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CASE REPORT

Walking performances and muscle oxygen desaturation are increased after supervised exercise training in Takayasu arteritis: a case report and a review of the literature

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Background Takayasu arteritis (TAK) is a rare chronic inflammatory vasculitis predominantly affecting the aorta and its main branches. Takayasu arteritis has been shown to increase cardiovascular risk. Supervised exercise training (SET) is a well-recognized and effective therapeutic tool improving walking performances in patients with chronic atherosclerotic disease; however, the effects of SET, and the underlying mechanisms, remain poorly documented in TAK patients.

Case summary We reviewed the literature and investigated the effects of a 12-week SET programme on walking performances, physical function, and calf muscle oxygen saturation (StO_2; assessed by near-infrared spectroscopy) during exercise in a 28-year-old man with TAK and symptoms of arterial lower limb claudication. The literature review evidences only two recent publications suggesting that exercise training is effective and well-tolerated in patients with arteritis. The treadmill pain-free (+22%) and maximal (+273%) walking distance, 6-min walking distance (+66%), and physical function of lower extremities (+20%) following SET were significantly improved in our patient. Moreover, we observed a greater muscle oxygen desaturation (increased oxygen extraction) during exercise.

Discussion Following SET, the increased oxygen extraction may be related to improved microvascular milieu leading to a better match between muscle oxygen supply and demand during exercise. These new results may contribute to mechanistic insights in peripheral adaptations following exercise training in TAK patients and may help to explain, at least partly, the increased walking performances. Although more studies are needed to better explore the impact of exercise training, these results suggest that exercise should be recommended in TAK patients.

Keywords Intermittent claudication • Vascular rehabilitation • Near-infrared spectroscopy • Muscle oxygenation • Exercise • Case report • Takayasu

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Learning points

- Exercise training increases walking performance and physical function and should be recommended in TAK patients.
- One of the possible underlying mechanisms may be an improved microvascular milieu leading to a better match between muscle oxygen supply and demand during exercise.

Introduction

Takayasu arteritis (TAK) is a rare chronic inflammatory vasculitis that predominantly leads to stenosis, occlusion, and/or aneurysm of the aorta and its main branches.[1] Takayasu arteritis mainly occurs in young females.[1] Clinical manifestations are diminished/absent peripheral pulses, asymmetric blood pressure in either upper or lower limbs, peripheral ischaemia, and arterial claudication.[1] Daily life activities may be compromised, with consequent reduced physical function, and decreased quality of life.[1–3] Patients with TAK are at higher risk of cardiovascular events.[4] It has recently been shown that exercise training is effective and well-tolerated in female patients with TAK[3] and that may increase walking performance and quality of life in a male patient with arteritis and symptoms of claudication of lower limbs.[5] However, the underlying mechanisms remain poorly investigated. In patients with lower extremity artery disease (LEAD), presenting similar symptoms of claudication than TAK patients, adaptations to exercise training mainly reside at the skeletal muscle level.[6] Therefore, one may hypothesize that similar adaptations may also occur in symptomatic TAK patients.

Near-infrared spectroscopy (NIRS) is a non-invasive system measuring muscle oxygen saturation [StO_2 (%)], indicative of tissue oxygenation.[7] Near-infrared spectroscopy-assessed StO_2 may therefore provide information on the balance between oxygen consumption and delivery within the skeletal muscle at rest and during exercise,[7] contributing to new mechanistic insights following exercise training in TAK patients.

We presented here a review of the literature in the topic of exercise training and arteritis and the first case of a 28-year-old man with TAK and symptoms of arterial lower limb claudication being evaluated with NIRS during exercise before and after a 12-week supervised exercise training (SET). In addition, physical function of lower extremities was also assessed.

