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Systemic Lupus, Metabolic Syndrome, Cardiac Disease, and Peripheral Artery Disease

Blaess J, Goepfert T, Geneton S, Irene E, Gerard H, Taesch F, Sordet C, Arnaud L. Benefits & risks of physical activity in patients with systemic lupus erythematosus: a systematic review of the literature. *Semin Arthritis Rheum.* 2023 Feb;58:152128. Epub 2022 Nov 19. doi:10.1016/j.semarthrit.2022.152128. PMID: 36436314

There has been little clinical exercise physiology research performed on individuals with systemic lupus erythematosus (SLE). Significant and severe fatigue is the primary symptom reported. Those with SLE are at increased risk of cardiovascular disease and metabolic syndrome because of progression of the disease and glucocorticoid treatment. Compared to healthy individuals, those with SLE exhibit higher brachial and carotid systolic blood pressure. Inactivity results in higher levels of inflammatory markers such as CRP, IL-2, and TNF- α . Due to the nature of SLE, inactivity is common, which further promotes a decline in health. Recent trials have evaluated the impact of physical activity (PA) on patients with SLE. This systematic review examined PA's benefits and potential risks in those with SLE.

Methods: This systematic review was performed in using MEDLINE (via PubMed). Only studies from 1989 through March of 2022 were used. The search strategy used terms "Exercise" and "Lupus Erythematosus, Systemic" as well as additional and relevant free text combinations such as "physical activity." Studies were included in the analysis if they investigated the relationship between PA and SLE (randomized, case-control, or cohort studies) and contained original data.

Results: The authors used 40 studies with varying design, published between 1989 and 2022 for the analysis with a total of 229 patients included.

PA Levels and Adherence to WHO Recommendations: Those with SLE had lower levels of PA compared to the general population. Only 11% to 30% met current WHO

recommendations. The reasons reported for not performing PA were poor fitness, pain, and fatigue.

Impaired Aerobic Capacities and Cardiorespiratory Fitness: The $\text{VO}_{2\text{max}}$ of physically active SLE patients was $35.5 \pm 1.9 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, significantly higher than sedentary patients with SLE.

Benefits of PA: Mixed training programs increase aerobic capacity and $\text{VO}_{2\text{max}}$. Resistance training programs tend to provide less significant improvement in aerobic capacity. However, resistance training improves symptoms and muscle function. Considering the risk of cardiovascular disease due to inactivity, when patients with SLE reallocated 10 minutes per day of sedentary behavior into moderate-vigorous PA, the decrease of the estimated 10-year cardiovascular risk was ~20%.

Safety of PA in SLE: No adverse events were reported across the included studies, and there was no increase in disease activity. This suggests exercise is generally safe in those with SLE.

Discussion: Patients with SLE have low levels of PA and spend the majority of their day in sedentary behavior resulting in impaired aerobic capacities, which increases the risk of SLE. The preferred solution is to replace a minimum of 10 minutes of sedentary behavior with moderate-vigorous PA to reduce their risk of cardiovascular disease.

Aerobic training programs provide benefits such as improved $\text{VO}_{2\text{max}}$ and reduced estimated cardiovascular risk, whereas resistance training programs improve strength and function. Combining both aerobic and resistance training may prove the most useful for individuals with SLE, and both appear to be safe to implement. Additionally, PA has demonstrated improvements in fatigue and depression, which are prevalent with SLE.

Reljic D, Dieterich W, Herrmann HJ, Neurath MF, Zopf Y. "HIIT the inflammation": comparative effects of low-volume interval training and resistance exercises on inflammatory indices in obese metabolic syndrome patients undergoing caloric restriction. *Nutrients*. 2022 May 10;14(10):1996. doi:10.3390/nu14101996. PMID: 35631137

Rinaldo L, Caligari M, Acquati C, Nicolazzi S, Paracchini G, Sardano D, Giordano A, Marcassa C, Corrà U. Functional capacity assessment and minimal clinically important difference in post-acute cardiac patients: the role of Short Physical Performance Battery. *Eur J Prev Cardiol*. 2022 May 25;29(7):1008–14. doi:10.1093/eurjpc/zwab044. PMID: 33846721

As the prevalence of obesity continues to rise, it is important to identify and understand the possible comorbidities that exist in this population. Metabolic syndrome (MetS), a risk related to obesity, is also associated with inflammation, which may contribute to the development of various secondary diseases. The primary mechanism of inflammation is the oversecretion of proinflammatory adipokines and cytokines from adipose tissue. Reducing this inflammation may reduce risk. The purpose of this study was to compare the effects of 12 weeks of low-volume high-intensity interval training (LOW-HIIT), single and 3 set resistance training (1-RT and 3-RT), and whole-body electromyostimulation (WB-EMS) on inflammatory and cardiometabolic measures in a cohort of obese patients with MetS.

