Physical Activity and Exercise for Cardiovascular Prevention — Where Do We Come from, where Do We Go?

Körperliche Aktivität und Training in der kardiovaskulären Prävention – Woher kommen wir, wohin gehen wir?

More than 60 years have passed since the landmark study of Morris et al. from 1953, who showed higher incidence of coronary heart disease in inactive bus drivers and telephonists compared to active conductors and postmen. Ever since, numerous studies have shown the importance of both, physical activity (PA) and exercise, in prevention and treatment of cardiovascular diseases. Still, the debate about the optimal type, amount and intensity of activity is controversially discussed and unresolved. So what is already known and which questions remain for the future?

Physical Inactivity is the New Smoking

Physical inactivity is characterized by a high amount of sedentary behavior and lack of PA. Its detrimental effects on healthy aging have been repeatedly demonstrated. Today, physical inactivity is amongst the four major promoters of aging-related non-communicable diseases (NCD) being associated with a similar number of deaths like smoking on a population level (18). Increased mobility, modern technology and the availability of almost everything via internet lead to reductions in occupation- and household-related energy expenditure of 140 and more than 250 kcal/d, respectively (5). These factors and the excessive use of media promote sedentary behaviors, like sitting, lying and not moving. Sedentary behavior is associated with unfavorable physiological changes, such as downregulation of arterial shear rate and blood flow as well as unfavorable alterations to glucose metabolism, inflammatory stress and oxidative stress (4). However, these negative effects seem not to be independent of and might be attenuated by an increase of PA and cardiorespiratory fitness (CRF), respectively.

The Type of Activity Matters!

The beneficial cardiovascular effects of an active life style are well-known. Although PA and CRF are partially interrelated, both have independent effects on cardiovascular risk reduction, with CRF being nearly twice as strong as PA (20). An adequate amount of both, PA and high-intensity exercise, leads to the most substantial reductions in shortand long-term risk of cardiovascular morbidity and mortality (20).

The Amount Matters

Three hours of moderate-intensity PA per week can reduce the risk for coronary heart disease, stroke and other cardiovascular diseases by 35% (13). All-cause mortality and other NCD, such as dementia, depression, colon cancer, breast cancer, diabetes and hip fractures can also be reduced for up to 50% (13). Thereby, a clear dose-response relationship is visible with the highest benefits in those, who increase their activity from sedentariness to three hours per week (10).

The Intensity Matters!

Twenty minutes of exercise at vigorous intensity exert the same beneficial effects on all-cause mortality as 80 minutes of exercise at low-to-moderate intensity (17). Furthermore, exercise at vigorous intensity effectively increases maximum oxygen consumption and, thus, CRF. Since the "Aerobics Center Longitudinal Study" we know, that good CRF protects against the influence of classical cardiovascular risk factors (2). Also, exercise at vigorous intensity has been shown to induce greater improvements of diastolic blood pressure and glucose control than exercise at moderate intensity, whereas this could not be demonstrated for systolic blood pressure and blood lipids (15).

Cardiorespiratory Fitness — the Strongest Predictor of Cardiovascular Risk!

The superior value of CRF for prediction of overall mortality in healthy people and in those with cardiovascular disease was demonstrated 17 years ago in the landmark study by Myers et al (11). Despite age and sex no other classical risk factor outmatched CRF in this regard. However, only very recently its potential to improve accuracy of cardiovascular risk scores was demonstrated for the first time in the "Henry Ford ExercIse Testing - FIT" project (1). This has also been shown for SCORE, a score to predict coronary arterial morbidity and mortality (7). Surprisingly, maximum oxygen consumption still has not been embedded in major risk scores such as the Framingham Risk Score or the EuroScore.

Understand the Molecular Response to Physical Activity and Optimize the Effects of Exercise

The adequate type, amount and intensity of exercise for maintenance of a healthy state is highly variable between individuals. We still lack an

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in-depth understanding of the molecular processes underlying physiological functioning and the impact of exercise on the determinants of cellular senescence. Better knowledge about the mediation of exercise on mitochondrial biogenesis, fiber transformation, autophagy, intercellular communication and other important factors of physiological aging is necessary to enable a precise characterization of a person's health status and for the prescription of individualized exercise-based treatment (6). The "Molecular Transducers of Physical Activity in Humans - MoTrPAC" project is currently the largest ongoing study that aims to create a "molecular map" of the effects of physical activity in humans.

Where Do We Go? Seeking the Recipe for Optimal Health!

Medicine is shifting from reactive towards proactive care. Instead of waiting for risk factors or diseases to occur, the establishment and maintenance of optimal health should be sought in order to minimize the DALY ("disability adjusted life years") and enhance health span (19). PA and CRF are key players in this context. In order to achieve a better understanding of the decrease of CRF with aging, the combined assessment with muscular strength and neuromuscular coordination is warranted to improve prevention of frailty at older age (16).

The acceptance of CRF as an independent cardiovascular risk factor and its implementation in the routine assessment of prediction of morbidity and mortality should therefore be a major concern for the upcoming generation of medical professionals. Accordingly, assessment of CRF in healthy people was introduced into several guidelines, especially those focusing on healthy living in children and adolescents (9) and on cardiovascular health (12). Databases on PA and CRF, like the FRIEND registry (8) and the currently ongoing COmPLETE Health project (16), need to be expanded to establish reference values in children and adults with optimal health.

Furthermore, there is an urgent need for translational studies, involving systems biologists, exercise physiologists and clinical scientists that cover the interactions of the human body with environmental exposures on every level from genotype to phenotype including studies in omics, e.g. metabolomics or proteomics (14). This will foster the understanding of the molecular effects of PA and lead to higher effectiveness of exercise treatment.

Finally, the next generation of medical professionals needs to be educated about the outstanding importance of PA and CRF in cardiovascular prevention. Sports and exercise medicine deserves a stronger place in the curricula of Human Medicine studies and should be accepted as a medical profession equally to e. g. internal medicine or pediatrics (3).

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