Timeline

Time	Events
Between 18 and 16 months prior to supervised exercise training (SET)	• Diagnosis of TAK • CRP = 292 mg L^{-1} • Lower limb claudication: 50 m • Treatment: i.v. corticosteroid therapy, Prednisone 45 mg day^{-1} (1 mg kg day^{-1}) and Methotrexate 10 mg $week^{-1}$
Between 16 and 12 months prior to SET	• Lower limb claudication: 200 m • CRP = 1 mg L^{-1} • Treatment: Methotrexate 10 mg $week^{-1}$; Prednisone decrease until 17.5 mg day^{-1}
Between 12 and 11 months prior to SET	• Abdominal pain • CRP = 91 mg L^{-1} • Treatment: Prednisone 40 mg day^{-1} and Tocilizumab 8 mg kg $month^{-1}$, Methotrexate was stopped
Between 11 and 7 months prior to SET	• Lower limb claudication: 200 m • No significant sign of inflammation • CRP = 1 mg L^{-1} • Treatment: Prednisone decrease until 10 mg day^{-1}, Tocilizumab 8 mg kg $month^{-1}$
Between 4 months to the beginning of SET	• Lower limb claudication: 200 m • No significant sign of inflammation • CRP = 1 mg L^{-1} • Treatment: Prednisone decreases until 5 mg day^{-1}, Tocilizumab 8 mg kg $month^{-1}$ • SET was initiated
Following SET	• Significant improvement in walking performances and physical function • No significant sign of inflammation • CRP <1 mg L^{-1}

Patient information

A 28-year-old man (body mass index 17.8 kg/m^2) with TAK, renal artery stenosis with hypertension and symptoms of arterial lower limbs claudication was investigated (*Figure 1*). The patient had no active comorbidities and was non-smoker. Eighteen months prior to SET, the patient was hospitalized for abdominal and lower extremity pain (claudication: 50 m), myalgia, and fever. Peripheral pulses were present only in femoral arteries; ankle-brachial index was 0.80 (right leg) and 0.57 (left leg). Vascular Duplex examination revealed thickness of the arterial wall and stenosis/occlusion of digestive, renal, and ilio-femoral arterial axes. Systemic inflammation (CRP) was 292 $mg\,L^{-1}$. Treatment included intravenous corticosteroid therapy, followed by Prednisone 1 $mg\,kg^{-1}\,day^{-1}$ and Methotrexate 10 $mg\,week^{-1}$. After 6 months, by reason of an adverse evolution, with abdominal pain, persistence of significant lower limb claudication and biologic inflammation, a treatment modification was proposed. In the following months, inflammation was reduced and stabilized. The patient was then proposed to participate to a SET programme.

Figure 1 Computed tomography angiography (maximum intensity projection 3D reconstruction) showing multiple stenoses/occlusions of iliac and femoral arteries.

Physical examination

Physical examination before beginning of SET revealed high blood pressure values (systolic blood pressure 151 mmHg; diastolic blood pressure 101 mmHg) with a normal resting heart rate. Peripheral pulses were present at the femoral artery level bilaterally and not perceived distally. Respiratory examination revealed no abnormalities.

Functional assessments

Functional assessments were performed before and following SET.

Walking performances

Constant-load treadmill test

This test was performed at 3.2 $km\,h^{-1}$ with a 12% slope to determine pain-free walking distance (PFWD) and maximal walking distance (MWD). Calf StO_2 was monitored both at rest and during exercise with continuous wave NIRS (PortaMon, Artinis, The Netherlands). Near-infrared spectroscopy probe was placed over the lateral gastrocnemius muscle corresponding to the maximum girth of the calf of the most affected leg. Near-infrared spectroscopy probe was positioned with 3.5 cm inter-optode spacing. The signal was recorded at 10 Hz and a differential pathlength factor of 6.0 was used.

Six-minute walking test

This test was performed in an indoor 50 m-corridor to determine the 6 min-walking distance (6MWD). Patient was asked to walk as much as possible within 6 min. At the end of the test, patient evaluated leg pain using a visual analogue scale ('no pain': 0 and 'worst imaginable pain': 10).

Physical function

Lower limb function was assessed by means of the Short Physical Performance Battery test and the stair climbing test.[8,9]

Table 1 Walking performances and physical function of lower extremities before and after the supervised exercise training programme

Variables	Before	After	Change (%)
Walking performance			
PFWD (m)	90.0	110.0	+22
MWD (m)	150.0	560.0	+273
6MWD (m)	352.0	585.0	+66
Resting time during 6MWT (s)	110	0	
$6MWT_{vas}$	6.2	2.0	-68
SPPB			
Stand test summed (s)	30.0	30.0	0
4-m velocity test ($m\,s^{-1}$)	1.1	1.6	+43
5× chair stand test (s)	14.0	5.9	-58
SPPB total score	10.0	12.0	+20
SCT (s)	5.5	3.1	-43

MWD, maximal walking distance; 6MWD, six-minute walking distance; $6MWT_{vas}$, visual analogical scale at the end of the 6-min walking test; PFWD, pain-free walking distance; SCT, stair climbing test; SPPB, short physical performance battery.

