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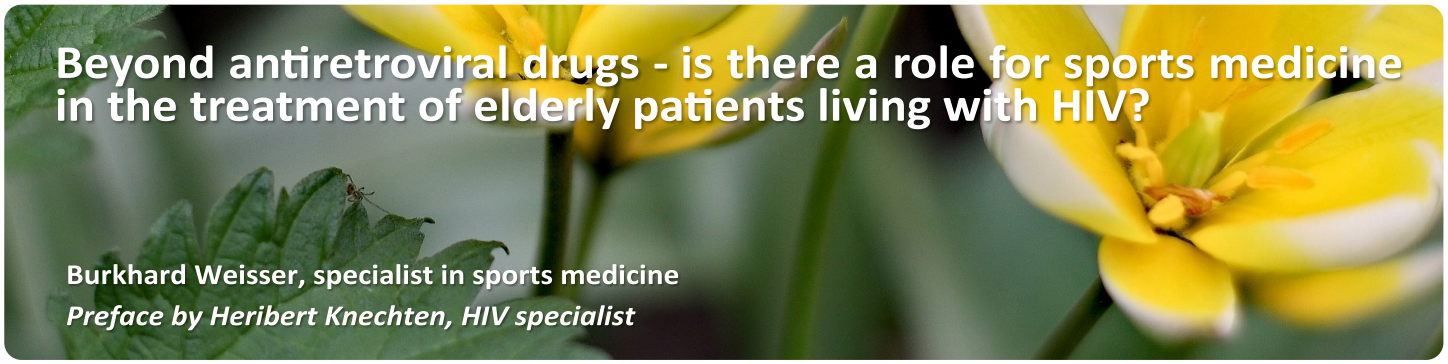

Beyond antiretroviral drugs - is there a role for sports medicine in the treatment of elderly patients living with HIV?

Burkhard Weisser, specialist in sports medicine
Preface by Heribert Knechten, HIV specialist

Heribert Knechten

Change is constant. But you have to be ready to face the future!
In times when antiretroviral therapy can be successful in over 95% of cases[1], the predominant topics of daily practice are changing.

Until 1996, we were concerned with AIDS-defining diseases (and this is still a problem in some countries of the world), but the current HIV infection has surprised us with heart attacks, obesity, high blood pressure and other complex issues. The often premature cases of malignant tumors and other diseases also influence the situation of HIV-infected people.

However, the almost normal life expectancy of people with HIV is not without its challenges:

Does the extra time gained translate into a higher quality of life? For this reason, PROMS (patient-related outcome measures) have become increasingly important in recent years. For some time now, clinical studies need measures of the health-related quality of life and all the effects on the life of the subject.

As doctors, we are also expected to make people with HIV aware of the latest findings on nutrition and the importance of physical and mental fitness for healthy ageing.

It should be made clear that for every disease, a little more fitness and increased muscle mass means fewer heart attacks, fewer strokes, fewer hospitalizations and fewer deaths. It is also important to realize that anyone who is able to get active will benefit, regardless of age, and depending on their level of commitment, may be able to achieve maximum gains compared to the inactive control group. Physical activities should be systematically incorporated into everyday life and every opportunity should be taken to do so.

As doctors, we should not try to overcome intrinsic resistance; the activation of personal responsibility can only come from the individual him/ herself; tips and suggestions for thinking about diet and exercise are effective.

In this context, the topic of "Beyond HIV" is becoming increasingly important in everyday treatment. Training in this area is therefore essential!

Burkhard Weisser

During the last decades, the medical treatment of persons living with HIV has been a success story. The Global Burden of Disease Study 2021[2] has demonstrated a substantial age-standardised reduction of disability-adjusted life-years (DALY = years lived with disability plus years of life lost) for HIV/AIDS (minus 47,8%). In western industrialized countries, the life expectancy of people living with HIV receiving effective combination antiretroviral therapy is approaching that of the general population and non AIDS-defining comorbidities are becoming of greater concern [3].

