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The effects of standing exposure on venous and muscular stress parameters: influence of dynamic muscle activity in the lower extremities, age and gender, in healthy individuals

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Widmung

Für meine Familie.

List of content

1 List of abbreviations

Bioelectrical impedance	BI
Chronic venous insufficiency	CVI
Discomfort developer	DD
Low back discomfort	LBD
Low back pain	LBP
Measurement	M
Musculoskeletal disorders	MSD
Non-discomfort developer	NoDD
Non-pain developer	NPD
Pain developer	PD
Standard deviation	SD
Surface electromyography	SEMG
Transforming growth factor	TGF
Tumor necrosis factor	TNF
TNF (tumor necrosis factor) receptor associated factor	TRAF
Venous diseases	VD
Waterplethysmography	WP

2 Structure of the thesis

This doctoral thesis deals with the influence of prolonged standing on surrogate parameters for an increased risk of venous diseases and musculoskeletal disorders as well as possible influences of age and gender.

The dissertation is separated in three parts. The first part explains the theoretical background and the rationale of the thesis. Part two provides the three research papers, all of them are published in international peer-reviewed journals. The first publication deals with the reproducibility of used measuring methods. Papers two and three provide data on the influence of standing work on the above-mentioned surrogate parameters, including age and gender aspects. Prior to each scientific paper a brief summary and the scientific aims of the study are given.

The last part of this work includes a comprehensive discussion of the results of the scientific program papers with regard to the found literature.

3 Background

The first part of the dissertation provides the theoretical background and rationale of this thesis. It is structured in four chapters. The first chapter shows the prevalence of standing work in today's global economy. In the second chapter adverse health outcomes associated with prolonged standing work and possible pathophysiological pathways are described. Further, recommendations for standing work of federal agencies and researchers are discussed in chapter three. The last part deals with measurement techniques and measures that can be used as surrogate parameters for the risk evaluation of the adverse health outcomes of standing work.

3.1 Standing work

Standing for prolonged periods of time is required in many of today's workplaces. In an Australian survey 62% of the study population (n=4500) reported that they usually were exposed to standing in one place while working (Safe Work Australia, 2011). A study with a Canadian working population (n=9425) in Québec similarly showed that 58% of respondents reported usually standing at work (Tissot *et al.*, 2005). Similar numbers were shown in a German survey (Wittig *et al.*, 2013) and the fifth European working conditions survey (Parent-Thirion, A., G. Vermeylen, G. van Houten, M. Lyly-Yrjänäinen, I. Biletta and J. Cabrita., op. 2012). Additionally, a study in Denmark objectively measured (using accelerometers) standing, sitting and walking in blue collar workers and found that the average time spent in a static standing position was 2.2 (SD 1.3) hours with some occupational subgroups standing up to 3.7 (SD 0.7) hours per workday (Munch Nielsen *et al.*, 2017). Occupations requiring static standing over significant periods of time are found across professions including the food, healthcare, retail, service and manufacturing industries and are widespread throughout industrialized countries.

3.2 Adverse health outcomes associated with standing work

Epidemiological studies show several risks when investigating people required to stand for prolonged periods of time during their work. Standing workers were shown to have an increased risk for venous diseases (Tabatabaeifar *et al.*, 2015; Tüchsen *et al.*, 2000; Tüchsen *et al.*, 2005) and musculoskeletal disorders (Coenen *et al.*, 2016). Additionally, perinatal health complications such as preterm delivery are discussed to be associated with prolonged standing (Palmer *et al.*, 2013; van Beukering *et al.*, 2014).

In the following two chapters the prevalence, socioeconomic costs and possible pathophysiological pathways for VD and MSD as well as the association with standing are discussed.

3.2.1 Venous diseases

In the vein consult program epidemiological data on the prevalence of VD were investigated worldwide based on the CEAP classification (clinical, etiological, anatomic, pathophysiologic; from C0 to C6; (Eklöf *et al.*, 2004)) in over 90,000 subjects. The authors report a worldwide prevalence of 83.6% (including the less severe stages C1-C2), showing that VD are very common in the general population (Rabe *et al.*, 2012). The German Federal Statistical Office calculated the total costs for VD to be 2.17 billion € in 2015 (Statistisches Bundesamt, 2018) which almost haven't changed since 2005 (Rabe and Pannier, 2010).

To date, the origin of a primary varicosis is still unclear. Whether a venous valve insufficiency is leading to an increase in venous hypertension or vice versa as the initial cause of a beginning varicosis is unresolved (Pfisterer *et al.*, 2014). There are several factors contributing to the development of VD such as varicosis or chronic venous insufficiency (CVI). These risk factors include family history, obesity, previous pregnancy and reduced mobility at work (sitting or standing) (Carpentier *et al.*, 2004; Lacroix *et al.*, 2003; Robertson *et al.*, 2013; Ismail *et al.*, 2016). Additionally, age is one of the main risk factors for the development of varicose veins and CVI, as exposure to biomechanical stress (explained in detail in the next paragraph) of the venous system might accumulate during lifetime, leading to diagnosis of VD in a higher age (Robertson *et al.*, 2013; Carpentier *et*

al., 2004; Davies, 2019). However, the data on the effect of gender are not as conclusive. While some studies show no differences in the prevalence of VD between males and females (Robertson *et al.*, 2013; Evans *et al.*, 1999) or at least not for more severe stages of CVI (Rabe *et al.*, 2012), more recent studies suggest an increased risk of VD in women (Wrona *et al.*, 2015; Davies, 2019). This association is debated to occur due to hormonal influences during previous pregnancy, as no gender differences in VD prevalence were shown for men and women with no previous pregnancy (Bromen *et al.*, 2004; Ismail *et al.*, 2016).

There are two biomechanical risk factors in the progression and arguably the initiation of a primary varicosis connected to static standing. During static standing, the physiological reaction of the venous system to the initial blood pooling due to orthostatic pressure, is stretching of the venous walls (Stick *et al.*, 1985). If this situation is maintained over a prolonged period of time, a further increase in venous pressure (venous hypertension) leads to circumferential stress of the venous walls which is known to trigger pathophysiological remodelling processes (Segiet *et al.*, 2015; Serralheiro *et al.*, 2017; Mansilha and Sousa, 2018). Several studies showed that venous hypertension stimulates an endothelial activation and the expression of growth factors and adhesion molecules such as matrix metalloproteinases (Bergan, 2007; Woodside *et al.*, 2003; Mannello *et al.*, 2014; Yasim *et al.*, 2008). These mechanisms lead to an inflammatory response which changes the extracellular matrix of the venous walls and reduces their elasticity (Takase *et al.*, 2004; Woodside *et al.*, 2003; Mannello *et al.*, 2014; Saito *et al.*, 2001; Aravind *et al.*, 2010; MacColl and Khalil, 2015). The possibility that these remodelling processes of the venous walls can be triggered only by inducing prolonged venous pressure was shown in a mouse model (Feldner *et al.*, 2011). Feldner et al. also found an increase in matrix metalloproteinases in their histological analysis which can be seen in humans with existing varicose veins (Saito *et al.*, 2001).