Methods: Patients were randomly assigned to different exercise regimens (including LOW-HIIT, 1-RT, WB-EMS, and 3-RT) performed for a duration of 12 weeks combined with nutritional counseling. This analysis focused on the impact of the different low-volume exercise programs on inflammation outcomes in a sample of patients. The primary outcome of this study was serum concentration of C-reactive protein (CRP), and secondary outcomes were further inflammatory markers, cardiometabolic indices, Vo_2max , and anthropometric variables as specified below. Additionally, the cardiometabolic risk status was quantified using the metabolic syndrome severity score (MetS z-score) for all subgroups. The MetS z-score represents a risk score that was developed to assess severity of MetS.

Results: Body Composition. All groups reduced body weight primarily from a decrease in fat mass (FM). The relative amount of weight loss did not differ significantly between groups. Skeletal muscle mass decreased significantly in the WB-EMS and control (CON) groups.

Inflammatory Markers. Significant reductions in serum concentrations of CRP, hsCRP, IL-6, and LBP in the LOW-HIIT group compared to the 1-RT, 3-RT, and WB-EMS group.

Cardiometabolic Markers. MetS z-scores were found to be reduced in the LOW-HIIT, 1-RT, and 3-RT group.

Discussion: There were 4 primary findings of this study: (a) all groups exhibited similar weight loss during the period of calorie restriction (3.6%); (b) serum concentrations of inflammatory markers decreased only in the LOW-HIIT group; (c) among the RT groups, only 3-RT was related to a reduction in inflammatory markers (hsCRP and LBP); and (d) MetS severity score improved in the LOW-HIIT, 1-RT, and 3-RT groups.

Developed by the National Institute on Aging, the Short Physical Performance Battery (SPPB) consists of a series of assessments aimed to evaluate lower extremity physical function in older adults. Physical function is associated with various biomarkers including functional decline, chronic disease, falls, hospitalization, and mortality. Exercise programs, such as cardiac rehabilitation, aim to improve physical function and reduce risk factors associated with chronic disease. This study had 2 objectives: to examine the relationship between SPPB and short-term outcomes in elderly patients admitted to cardiac rehabilitation, and to determine the minimal clinically important difference (MCID) in SPPB scores for this population.

Methods: Data obtained from cardiac patients (≥ 75 years) admitted to cardiac rehabilitation in the postacute phase following a cardiac event were retrospectively examined. Patients completed a personalized exercise program which included a 6-day rehabilitation phase consisting of activities such as calisthenics, stair climbing, cycling, and assisted walking twice a day for 6 days. The SPPB was administered upon admission and again prior to discharge to assess standing balance, gait speed, and chair rise tests. Short-term outcomes included rate of in-hospital cardiac and noncardiac complications, resources used, changes in SPPB, and duration of hospitalization. The Patient Global Impression of Change (PGIC), which asks patients to rate their health status and physical function since admission, was used as the anchor to determine the MCID in SPPB.

Results: Patients ($N = 385$) 80.1 ± 3.7 years of age (58% males) and were admitted to cardiac rehabilitation following cardiac surgery (70.9%), acute coronary syndrome (17.7%), or congestive heart failure (10.4%). Short-term outcome data revealed a longer average length of stay (31.1 ± 16.1 , 20.2 ± 6.1 , 24.9 ± 10.2 , 17.1 ± 5.9 days) and greater major complications rate (63%, 47%, 34%, 27%) based on SPPB scoring categorization of severe, moderate, mild, minimal/no limitations, respectively. SPPB scores from admission to discharge improved significantly ($P < 0.001$) for the entire study cohort. An increase of >1 on SPPB was determined to be the MCID for the SPPB. Clinically significant improvements were observed in 74.2% of patients completing cardiac rehabilitation, however the degree of improvement based on changes in SPPB scores was inversely related to level of functional impairment upon admission.

