearm blood flow and decreased levels of oxygen uptake have been reported in other clinical populations.\(^{11,13,29}\) Another explanation for lower oxygen consumption at baseline and after exercise may be related to the presence of muscle damage. Muscle biopsy studies revealed the occurrence of "moth-eaten" fibers, a marker for muscle damage\(^{10,13,19}\) in forearm muscles in patients with chronic epicondylitis\(^{10}\) and in the trapezius muscle of individuals with trapezius myalgia.\(^{12,15,19,19}\) Future studies should further examine the underlying mechanisms for the lower baseline and exercise-induced forearm oxygen consumption in patients with RSI.

Muscle oxygen consumption is directly related to the amount of work performed by the forearm musculature.\(^{3,5,20}\) Therefore, a potential explanation for the lower oxygen consumption and blood flow in patients with RSI may be related to the lower workload in patients with RSI. However, no differences were found for MVC between the affected forearm in patients with RSI and the dominant forearm in controls \(P = .77\), nor between both forearms within patients with RSI \(P = .53\). Therefore, our results cannot be explained by differences in muscle force between arms or between groups.

Our study adds the important novel finding that oxygen consumption and blood flow after incremental handgrip exercise are similarly impaired in both arms in patients with unilateral RSI. This suggests that impaired oxygen consumption and blood flow after exercise are related to systemic changes rather than localized adaptations in the affected region alone. This finding of systemic changes in RSI raises an important question related to the mechanism of RSI. Studies have reported impaired vascular responses after typing in the affected arm of patients with RSI (evidenced by a lower hand temperature)\(^{6,26}\) and after a brief application of an ice pack to the C7 area of the cervical spine.\(^{9}\) Although no direct evidence was provided, these changes
were hypothesized to relate to inappropriate reflex vasodilatation, possibly via the sympathetic nervous system. Another hypothesis is related to an impaired ability to relax muscles in patients with RSI. Veiersted et al. found that healthy women with lower rates of brief unconscious interruptions in muscle activity, monitored with electromyography, were prone to develop RSI symptoms over time. The finding suggests that continuous muscle activation during muscle tasks is a predisposing factor for the development of RSI symptoms. Accordingly, patients with RSI in our study might not have fully relaxed the forearm muscles between repetitive handgrip exercises, leading to vascular blockade. Muscle circulation is obstructed at a relatively low exercise level of 10% MVC. Therefore, continuous muscle tensions may impair muscle blood flow and thereby cause a decrease in oxygen consumption. However, whether poor muscle relaxation in RSI explains such high differences in oxygen consumption found in our study remains disputable.

Clinical Relevance
Our novel findings suggest the presence of systemic changes in the vasculature in patients with unilateral RSI. Whether these changes are indicative of a predisposing factor for RSI or represent a direct consequence of RSI cannot be answered by the results of our study. The fact that unilateral RSI is accompanied by bilateral changes in oxygen consumption and blood flow suggests a progression to a bilateral condition, and systemic changes could be an indication that a person with unilateral symptoms may progress to bilateral symptoms in the future. These findings suggest that the management of RSI symptoms should not focus on the affected region only. For example, treatment strategies, such as whole-body exercise training, represent a well-established and potent stimulus to induce systemic improvements in the vasculature. Exercise training may therefore be recommended in addition to current treatment guidelines to improve the vascular impairments found in patients with RSI.

Limitations
Our study benefits from inclusion of a large group of patients, well-controlled experiments using a within-subject design (allowing for comparison between the affected and nonaffected forearm), and measurements performed at baseline as well as after physical activity. A potential limitation is that RSI is a nonspecific diagnosis. We tried to include a homogeneous group of patients by focusing on RSI symptoms related to computer work only. Other pathologies often associated with RSI, like lateral epicondylitis, were not included in our study. Therefore, our results apply to patients with nonspecific RSI-related arm pain occurring or sustained by computer work activities only. Other factors, such as high perceived work stress, non–work-related work stress, and high job demands, and personal characteristics such as psycho-neurosis and neurotic perfectionism, are also suggested to play a role in the development or continuation of RSI symptoms. However, these psychological factors were not taken into account in our study.

CONCLUSION

Patients with RSI demonstrate impaired oxygen consumption and blood flow in the affected forearm at rest and after incremental levels of handgrip exercise. These pathophysiological impairments are present to a similar extent in the symptom-free, nonaffected forearm. This finding suggests
that, despite the unilateral character of the clinical symptoms, patients with unilateral RSI demonstrate a similar impairment in forearm oxygen consumption and blood flow in both forearms. Because changes in muscle circulation in RSI are not exclusively limited to forearm muscles affected by RSI, the implications for clinical management of RSI are that it should not be exclusively targeted to the local structures.

**KEY POINTS**

**FINDINGS:** Impaired oxygen uptake and blood flow at baseline and after exercise are present in the affected, but also to a similar extent in the symptom-free non-affected, forearm of patients with RSI.

**IMPLICATIONS:** This finding suggests that despite the unilateral character in clinical symptoms, RSI is potentially associated with systemic changes in forearm blood flow and oxygen consumption. Management of this condition should consider incorporating interventions at the systemic level.

**CAUTION:** Our results only apply to patients with non-specific RSI-related arm pain occurring with, or sustained by, computer-work activities.

**ACKNOWLEDGEMENTS:** We thank all patients and control subjects who participated in this study.

**REFERENCES**