The second biomechanical risk factor is connected to a decrease in haemodynamics during static standing. Usually, blood flow produces shear stress between the intima (inner layer of the venous wall) and the circulating blood. This shear stress was shown to initiate the release of nitric oxide which has an anti-

inflammatory effect by reacting with reactive oxygen species (Pfisterer *et al.*, 2014). Further, shear stress induces specific protein (TRAF-3) and transforming growth factor (TGF-beta1) production. TRAF-3 is inhibiting pro-inflammatory mechanisms whereas TGF-beta1 is further contributing to matrix accumulation in the venous walls (Urbich *et al.*, 2001; O'Callaghan and Williams, 2000). Without this physiological shear stress, it is believed that inflammatory responses are further contributing to venous wall remodelling including fibrosis, thickening of the venous wall and atrophy of elastic fibres which makes veins susceptible to varicosis (Pfisterer *et al.*, 2014; Mansilha and Sousa, 2018; Serralheiro *et al.*, 2017). Both described biomechanical risk factors are prevalent in prolonged static standing and can be considered as a major contributing factor in the development of VD regarding the underlying evidence.

3.2.2 Musculoskeletal complaints

According to several German health insurances, musculoskeletal diseases were the second most frequent reason for incapacity to work with about 15 to 16.4 cases per 100 insured persons in one year (Grobe *et al.*, 2018; Marschall *et al.*, 2017). In Germany the total costs for all musculoskeletal diseases combined were the second highest after mental diseases in 2015 with 34.2 billion €, and 4.5 billion € for back pain alone according to the German Federal Statistical Office (Statistisches Bundesamt, 2018).

Although being a major epidemic in the general population with a one year prevalence up to 65% (March *et al.*, 2014; Walker, 2000) and a lifetime prevalence up to 84% (Balagué *et al.*, 2012), people working in standing occupations are even more likely to suffer from low back pain/ low back discomfort (LBP/ LBD) (Coenen *et al.*, 2016; da Costa and Vieira, 2010; McCulloch, 2002). Other occupational contributing factors associated with LBP are lifting, pushing, pulling, constraint postures and repetitive manual work (da Costa and Vieira, 2010; Griffith *et al.*, 2012; Lötters *et al.*, 2003), besides psychosocial factors like high job demands and low social support (da Costa and Vieira, 2010; Lang *et al.*, 2012). Further, epidemiological data suggests a higher risk of LBP among older adults (Wong *et al.*, 2017; Dionne *et al.*, 2006) who additionally show longer duration of sick leave

compared to a younger demographic (Leboeuf-Yde *et al.*, 2011). Moreover, females tend to have a higher prevalence of acute and chronic back related pain compared to men (Palacios-Ceña *et al.*, 2015; Stewart Williams *et al.*, 2015; Wong *et al.*, 2017).

Several laboratory studies show that healthy, previously asymptomatic persons, develop acute transient LBP/ LBD in two-hour static standing periods at a rate between 32% and 70%. These persons are mostly described as pain or discomfort developers (PD/ DD) (Aghazadeh *et al.*, 2015; Bussey *et al.*, 2016; Nelson-Wong *et al.*, 2008; Nelson-Wong and Callaghan, 2010a; Gallagher *et al.*, 2011).

Several mechanisms for the association of LBP/ LBD and prolonged standing are discussed. Some studies suggest an influence of fatigue in the back musculature (Antle and Côté, 2013; Balasubramanian *et al.*, 2009) or constraint static posture and a lack of variation in movement that could protect from fatigue (Balasubramanian *et al.*, 2009; Gallagher *et al.*, 2011; Gregory and Callaghan, 2008). Coenen et al. summarized additional possible mechanisms for PD/ DD in their review paper. The authors categorized possible LBP/ LBD development mechanisms during standing with four different options, namely: muscle, postural, loading and blood flow (Coenen *et al.*, 2017). Concerning the muscle category, an increase in co-contraction of the left and right gluteus medius and of the trunk muscles was found in the PD group, in comparison to the non-pain developer group (NPD) (Aghazadeh *et al.*, 2015; Bussey *et al.*, 2016; Nelson-Wong *et al.*, 2008). No such relationships were found in other studies (Marshall *et al.*, 2011; Aghazadeh *et al.*, 2015). Equally inconclusive are findings of increased trunk muscle activity (Hansen *et al.*, 1998), reduced gluteus medius muscle strength and endurance (Marshall *et al.*, 2011) and smaller hip range of motion (Bussey *et al.*, 2016) with opposite findings in other studies (muscle activity: (Gregory and Callaghan, 2008); strength and endurance: (Bussey *et al.*, 2016) range of motion: (Raftry and Marshall, 2012)). Further, some authors suggest an increase in body sway (Antle and Côté, 2013), lumbar flexion (Gregory and Callaghan, 2008; Gallagher and Callaghan, 2016) and more spinal axial rotation (Gregory and Callaghan, 2008) during prolonged standing in PD, whereas two studies found no differences in body sway (Gallagher and Callaghan, 2015; Madeleine *et al.*, 1998). Finally, it was

suggested that there might be some postural changes like a decrease in body weight shifting (Gallagher *et al.*, 2011) and an increase in spinal loading during standing (Gregory and Callaghan, 2008). Concerning the aforementioned blood flow category, no study could be found that showed an association with LBP (Coenen *et al.*, 2017). In summary, the mechanisms contributing to the development of transient LBP/ LBD in healthy people during prolonged standing are unclear and seem to be multifactorial or individual.

Another body region that is associated with detrimental effects after prolonged occupational standing, are the lower extremities. Especially, complaints of the feet and lower legs are often evident (McCulloch, 2002; Pensri *et al.*, 2009; Chee *et al.*, 2004; Graf, 2015). The underlying mechanisms that are discussed in the literature are partly similar to those of the lower back region. It was suggested that fatigue in the calf muscle may contribute to discomfort (Garcia *et al.*, 2016; Garcia *et al.*, 2015; Wiggermann and Keyserling, 2013; Halim *et al.*, 2012; Madeleine *et al.*, 1998). It is also mentioned that an increase in lower leg volume through orthostatic pressure and the lack of muscle-venous pump function (Chester *et al.*, 2002; Karimi *et al.*, 2016; Garcia *et al.*, 2018) is putting stress on passive structures, causing lower leg symptoms (Coenen *et al.*, 2017; Friden *et al.*, 1986).

From a physiological perspective, both lower back and lower leg symptoms could arise due to a restricted freedom of movement combined with a continuous static, low-level muscle activity, using primarily type I muscle fibres. A resulting decrease in blood flow can lead to a metabolic overload with pain or discomfort symptoms. This process was previously shown to elicit fatigue in the upper extremities and is known as the ‘Cinderella Hypothesis’ (Hägg, 1991; Zennaro *et al.*, 2003; Visser and van Dieën, 2006).