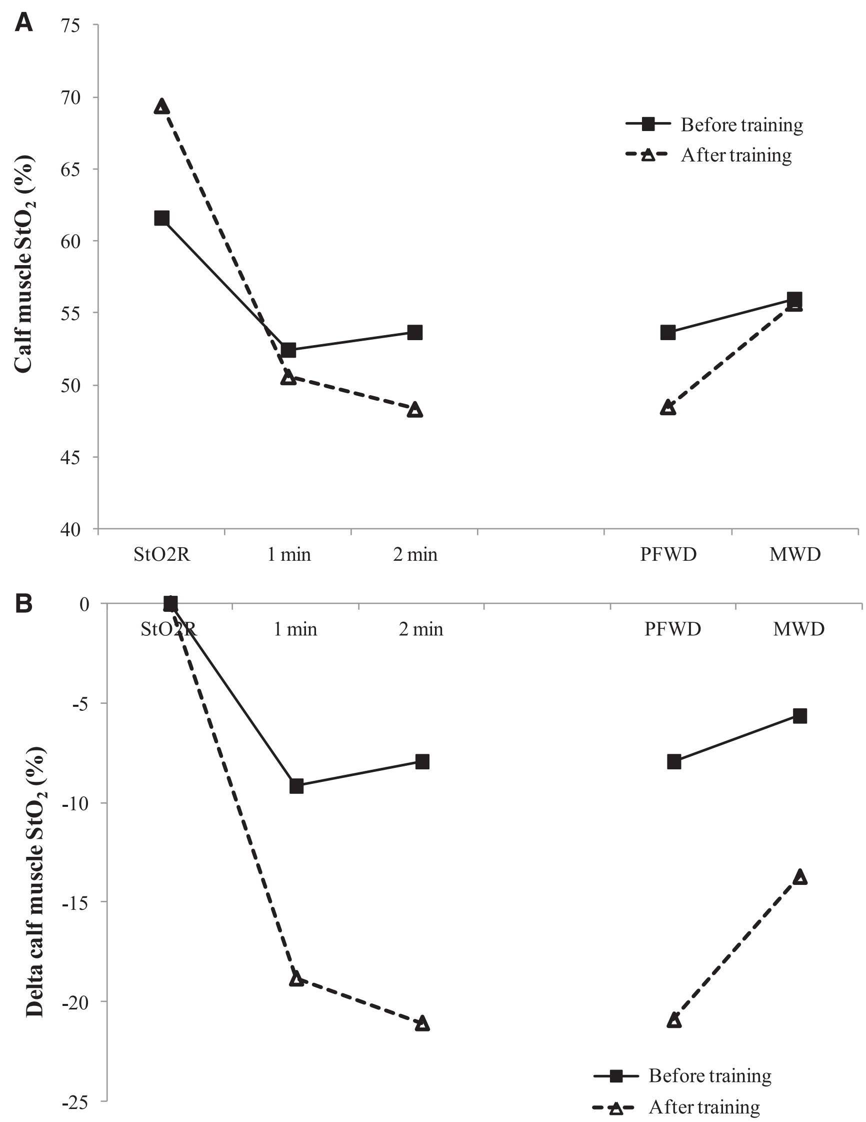

Figure 2 Calf muscle oxygen saturation (StO_2) (*A*) and delta StO_2 (ΔStO_2) (*B*) at rest (StO_{2R}), during the first 2 minutes of effort and at the pain-free walking distance (PFWD) and maximal walking distance (MWD). StO_{2R} was recorded after 3 min of standing before exercise. Each time point was calculated as the average StO_2 during the last 15 s and ΔStO_2 was calculated as the StO_2 at each time point minus the baseline StO_2.