Age-related diseases of the increasingly elderly group of patients living with HIV include typical cardiovascular and metabolic diseases and other geriatric entities. Furthermore, a consistent treatment of cardiovascular risk factors has been neglected in the past since virus suppression was the focus of therapy. In addition, there seem to exist HIV-typical co-morbidities such as premature frailty, sarcopenia, low physical fitness, and mental health problems. HIV is increasingly considered as a chronic illness [4].

Frailty in elderly people living with HIV – immune mechanisms?

People living with HIV are getting older. In addition, they seem to experience accelerated aging probably due to chronic activation of the immune system. Increased markers of immune exhaustion and immune senescence have been demonstrated in frail HIV-patients compared with non-frail elderly patients[5]. T-cell exhaustion seems to lead to impaired T-cell function, lack of telomerase and telomere shortening. In addition to specific immune mechanisms, a systemic inflammation might induce a variety of organ dysfunctions such as loss of muscle mass (sarcopenia), changes of the vascular wall (atherosclerosis), and microvascular/endothelial disfunction leading to ischemia [6]. Loss of muscle mass and strength is probably one of the most important risk factors for frailty. Some authors call the increase of frailty among people living with HIV a "silent epidemic" [7].

Possible effects of exercise and other life style factors on systemic inflammation, telomere length, and other immune mechanisms

It has been suggested that short telomere length is associated with progressive acceleration of aging, including an increase in age-related diseases such as osteoporosis, cancer, and dementia. Therefore, it seems evident that controlling telomere length could be a key factor in the aging process and health care. Telomere shortening has also been demonstrated in elderly HIV patients. At least in healthy subjects, a current systematic review has shown a favorable effect of exercise on telomere length [9]. Although there is little data for people living with HIV (PLWH), the anti-inflammatory effect of exercise in other chronic diseases has been very well documented. This is particularly true for patients with cardiovascular risk factors such as obesity, diabetes, hypertension and sedentary life style. These risk factors continue to increase in the elderly HIV population in industrialized countries. Another life style factor influencing a systemic inflammation is the diet. The Mediterranean diet is not only associated with anti-inflammatory effects but might also have a protective effect against sarcopenia [10]. Recently, a dietary anti-inflammatory index has been proposed (DII). Therefore, in addition to further exercise studies, dietary interventions might be needed in patients living with HIV to control low-grade systemic inflammation [11]. Foods with the highest anti-inflammatory potential include tomatoes (- 0.78), apples and berries (0.65), deep yellow or orange vegetables (0.57), and poultry (0.45). Among the worst inflammatory foods are processed red meat (+0.68) and added sugar (+0.56) with + meaning pro-inflammatory.

Trainability of cardiovascular fitness in people living with HIV

Low cardiovascular fitness is one of the most important risk factors for the development of frailty, sarcopenia and reduced quality of life particularly in elderly patients with HIV. In an intervention study, it was investigated, whether older people living with HIV can achieve similar functional benefits with exercise as their uninfected peers. Sedentary adults (50–75 years) with or without HIV were recruited for 24-weeks of supervised endurance/resistance exercise [12]. Among others, the initially low VO2 max. (25.2 ml/kg/min) increased from week 0-12 by 10% in PLWH as compared to 5% in uninfected people. VO2 max is the best parameter for the cardiovascular and muscular fitness and refers to the maximum volume (V) of oxygen (O2) that an individual can utilize during exercise. From week 13-24, HIV patients had either equal improvements in physical function (e.g. bench press, leg press, and lat pulldown) or greater training effects than the control group (stair climb, grip strength, and 400m walk time). The study used a modified version of the Short Physical Performance Battery that improves discrimination of physical function at the higher end of the functional spectrum. Thus, not only pure strength and endurance was measured but also physical function parameters important for daily living (e.g. 10 repeated chair stands). In addition, a reduction in the number of frailty criteria was shown in the HIV group. The authors concluded that among sedentary, older adults, the effects of exercise on physical function are not attenuated among patients living with HIV.