3.2.3 Interventions against detrimental effects of standing work

Previously investigated interventions include a variety of approaches. To counteract musculoskeletal complaints of the lower extremities, studies tested different flooring conditions (e.g. so called ‘anti-fatigue’ mats) and shoe insoles. The systematic review of Speed et al. found moderate evidence for the reduction of subjective ratings of discomfort with slightly better outcomes for the shoe insoles

(Speed *et al.*, 2018). Several studies showed that sloped surfaces can reduce lower back discomfort, probably through changes in hip and lumbar posture (Nelson-Wong and Callaghan, 2010b; Gallagher *et al.*, 2013; Fewster *et al.*, 2017; Gallagher and Callaghan, 2016). Seated breaks to reduce LBP were only effective in short term (Gallagher *et al.*, 2014). If the 'Cinderella Hypothesis' is true for the development of complaints in the lower back and lower legs, bouts of increased muscle activity could counteract the fatiguing process of continuous low-level activation. Studies comparing stationary standing with walking bouts in between stationary standing showed positive effects on subjective ratings of discomfort and lower leg and lower back fatigue of the dynamic working situation (Balasubramanian *et al.*, 2008; Balasubramanian *et al.*, 2009).

A very common intervention to prevent lower leg swelling, are compression stockings. They have shown to be effective, even with rather low exerted pressure (Partsch *et al.*, 2004; Mosti and Partsch, 2013; Krijnen *et al.*, 1997; Steinhilber *et al.*, 2017) and a synergistic effect with continuous walking (Ema Quilici Belczak *et al.*, 2012). Despite the positive effects, stockings are fighting with compliance and adherence problems mainly because of low comfort (Kankam *et al.*, 2018; Allegra *et al.*, 2014). Moreover, dynamic movement alone was shown to prevent lower leg swelling through activating the muscle-venous pump either through stationary leg movements like knee bending (Uda *et al.*, 1997; Stick *et al.*, 1989) or by continuous cycling (Stick *et al.*, 1989).

In both MSD and VD, increasing movement (e.g. by walking bouts) seems to be a promising approach to counteract pathophysiological mechanisms without a need for further aids (like compression stockings or floor mats etc.).

3.2.3.1 Summary of Chapter 1.1 and 1.2

Standing is required in plenty of today's workplaces across professions and industries. Prolonged static standing is associated with VD and MSD of the lower back and lower extremities, resulting in substantial socio-economic costs. Continuous circumferential stress of the venous wall (increased venous pressure) and decreased blood flow, resulting from static standing, facilitate pathophysiological mechanisms which lead to pro-inflammatory responses. The result of

these mechanisms is venous wall remodelling with fibrosis, thickening of the venous walls and atrophy of elastic fibres, making veins susceptible to varicosis. The mechanisms behind LBP/ LBD and lower extremity complaints are not fully understood, yet. Most hypothesis assume that continuous static posture is playing a major role. In this regard, the 'Cinderella Hypothesis' might be a reasonable explanation for fatigue of type I muscle fibres through prolonged low-level activation, leading to a metabolic overload and thus pain or discomfort. Promising interventions to reduce discomfort are a soft underground (cushioned shoe insoles), sloped surfaces, seated breaks (only short term) and increased movement. In order to reduce objective risks like e.g. oedema, compression stockings and activation of muscles and the muscle-venous pump by e.g. walking, seem to be effective.

3.3 Recommendations for standing work

Federal agencies that take care of worker safety and health regard standing work as problematic and therefore give advice on workplace design. In Germany for example, the Commission for Occupational Safety and Safety Engineering of the Federal States (LASI) recommends a ratio for standing vs. sitting/ walking of 1:2 or a distribution of 60% sitting, 30% standing and 10% walking during a regular working shift (Berger *et al.*, 2009). Further, it is suggesting four different risk areas:

- 1: up to 2.5 hours → low standing load/ stress
- 2: 2.5 – 4 hours → increased standing load/ stress
- 3: 4 – 5.5 hours → significantly increased standing load/ stress
- 4: more than 5.5 hours → high standing load/ stress

However, when looking at the citations given in the LASI guideline, only a reference to the Swiss National Accident Insurance Fund (SUVA) recommendation can be found, which also states that the 60% sitting, 30% standing and 10% walking distribution is optimal (Suva, 2014). Likewise, other federal institutions have made recommendations like job enrichment, job rotation and seated breaks (Dicke, 2008; DOSH, 2002; CCOHS, 2018). Unfortunately, neither of those institutions are providing any evidence or literature to back up their very specific claims. Their suggestions are therefore most probably based on expert opinion, at best.

There are scientific approaches for recommendations of the design of standing work. Joy Ebben tried to give suggestions based on findings of mostly laboratory studies in a paper from 2003. Frequent and sufficient rest breaks in sitting or lying position, changes in posture, encouraging walking, proper footwear and footrests were recommendations resulting from a rather low number of studies (Ebben, 2003). Halim and Omar developed a prolonged standing strain index based on a review of scientific and professional literature as well as expert opinions. This index defines ≤1 hour of static standing as safe, >1 hour of static standing as slightly unsafe, and >1 hour static standing combined with >4 hours total standing time per day as unsafe (Halim and Omar, 2012). Again, the basis for these

recommendations is quite unclear because no dose-response relationships were investigated in the systematic review. Finally, a very recent review of laboratory studies by Coenen et al. investigated the time when the threshold for clinically relevant (9 mm on a 100 mm visual analogue scale; (Kelly, 1998)) increases in low back pain intensity was reached. They found that after 42 min of continuous standing, a clinically relevant pain intensity was exceeded and thus standing time should not last over 40 min in order to prevent LBP from developing (Coenen *et al.*, 2017). Because of limited data available, no such threshold was calculated for lower extremity pain.

Based on the given evidence, it is difficult to give substantial advise for the design of standing work. Interpretations of the underlying pathophysiological mechanisms seem to be the best approach available to date, without knowing the exact effects or dose-response relationships.

3.3.1.1 Summary of chapter 1.3

Recommendations and guidelines from federal work safety and health institutions are based on low evidence (expert rating at best). More scientific approaches recommend sufficient rest breaks, posture changes, encouraging walking, proper footwear and footrests, and define >1 h static standing combined with >4 h total standing time per day as unsafe, based on low to medium evidence from a small number of studies. Another review calculated that static standing over about 40 min should be avoided to prevent LBP/ LBD development, based on laboratory studies. In order to give substantial advise for workplace design, more evidence is needed.

