

Sit Less or Exercise More?

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SUMMARY

In the last decades, our society has become increasingly more sedentary. The majority of the western population spends approximately half of the waking day sedentary, e.g. driving the car, doing office work and watching TV. In order to increase physical activity, the World Health Organization advises to perform 150 min/week of moderate-to-vigorous physical activity (MVPA). Despite its positive health benefits, adherence to the physical activity guidelines is low. Even for people adhering to these guidelines, there are about 15.5 waking h/day left that can be spent sitting. Epidemiological studies suggest that prolonged sitting is detrimental to health, independent of the time spent in MVPA. In addition to sitting and MVPA, the other part of our waking day is spent in light physical activity (LPA). However, in contrast to MVPA, little is known about LPA. Observational studies reported that increased time spent in LPA, like standing and light walking, has been associated with lower risk of cardiovascular disease and mortality. However, few intervention studies have been performed on the health effects of substituting sitting with LPA. Moreover, it was not known whether the health effects of prolonged sitting were independent of energy expenditure. Therefore in this dissertation, I compared the effects of substituting sitting with LPA (standing and slow pace walking) and MVPA (cycling on ergometer at 50-60% W_{\max}) on cardiovascular risk factors when estimated energy was comparable between LPA and MVPA. The studies described in this dissertation had a comparable design but the investigated population and/or the outcome measures differed between the studies. In all studies, the participants followed a Sit and a SitLess (LPA) regimen in a randomised order (chapters 2-4). In two of the three studies, the participants also followed an Exercise (MVPA) regimen (chapters 2 and 4). Each intervention lasted 4 days; physical activity (objectively measured with accelerometry), energy expenditure and diet were standardised during each intervention.

In **Chapter 2**, we investigated the effects of substituting sitting with LPA (standing and light walking) and MVPA (cycling) on biomarkers of glucose and lipid metabolism. In this study, we observed that substituting sitting with LPA improved plasma insulin and lipids (triglycerides, non-HDL cholesterol and apolipoprotein B) in healthy young subjects with normal weight. In contrast, this study showed that 1 hour of daily MVPA combined with a high sitting time did not significantly improve biomarkers of glucose and lipid metabolism compared to a sitting regimen. These results suggest that substituting sitting with standing and light walking is an effective approach to improve cardiovascular risk factors. In addition, these results suggest that the negative effects of prolonged sitting on glucose and lipid metabolism cannot be fully compensated by MVPA only.

In **Chapter 3**, we investigated the effects of substituting sitting with LPA in overweight/obese subjects on blood pressure, glucose, and lipid metabolism. In this study, we observed that substituting sitting with standing and light walking improved insulin sensitivity (Matsuda index), several biomarkers of lipid metabolism (triglycerides, free

fatty acids, HDL-cholesterol, non-HDL cholesterol and apolipoprotein B) and diastolic blood pressure. We also explored the effects of LPA on mood and cognition but only observed a small improvement in mood after the LPA intervention.

In **Chapter 4**, we investigated the effects of substituting sitting with LPA and MVPA in overweight/obese subjects with type 2 diabetes. Outcome measures included 24-hour glucose regulation (measured with continuous glucose monitoring), insulin sensitivity (HOMA2-IR) and biomarkers of lipid metabolism. Substituting sitting with LPA (standing and walking) for 4 days improved 24-hour glucose regulation and plasma lipids (triglycerides and free fatty acids) to a comparable degree as MVPA (cycling). Moreover, LPA improved insulin sensitivity more than MVPA. The results observed in this study are promising as many patients with type 2 diabetes have difficulties to perform MVPA.

In **Chapter 5**, we combined the results of the studies described in chapters 2-4 and compared the effects of LPA vs. MVPA on circulating biomarkers of endothelial function, insulin sensitivity and lipid metabolism. In line with the results previously described, we observed that LPA –but not MVPA- was effective in improving insulin sensitivity and biomarkers of lipid metabolism. Interestingly, however, MVPA –but not LPA- improved biomarkers of endothelial function. These data indicate that reducing sitting time with LPA and MVPA have differential effects on cardiovascular risk factors.

In **Chapter 6**, I discussed the main findings, methodological considerations and clinical implications of the studies presented in this dissertation by relating them to existing literature. The studies described in this dissertation investigated the effect of different activity strategies on cardiovascular risk factors. Strengths of my studies include the strict adherence to the activity regimens in free-living conditions, objective measurement of physical activity by accelerometry and standardisation of diet. Limitations of the studies include the estimation of energy expenditure and the short duration of the intervention studies. Future studies are needed to investigate underlying biological mechanisms and the feasibility and cardiovascular effects of light activities on the longer-term.

In conclusion, the results described in this dissertation suggest that the negative health effects of too much sitting cannot be compensated by structured exercise only. The results suggest that interrupting sitting regularly with light activities improves cardiovascular risk factors, independent of an increase in energy expenditure. Moreover, the results suggest that substituting sitting with light versus moderate-to-vigorous physical activity have different effects on cardiovascular and metabolic health. As a consequence, not only structured exercise but also reducing sitting time and substituting it with light activities seem also important to improve cardiometabolic health. In one short sentence: sit less and move more!