Supervised exercise training

Supervised exercise training consisted of 36 sessions, three times a week, over a 12 week period. Each training session started with a 5–10 min warm-up and ended with a 5-min stretching cool-down period. One session weekly was mainly focused on strengthening of lower limbs and include different type of walking (heel and toe walking, skipping walking, side-to-side walking, power-jogger walking) and resistance exercises focused on the main muscle groups of the lower limbs performed with an elastic band. During the two other weekly sessions, outdoor Nordic walking was performed. Training session duration was progressively increased (from 30 to 55 min) according to patient's tolerance. The intensity was mainly set at 12–14 on the 15-grade Borg scale (moderate intensity).[10]

Follow-up and outcomes

The patient completed the training programme. Walking performances (PFWD: +22%; MWD: +273%; 6MWD: +66%) and physical function of lower extremities (+20%) significantly increased (*Table 1*) and muscle oxygen desaturation during exercise was greater after SET (*Figure 2A and B*).

Review of the literature

We performed a review of the literature on the topic of exercise training and arteritis in Pubmed and Embase (Supplementary material online). After screening procedure, we found two publications (one article and one case report; *Table 2*).

Table 2 Summary of studies

References	Arteritis	*n*	Gender	Age	BMI	Exercise training	Main findings
Lima *et al.*[5]	Arteritis with no identifiable cause	1	Male	33	29.4	• 16-week unsupervised ET • Patient were instructed to walk 1 h/day until maximum claudication pain at least five times per week • Weekly phone to monitor training adherence	↑ in claudication distance and total walking distance during treadmill and 6-min walking test ↑ in QoL (assessed with SF-36) ↓ SBP, DBP, rate pressure product, and LF/HF ratio
Oliveira *et al.*[3]	TAK	6	Female	35.3 ± 6.6	26.6 ± 4.6	• 12-week SET (2×/week) • 30–50 min (gradually increased) of treadmill walking • HR between the VT and RCP was used to determine exercise intensity during the training sessions	↑ muscle strength and physical function ↑ time to reach VT = $V'O_{2peak}$, time-to-exhaustion = endothelial function = QoL (assessed with SF-36 and HAQ) ↓ TNF ↑ VEGF and PDGF AA

DBP, diastolic blood pressure; HAQ, Health Assessment Questionnaire; HR, heart rate; LF/HF ratio, ratio of the low- and high-frequency bands in heart rate variability; PDGF AA, platelet-derived growth factor; QoL, quality of life; RCP, respiratory compensation point; SBP, systolic blood pressure; SET, supervised exercise training; SF-36, medical Outcome Study Short-Form 36 General Health Survey; TAK, Takayasu arteritis; TNF, tumour necrosis factor; VEGF, vascular endothelial growth factor; $V'O_{2peak}$, peak oxygen uptake; VT, ventilatory threshold; ↑, increase; ↓, decrease; =, similar.

Discussion

Exercise training is poorly investigated in patients with arteritis. Present results show that walking performances and physical function increase after SET in a TAK patient. In addition, we observed a greater muscle oxygen desaturation during exercise in the post-training condition.

The improvements of walking performance are in line with previous observations reported in LEAD patients.[11] One of the possible underlying mechanism associated with walking improvement may reside at the skeletal muscle level. It has recently been shown that exercise training may increase microvascular skeletal muscle blood flow during exercise in LEAD patients.[12] This is probably related to improvements in endothelium-dependent vasodilation and increased capillary density.[6,12,13] These adaptive responses may lead to increased oxygen extraction from the skeletal muscle, and therefore improve muscle oxidative metabolism during exercise.[6,12–15] Therefore, the greater muscle oxygen desaturation (i.e. increased oxygen extraction) during exercise observed after SET in our patient, may be related to an improved microvascular milieu leading to a better match between muscle oxygen supply and demand during exercise. These results may help to explain, at least partly, the observed increased walking performances and exercise tolerance and contributing to new mechanistic insights following exercise training in TAK patients. In addition, physical function of lower extremities also increased after SET, confirming recent results in TAK patients.[3]

Conclusion

Beneficial effect of SET in non-atherosclerotic patients will need to be confirmed in a properly conducted randomized control trial. However, based on our findings and on previous results, SET seems to be beneficial and may be recommended in TAK patients.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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