3.4 Measurement techniques and surrogate parameters

In order to evaluate risks of developing VD and MSD, it is necessary to find valid and reliable surrogate parameters, because direct measurements of, for example VD progression in healthy people, would need years or decades of observation in an occupational setting. Regarding the described (see Chapter 1.2) pathophysiological mechanisms present in the development of VD, lower leg oedema seems to be a valid surrogate parameter to make assertions about venous wall stretching and reduced blood flow (Kanai *et al.*, 1987; Tomei *et al.*, 1999). The gold standard in lower leg volume measurement is still regarded to be waterplethysmography (WP) (Petersen *et al.*, 1999; Henschke *et al.*, 2006). It is based on the Archimedean principle of water displacement and has been used widely before (Belczak *et al.*, 2009; Brijker *et al.*, 2000; Rabe *et al.*, 2010). The disadvantages of WP are that it is very time consuming and susceptible to errors like water splashing due to leg movement of subjects e.g. (Rabe *et al.*, 2010). Good standardization of the procedure and subject placement is essential to ensure good reliability (Rabe *et al.*, 2010; Petersen *et al.*, 1999). A faster method of measuring lower leg oedema is bioelectrical impedance (BI). This technique uses a four electrode setup to measure changes in water distribution in human limbs indirectly (Kanai *et al.*, 1983; Kanai *et al.*, 1988; Kanai *et al.*, 1987; Seo *et al.*, 1995; Seo *et al.*, 2001). Two stimulation electrodes are used to apply a constant low intensity electrical current into the lower leg. Another two measuring electrodes capture the resulting voltage in the stimulated area. If an orthostatic oedema occurs, the impedance in the tissue decreases as well as the measured voltage (Kanai *et al.*, 1983). BI only gives information in relative terms but can be measured within a couple of seconds and therefore shows the progression of an oedema.

MSD can be measured subjectively via numeric rating scales which are very common in studies for occupational health. Usually subjects are asked to rate their level of discomfort or pain on a scale from 0= no pain/ discomfort to 10= highest imaginable pain/ discomfort (Wiggermann and Keyserling, 2013; Cham and Redfern, 2001). Alternatively, subjects are asked to draw a line on a 0 mm to 100 mm

visual analog scale with the same defined endpoints (Nelson-Wong and Callaghan, 2010a; Marshall *et al.*, 2011).

Finally, muscle activity measurements with surface electromyography (SEMG) can be used to estimate whether continuous low-level activity is present during static standing in the muscles susceptible to discomfort and pain (Visser and van Dieën, 2006; Zennaro *et al.*, 2003). Additionally, a gravimetrical position sensor can measure three dimensional movements of PD/ DD and NPD/ NoDD subjects in the lower back region, gaining information about movement patterns and possible mechanisms in the development of LBP/ LBD (Balasubramanian *et al.*, 2009; Gallagher *et al.*, 2011; Gregory and Callaghan, 2008). This would allow to verify or dismiss the model of fatigue of type I muscle fibres and metabolic overload, being a possible explanation for the development of complaints in the lower leg and lower back region.

3.5 Research questions

This doctoral thesis deals with the following general research questions:

- How does multiple hours of static standing effect surrogate parameters of venous diseases of the lower extremities in healthy individuals?
- How does multiple hours of static standing effect surrogate parameters of musculoskeletal disorders of the lower back and lower extremities in healthy individuals?
- Does low pace walking influence surrogate parameters of musculoskeletal disorders and venous diseases in healthy individuals?
- Does age and gender have an influence on investigated parameters?

In order to answer these general research questions a first study was conducted to investigate some of the used measurement techniques with the following research question published in the first paper:

- Is intra- and inter- rater reliability for the waterplethysmography and bioelectrical impedance measurements sufficient to investigate possible changes in lower leg oedema during static standing?

Answering these research questions may increase the knowledge about prevention measures for standing workplace design to reduce musculoskeletal and venous risk factors and to create a basis for further studies.

All measurements were conducted after the approval of the ethics committee of the Faculty of Medicine of the University Hospital Tübingen (project number: 591/2014BO1).

4 Scientific program – research paper

The second chapter deals with the cumulative research of the three research papers. The first one refers to the used measurements and their reproducibility. In the second and third paper the influence of prolonged standing on used surrogate parameters is investigated. Table 1 shows a general overview of these papers and the author's contribution. All the research papers are consistent with the version accepted by the corresponding journal.

Table 1: Research papers that are included into the scientific program

Authors	Year	Status	Journal	Author's contribution
Wall R, Lips O, Seibt R, Rieger M A, Steinhilber B	2017	Published	Physiological Measurement (Impact Factor 2017: 2.006)	• Development of the study design (in cooperation with co-authors) • Data acquisition and data analysis • Preparation of the manuscript
Wall R, Läubli T, Seibt R, Rieger M A, Steinhilber B	2019	Published	International Journal of Industrial Ergonomics (Impact Factor 2018: 1.571)	• Development of the study design (in cooperation with co-authors) • Data acquisition and data analysis • Preparation of the manuscript
Wall R, Garcia M, Läubli T, Seibt R, Martin B, Rieger M A, Steinhilber B	2020	Published	Ergonomics (Impact Factor 2018: 2.181)	• Development of the study design (in cooperation with co-authors) • Data acquisition and data analysis • Preparation of the manuscript

4.1 Research paper 1: Reproducibility of lower leg waterplethysmography and bioelectrical impedance measurements

Waterplethysmography is regarded as the gold standard of volumetry (Petersen *et al.*, 1999; Henschke *et al.*, 2006). A self-made device for WP measurement was built for the planned studies on prolonged standing. Furthermore, BI measurement was conducted with a self-developed setup. In order to interpret results of upcoming studies, reproducibility must be assured for WP and BI.

Therefore, the first study investigated intra- and inter-rater reliability of WP and BI measurements comparing the standard errors of measurement of two separate investigators in a test-retest design.

The aims of study 1, relevant to this dissertation were:

- To investigate the inter-rater reliability of two separate raters, measuring waterplethysmography and bioelectrical impedance on the lower leg.
- To investigate the intra-rater reliability for each rater, measuring waterplethysmography and bioelectrical impedance of the lower leg.

Wall, R., Lips, O., Seibt, R., Rieger, M. and Steinhilber, B. (2017), “Intra- and inter-rater reliability of lower leg waterplethysmography, bioelectrical impedance and muscle twitch force for the use in standing work evaluation”, *Physiological Measurement,* Vol. 38 No. 5, pp. 701-714.

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Intra- and inter-rater reliability of lower leg waterplethysmography, bioelectrical impedance and muscle twitch force for the use in standing work evaluation

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Abstract

Objectives. Prolonged standing is associated with multiple risk factors for musculoskeletal and venous disorders. In Germany over 50% of the working population spend most of their working time in a standing position. Basic understanding of prolonged standing physiology is lacking. We therefore plan to investigate the influence of 5 h standing (including breaks) on lower limb oedema measured by waterplethysmography (WP) and bioelectrical impedance (BI) and fatigue in the triceps surae muscle using muscle twitch force (MTF). In order to interpret our results, test-retest and inter-rater reliability of these measurement methods was evaluated first. *Approach.* 20 subjects (9 female) were included to test each method three times (M1, M2, M3) in 30 min periods with two raters (R1, R2) on separate days. Intraclass correlation coefficient (ICC; 2,1), standard error of measurement (SEM) and smallest real difference (SRD) were calculated for both raters. *Main results.* The SEM and SRD calculated for WP were 27 and 75 ml, respectively, for R1 and 23 and 64 ml, respectively, for R2 with an ICC of 0.98 ($p < 0.0001$). Statistically significant mean differences between M1 and M2 (R1 = 23 ml, $p = 0.004$; R2 = 19 ml, $p = 0.027$) but not significant mean differences between M2 and M3 (R1 = −6 ml, $p = 0.45$; R2 = 4 ml, $p = 0.27$) were calculated for both raters. BI data revealed SEM and SRD values of 3.8 and 10.5 Ω, respectively, for R1 and 3.4 and 9.4 Ω, respectively, for R2 with an ICC of 0.24 ($p = 0.001$). The differences between M1 and M2 (R1 = 3.9 Ω, $p = 0.0001$; R2 = 2.4 Ω, $p = 0.049$) and between M2 and M3 (R1 = 2.3 Ω, $p = 0.012$; R2 = 2.0 Ω, $p = 0.008$) were found to be statistically significant for both raters. SEM and SRD for MTF were 0.19 and 0.53 N, respectively, for