Discussion: Physical function assessments such as the SPPB can offer clinicians an objective measure to evaluate a patient's risk for various negative health outcomes. In the current study, older adults with lower SPPB scores following a cardiac event experienced more complications and were

hospitalized longer. While research tends to focus on statistical significance, establishing criteria for MCID may be more useful in an applied setting such as cardiac rehabilitation. To aid in determining a meaningful change in SPPB scores following cardiac rehabilitation in the postacute phase, the current study determined an increase greater than 1 in SPPB score was meaningful in terms of patients' health status and physical function. Additionally, cardiac rehabilitation was successful at eliciting a clinically significant improvement in 83% of patients classified as severe or moderate limitations. Research should be expanded to include later phases of cardiac rehabilitation and include a wider population for greater application of MCID for SPPB.

Lanzi S, Belch J, Brodmann M, Madaric J, Bura-Riviere A, Visonà A, Mazzolai L. Supervised exercise training in patients with lower extremity peripheral artery disease. *Vasa*. 2022 Sep;51(5):267–74. doi:10.1024/0301-1526/a001024. PMID: 36059219

Reduced blood flow as the result of atherosclerotic narrowing of arteries supplying the lower limbs, known as peripheral arterial disease (PAD), often leads to exertional leg pain or intermittent claudication (IC). Consequently, PAD negatively impacts lower limb function including altered gait patterns, and reduces strength, balance, and walking performance. Supervised exercise therapy (SET) should be considered as a tool for initial management of PAD, as it is successful at improving ambulatory parameters and quality of life. This study sought to determine perceptions of SET as well as its availability and use in European countries.

Methods: A link to an anonymous web-based 21-question survey, developed by specialists (clinical exercise physiologist and vascular physicians) in vascular rehabilitation, was published in the European Society for Vascular Medicine (ESVM) and distributed to vascular medicine national societies via ESVM board members. The questionnaire focused on awareness, referral, insurance coverage, and programmatic topics.

Results: The study team received 131 responses from 17 European countries, with highest responses from France (52%), Switzerland (13%), and Italy (11%). The majority of

responders were angiologists (80%; 105/131). Awareness of SET as a first-line treatment option, and its ability to improve function and walking parameters was reported by 95% and 96% of responders, respectively. Additionally, 95% indicated they would refer those with PAD to SET if available. The majority of SET program coordinators were either vascular physicians (48%) or cardiologists (26%). Responders from 6 countries reported that SET is reimbursed by health insurance, while responders from 10 countries indicated SET is not reimbursed. One country reported SET is funded by a national insurance program. Of the 131 responders, 22 were unaware of SET insurance coverage. SET was available in 10 countries. In 7 countries, SET availability in their country was unknown by 7% of responders. Characteristics of the SET programs included: 34% are stand-alone programs specific for PAD patients, 26% were a form of individual practice, 23% were a part of cardiac rehabilitation, and 17% did not offer (or were unaware of) a SET program; 65% enrolled only symptomatic patients, 9% enrolled both symptomatic and asymptomatic patients, 8% only enrolled patients following revascularization, and 1% only enrolled asymptomatic patients. Some responders (17%) were unaware of which patients were eligible. Length and frequency of SET programs were 12 weeks or less (67%), most commonly offered 2–3 times per week (37%), and predominantly utilized walking only (26%), or combined walking and resistance training (47%).

Discussion: Although very strong evidence exists for the benefits of SET for PAD, and most clinicians recognize it as a valuable component of initial disease management, this paper highlighted large variability in availability and reimbursement for SET in European countries. While 59% reportedly have SET for PAD, reimbursement is only available in 41% of countries. This is paradoxical considering SET is a Class 1A recommendation for chronic PAD patients. Interestingly, the inconsistent availability and utilization of SET for PAD may not be unique to Europe, as data from a recent study in the United States revealed SET was not available according to 54% of responders surveyed. This study demonstrates the need for improvements in SET for those with PAD in terms of clinician awareness of program availability and reimbursement, eligibility criteria, and consistency in programming.