Treating sarcopenia and frailty is a central goal

There is a close association between loss of muscle mass (sarcopenia) and frailty in elderly people with HIV. In the study presented in the previous paragraph, a preserved trainability for muscle strength and physical function was shown. These parameters are important for the health-related quality of life. However, an increase in muscle mass to treat sarcopenia might be more difficult to achieve. In a recent meta-analysis with a total of n=258 PLWH [13], seven RCTs (randomized clinical trials) were included lasting between six and 24 weeks. In comparison to no exercise, resistance training not only improved muscle strength but also lean body mass (mean difference 2.96 kg, 95%CI 0.98 to 4.94). In addition to this substantial increase in muscle mass, a reduction in body fat mass and an increase in $CD4^+$ cells count (mean difference of 100 cells/mm^3, 95% CI 12 to 188) have been observed. The optimal intensity for strength training for older adults and those with sarcopenia remains to be determined. Studies systematically comparing different training intensities for the treatment of sarcopenia in PLWH are lacking. In the general elderly population without HIV, previous work has suggested that higher intensities may be most effective for improving muscle strength, however, both moderate and low intensities can also induce substantial improvements.

Table 1: Resistance exercise training plan for elderly patients with sarcopenia. Modified according to Hurst C et al.[14]
1 RM one repetition maximum, RPE (rate of perceived exertion) on a scale 1-10.

Training frequency	2-3 sessions per week	
Exercise selection	*Lower body* Squat/leg press Knee extension Leg curl Calf rise	*Upper body* Chest press Seated row Lat pull down
Exercise Intensity	*Prescription based on 1 RM* 40-60% of 1 RM progressing to 70-85% of 1 RM	*Prescription based on RPE* RPE 4-6 progressing to RPE 6-8 on CR 10 scale
Exercise volume	1-3 sets of 6-12 repetitions	
Rest periods	Within sessions: 60-120 s between sets At least 2-3 min. between exercises Between sessions: At least 48 h	

Guidelines and recommendations for exercise

Although there is increasing evidence for the need of a prescription of physical exercise in elderly and frail patients with sarcopenia, the current EASC 12.0 guidelines do not include a separate exercise section. Exercise is generally recommended among other lifestyle measures in different chapters. For frailty and sarcopenia, it is recommended "to sustain and recover physical function impairment and sarcopenia by prescribing physical exercise with a resistance training component." At least in Germany, there is partial reimbursement of rehabilitation exercise.

As in elderly uninfected persons, people with HIV should engage in at least 150 min. of moderate or 75 min. of vigorous physical activity per week and should be active almost every day. Endurance exercise may include (nordic) walking, running and biking. In addition to these endurance recommendations, resistance training is of particular importance (see table). Most elderly patients will probably have no experience with resistance training. Therefore, a training supervised by physical therapists or exercise physiologists is recommended. There is a tendency towards using higher intensities for muscle growth. Although responses to exercise seem to be not adversely affected by ART therapy, little is known about interactions between drugs and exercise[14]. The lowest possible number of antiretroviral substances and further drugs treating cardiovascular risk factors might be beneficial for patients engaging in exercise programs.

Conclusion

People with HIV are getting older. There seems to be accelerated aging mechanisms in this group including chronic inflammation and changes of the immune system. A common complication is sarcopenia leading to loss of physical function and reduced quality of life. The effect of exercise, particularly resistance training in elderly patients with HIV has been well documented. There is an urgent need for general recommendations for exercise programs to reduce cardiovascular risk factors, sarcopenia and frailty in patients living with HIV [15].

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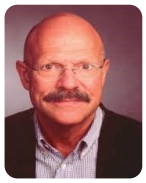

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