R1 and 0.23 and 0.64 N, respectively, for R2 with an ICC of 0.71 ($p < 0.0001$). Mean differences between M1 and M2 were statistically significant for rater 1 but not for rater 2 (R1 = 0.13 N, $p = 0.022$; R2 = 0.12 N, $p = 0.082$) and the same was found for the difference between M2 and M3 for both raters (R1 = 0.04 N, $p = 0.37$; R2 = 0.08 N, $p = 0.12$). *Significance.* All three measurement methods showed good reliability and should be suitable for detecting effects of standing work on oedema development and fatigue as seen in previous results of long term standing experiments. Inter-rater reliability is found to be satisfactory as well, demonstrated by the small differences in SEM values of R1 and R2. Statistically significant differences shown for all three measurement methods could be due to lacking standardisation of leg placement and thus an actual lower leg volume change between measurements, indicating possibilities for further improvement of SEM values.

Keywords: waterplethysmography, bioelectrical impedance, muscle twitch force, reliability, standing work, lower leg

(Some figures may appear in colour only in the online journal)

Introduction

Prolonged standing is associated with multiple musculoskeletal disorders (MSDs) of the lower limbs and lower back region (Andersen *et al* 2007, Pensri *et al* 2009, Werner *et al* 2010) as well as venous diseases like varicosis or chronic venous insufficiency (Tüchsen *et al* 2000, Bahk *et al* 2012). Thus, work-related exposure to standing has been found to increase the risk for developing these disorders (McCulloch 2002). Studies have shown that even short time exposure to static standing can induce muscle fatigue and lower leg swelling, which are discussed as being indicators of an increased risk for MSDs and venous disorders (Atsumi *et al* 1987, Ganasegeran *et al* 2014, Ringheim *et al* 2015). A survey by the German Federal Institute for Occupational Safety and Health (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin—BAuA) underlines the high prevalence of standing work in Germany. 54.7% of employees surveyed indicated that they often work in a standing position (Wittig *et al* 2013). In addition, international publications on prevalence of standing work show similar results for their respective labour forces (Krijnen *et al* 1997, Tissot *et al* 2005).

As already mentioned, muscle fatigue and lower leg swelling are regarded as important surrogate parameters of an increased risk for MSDs and venous disorders during standing work. In previous studies addressing health risks due to occupational standing, multiple methods to measure muscle fatigue and lower leg swelling were used (Tomei *et al* 1999, Andersen *et al* 2007).

Swelling—lower leg volume

Waterplethysmography (WP) is a method to measure lower leg volume (LLV) by water displacement. It is regarded as the gold standard of volumetry (Petersen *et al* 1999, Henschke *et al* 2006). Measurement error has been reported to be between 0.1 and 1.0% depending on experimental setup and execution (Rabe *et al* 2010). The water tank used for the present research covers a large part of the lower leg (more than 40 cm from plantar), increasing the amount of displaced water compared to setups described in previous studies (Rabe *et al* 2010), therefore possibly increasing measurement error. The disadvantages of this procedure

include the time consuming steps of filling the tank with water, placing the subject's leg into the tank, draining the water and then refilling the tank again, making it challenging to use in a field setting.

Bioelectrical impedance (BI) measurement can also be used as a method for evaluating volume changes in human limbs (Kanai *et al* 1983, Seo *et al* 1995, Seo *et al* 2001). It is an indirect approach whereby a low intensity constant electrical current is applied to a subject's limb, and surface electrodes measure the resulting voltage. This can be used as a relative estimate for changes in liquid distribution, which are related to a change in limb volume (Kanai *et al* 1983, Kanai *et al* 1988). A reduction of BI (lower voltage compared to baseline) corresponds to an increase of LLV and vice versa. At measuring frequencies below 1 kHz, current flows mainly through extra-cellular fluid due to the high impedance of cell membranes according to the Cole model (Cole 1972, Kanai *et al* 1987, Jaffrin and Morel 2008). This method has a significant time advantage compared to WP and may therefore be used as an alternative if reliability can be assured.

Muscle fatigue

Muscle twitch force (MTF) is a method to elucidate muscle fatigue induced by prolonged low level muscle exertion (Søgaard *et al* 2003, Blangsted *et al* 2005, Johnson *et al* 2013). Through electrical stimulation at low frequencies, (<20 Hz) muscle contractions are provoked leading to joint movement. Resulting force is measured by a force transducer and used as an estimate for muscle fatigue status. A decrease in twitch force is regarded as an indication for muscle fatigue (Adamo *et al* 2002, Adamo *et al* 2009, Kim and Johnson 2014).

The aim of the present study was to investigate the intraday test-retest reliability and the inter-rater reliability of two methods to quantify changes in lower leg volume as an indication of lower leg swelling (WP and BI) and one method to determine the amount of muscle fatigue (MTF). Knowledge about test–retest and inter-rater reliability is crucial for the selection of suitable methods and for the interpretation of changes in lower leg oedema and/or muscle fatigue caused by working in a standing position.

Methods

Subjects

20 healthy subjects (9 women and 11 men, age: 26.6 ± 7.1 years; height: 174.9 ± 8.8 cm; weight: 68.2 ± 11.6 kg) were recruited to participate in the present study. Exclusion criteria were severe venous diseases, age under 18 or over 67, and medication including diuretics, venotonics, vasodilators or antihypertensive drugs. The study was approved by the local ethics committee of the Medical Faculty, University of Tuebingen. All subjects signed informed consent prior to investigations and received financial compensation for their participation.

Raters

Both raters were experienced in conducting all three measurement procedures. Prior to this study rater 1 and rater 2 had carried out more than 50–100 measurement procedures within the past 9 months for WP, BI and MTF.

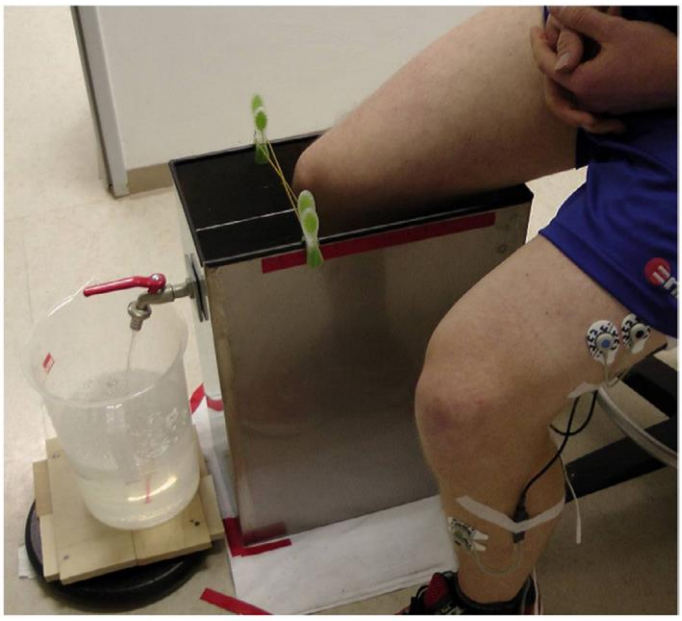

Figure 1. Experimental setup of waterplethysmography measure.

Measurement procedures

Lower leg volume.

Waterplethysmography. For WP measurement, a water tank of 50 cm height (water tap at 40 cm), 19 cm width and 36 cm length was used. An overflow valve (water tap 1/2-inch diameter) was installed at the height of 40 cm to purge the water displaced by the leg. Before the measurement was conducted, the tank was filled above level of the closed overflow valve with regular tap water (temperature: 25–30 °C). Then the valve was opened until the water level dropped down to the level of the outlet. The valve was closed when less than 1 drop per 10 s flowed out of it. In order to lower the water surface tension, which could impair water flow from the tank, a few drops of a detergent (surfactants) were added. Then the subject's lower leg was inserted into the tank carefully. Two scales, one on the bottom of the tank and a second one with an adjustable rubber band to monitor the subject's knee position at the upper side of the tank, were used to individually standardize and document an upright position of subject's lower leg (see figure 1). Subjects were advised to keep contact with the bottom of the tank with the entire sole of their foot without putting load on it and to keep contact to the rubber band with their knee. Chair position and height were set individually to avoid any contact of the thigh with the edge of the tank and were not changed between successive measurements. Then, after water surface has calmed, the overflow valve was opened and the displaced water was collected for exactly 5 min. During this time subjects were requested to avoid any kind of movement. Volume was quantified by weighing the amount of displaced water (measurement error ± 1.5 g approx.) with the assumption of 1 g corresponding to 1 ml of volume.

Impedance. Bioelectrical impedance measurements were conducted with a four electrode setup. Two electrodes (4×4 cm adhesive electrodes, Axion GmbH) were placed on the triceps surae muscle, one at the Achilles tendon distal of the muscle belly and the other at the proximal end of the medial caput of gastrocnemius muscle. Another pair of electrodes with an active area of 15 mm diameter (Covidien™, Kendall™ ECG electrodes H93SG, distance

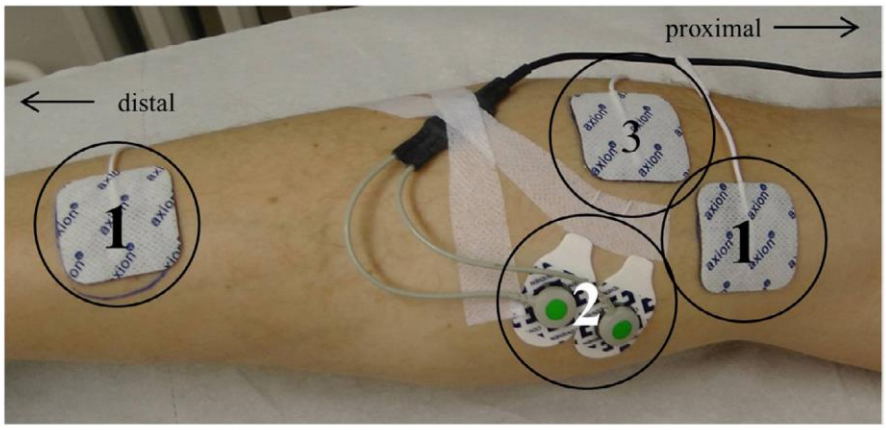

Figure 2. Electrode setup of Impedance measure on lower leg. (1) Stimulation electrodes, (2) measuring electrodes, (3) additional stimulation electrode for muscle twitch force measure.

between electrodes: 25 mm) was placed in direction of muscle fibres on the centre of the medial caput of gastrocnemius muscle belly (as recommended by SENIAM for the use in surface electromyography measurements, Hermens (1999)) in between the stimulation electrodes (see figure 2). A constant current square pulse (300 μA) with 1 ms duration and a repetition frequency of 13 Hz was applied for 20 s through the stimulation electrodes (Train/Delay Generator DG2A, square pulse; Constant Current Stimulator DS7A, Digitimer Ltd, England). Prior to electrode placement the skin was prepared with abrasive paste (Nupreb, Weaver and Company) to improve stimulation and measuring signal. Voltage was measured over a bandwidth of 4 to 650 Hz (PS11, THUMEDI GmbH & Co. KG, Germany, sampling rate 2048 Hz, high pass @ 4 Hz| − 3 dB|4th order, low pass @ 650 Hz| − 3 dB|11th order, passband ripple below 0.25 dB @ 20–500 Hz, noise below 0.6 μV rms, CMMR $>$ 100 dB). Measurement uncertainty of the device is below 1% of the measured voltage. During measurement, participants were seated comfortably in an armchair in a relaxed position. The chair was adjusted to ensure a leg position of 120° knee angle and 90° ankle angle (see figure 3). Subjects were asked to relax and to avoid any movement during the measurement procedure to reduce noise and electrical signals by muscle activity.

Previously conducted test measurements showed 370–372 Hz to be the frequency band with least variation compared to nine other tested bands from 12 to 650 Hz and was therefore chosen for the present study.

Data was processed with custom-made software (THUMEDI GmbH & Co. KG, Thum, Germany). First, raw data was transformed from time to frequency domain using Fast Fourier Transformation (FFT) after applying a rectangular window with a size of 2048 samples—which results in a frequency resolution of 1 Hz. Finally, voltage was calculated for a specific frequency band (370–372 Hz) using root mean squares to determine lower leg Impedance. Since the current as well as the shape of the pulses were constant, the measured frequency-specific voltages were only influenced by the impedance and are always in a strict linear relation to it. Thus, measured voltage can be used as an estimate to determine lower leg liquid distribution changes (oedema increase or decrease). Impedance was finally calculated by dividing the effective value of the voltage in the Range of 370–372 Hz by the effective value of the applied constant current. Considering the currents pulse shape, pulse duration, amplitude and repetition rate the effective current in the Range of 370–372 Hz is 0.465 μA (rms).

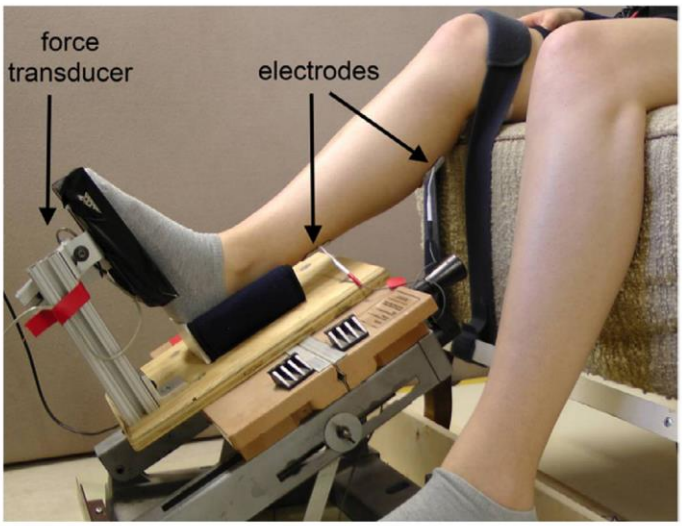

Figure 3. Experimental setup for measuring muscle twitch force of the triceps surae muscle. Subject positioning was the same during muscle twitch force and Impedance measurement.

Muscle twitch force. MTF was measured by electrically stimulating the triceps surae muscle every 500 ms using a rectangular pulse of 1 ms duration and a constant current limited to 30 mA individually adjusted for each participant. The location of stimulation electrodes was first gauged by palpation and then by determination of the area corresponding to the maximum tolerable discomfort induced by stimulation yielding the maximum twitch force. Stimulation intensity was selected individually for each subject and remained constant for the three measurements. The resulting plantar flexion force (twitch force) was measured at the bottom of the forefoot using a custom-made device with a force transducer (strain gauge). Twitch forces were sampled at 1000 Hz and collected using custom software based on LabVIEW (National Instruments Corp., USA).

The means of three series of 30 twitches with a coefficient of variation under 3% after potentiation were used as MTF values (Garcia *et al* 2015). MTF measurement took about 3–4 min in total.

Subject positioning was the same as during BI measurement with the exception of fixating the leg with a strap to avoid upward movement generated by stimulation.

Procedure. All described measurements were recorded successively during three measurement periods by one of two different raters (R1 and R2). The measurements were repeated on a second experimental day (not more than 4 weeks apart from day one) by the other rater. Randomization ensured that 10 subjects were first investigated by R1 and consequently the other 10 subjects were first investigated by R2. Further, the subjects' leg for WP was randomized (but was the same on both days), and then BI and MTF measurements were conducted on the other leg due to electrode placement.

Each experimental day started with the assessment of WP. After the first measurement the tank was refilled and the valve was opened to prepare for the second measurement. Meanwhile, subjects remained seated as pictured in figure 3. After attaching electrodes, testing signals and adjusting for sufficient stimulation intensity, BI and MTF were conducted consecutively. The next WP measurement followed approximately 30 min after WP 1. Directly after WP 2 and during tank preparation for WP 3, BI 2 and MTF 2 followed. Another 30 min after WP 2, the

third and last round of measurements was conducted. On a second day, the same subjects were assessed by the other rater at the same time of day (±1 h). R1 and R2 each tested ten people on day one and day two. Subject positioning, electrode placement and MTF intensity were carried out by R1 and R2 separately.

Statistical analyses. Alpha level to determine statistical significance was set to 0.05. Results were analysed using JMP 11 (SAS Inc. Cary, NC, USA) and SPSS Version 21 (IBM SPSS Inc., Chicago, IL, USA). Heteroscedasticity and systematic bias were inspected visually using Bland–Altman plots, which include the differences of consecutive measurements plotted against their mean absolute values (Bland and Altman 1999). Furthermore, a dependent *t*-test was conducted to control for systematic bias (statistically significant differences) between M1 and M2 as well as M2 and M3 separately.

A one way analysis of variance (ANOVA) with the factor subject was calculated to describe within-subject standard deviation by residual mean square, which is also known as standard error of measurement (SEM) (Bland and Altman 1999). Some researchers describe this as 'the most important type of reliability measure […] because it affects the precision of estimates of change in the variable of an experimental study' (Hopkins 2000). The SEM value multiplied by 2.77 is called the repeatability coefficient, also known as smallest real difference (SRD), which describes the individual difference upon retesting and can therefore serve as a cut-off for change with 95% confidence. The inter-rater reliability was calculated using the intra-class correlation coefficient (ICC 2,1; two way random, single measures, Weir 2005) and the confidence intervals (CI), and by comparing SEM values. Datasets of R1 and R2 were tested for normal distribution using the Shapiro–Wilk-Test and additionally rated by histograms.

Results

Subjects

All subjects completed the entire procedure with both raters. All data from WP and MTF were available for data analysis. BI data showed some extreme values so that data from two subjects measured by R2 had to be excluded from data analysis. In another three subjects, BI data were not plausible for one of the three measurements. Table 1 shows the means (MN) and standard deviations (SD) of the three measurements by rater one and two for WP, MTF, and BI.

Waterplethysmography

WP results showed normal distribution for all data. Visual control of Bland–Altman plots showed homoscedastic distribution in each of the test–retest differences. Mean differences were statistically significant for both raters between M1 and M2 (R1 = 23 ml, $p = 0.004$; R2 = 19 ml, $p = 0.027$) but not significant between M2 and M3 (R1 = −6 ml, $p = 0.45$; R2 = 4 ml, $p = 0.27$) (see figures 4(a) and (b) for rater 1). SEM and SRD values for R1 were 27 and 75 ml, respectively, and for R2 23 and 64 ml, respectively. The inter-rater reliability for WP described by the ICC was 0.99 (CI: 0.98–0.99, $p < 0.0001$) (see table 2).

Bioelectrical impedance

Two datasets could not be analysed so that the number of subjects was reduced to 18. Shapiro–Wilk-Test also revealed normally distributed BI data for R1 and R2. Homoscedasticity and statistically significant differences between M1 and M2 (R1 = 3.9

Table 1. Mean (MN) and standard deviation (SD) for all three measurements of waterplethysmography (WP), impedance (BI) and muscle twitch force (MTF) measures for both raters (R1, R2).

	WP in ml				BI in Ω				MTF in N			
	R1		R2		R1		R2		R1		R2	
Measure Rater	MN	SD	MN	SD	MN	SD	MN	SD	MN	SD	MN	SD
M1	3077	321	3082	315	69.8	13.9	60.8	13.5	1.68	0.53	1.73	0.51
M2	3100	327	3101	323	73.7	15.0	63.3	16.2	1.81	0.55	1.85	0.63
M3	3094	328	3105	325	76.0	13.7	65.2	15.8	1.85	0.59	1.93	0.66

Ω, $p = 0.0001$; R2 = 2.4 Ω, $p = 0.049$) and between M2 and M3 (R1 = 2.3 Ω, $p = 0.012$; R2 = 2.0 Ω, $p = 0.008$) occurred for BI data of both raters (see figures 4(c) and (d) for rater 1). SEM and SRD values for R1 were 3.8 and 10.5 Ω, respectively, and for R2 3.4 and 9.4 Ω, respectively. Intraclass correlation for R1 and R2 was 0.24 (CI: 0.07–0.51, $p = 0.001$) (see table 2).

Muscle twitch force

Normal distribution was given for datasets of both raters. MTF data also showed homoscedastic distribution of test–retest differences and statistically significant mean differences between M1 and M2 for rater 1 but not rater 2 (R1 = 0.13 N, $p = 0.022$; R2 = 0.12 N, $p = 0.082$) and no significant difference between M2 and M3 for both raters (R1 = 0.04 N, $p = 0.37$; R2 = 0.08 N, $p = 0.12$) (see figure 4(e) and (f) for rater1). SEM and SRD values for R1 were 0.19 and 0.53 N, respectively. R2 had a SEM of 0.23 N and a SRD of 0.64 N. The inter-rater reliability for MTF was 0.71 (CI: 0.55–0.85, $p < 0.0001$) (see table 2).

Discussion

Swelling—lower leg volume

Waterplethysmography. Waterplethysmography has previously been used to determine lower leg oedema development while standing (Man *et al* 2003, Mosti and Partsch 2013). There are no standardised protocols in the literature recommending measurement procedure, basin volume/design or water draining time. Additionally, wide variations of water displacement based volumetry procedures are described in previous studies. Subject placement could either be sitting (Brijker *et al* 2000) or standing (Belczak *et al* 2009). Positioning of the foot and lower leg varied from touching the ground (Henschke *et al* 2006) to lifting the foot to a certain mark on the lower leg level to the surface of the water (Hartmann and Huch 2005). Another inconsistent measurement factor is the water draining time. Durations vary from 20 s using a special construction (Goldie *et al* 1974) to 2 and 5 min, respectively (Hartmann and Huch 2005, Belczak *et al* 2009) or until water was drained completely (Henschke *et al* 2006). In most cases waterplethysmography measurements only included the distal lower leg up to a few centimetres above ankle level depending on the design of water tanks (Petersen *et al* 1999, Henschke *et al* 2006, Mosti and Partsch 2013). In order to measure oedema of a large part of the lower leg in the present study the authors chose to use a water tank with 50 cm height in contrast to previous studies using devices only covering the distal lower leg up to a few centimetres above ankle level (Petersen *et al* 1999, Henschke *et al* 2006, Mosti and Partsch 2013).

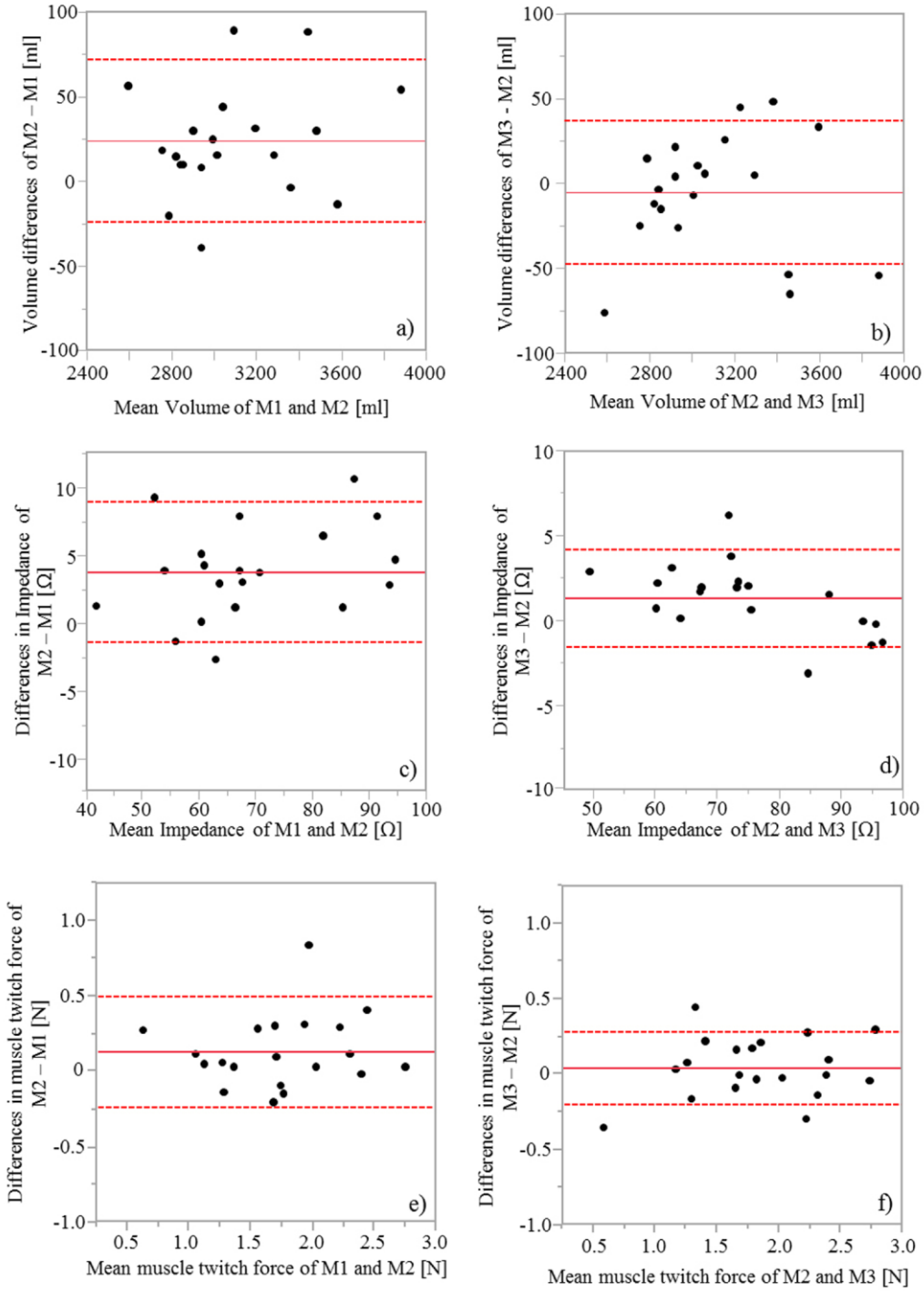

Figure 4. (a)–(f) Bland–Altman plots of waterplethysmography (a) and (b), impedance (c) and (d) and muscle twitch force (e) and (f) measurements showing differences and mean values in volume, voltage and twitch force of each subject measured by rater 1.

Table 2. Standard error of measurement (SEM) and smallest real difference (SRD) values of both raters (R1, R2) for waterplethysmography (WP), impedance (BI) and muscle twitch force (MTF) measures. (WP and MTF $n = 20$; BI $n = 18$).

Measure	WP (ml)		BI (Ω)		MTF (N)	
Rater	R1	R2	R1	R2	R1	R2
SEM	23	27	3.8	3.4	0.19	0.24
SRD	64	75	10.5	9.4	0.53	0.66
ICC	0.98 ($p < 0.0001$)		0.24 ($p = 0.001$)		0.71 ($p < 0.0001$)	

Water temperature of 25–30° C was chosen consistent with previous studies (Rabe *et al* 2010). Additionally, limiting water draining time to 5 min allows measurements in the course of standing work without excessively interfering with the work process. Evaluating the planned investigation and previously conducted test measurements, the authors chose the procedure and setting described above.

Our results showed a standard error of measurement of 23 and 27 ml corresponding to a 0.7 and 0.9% error, respectively (see table 1 for mean values of the measurements). Rabe *et al* (2010) report in their review about lower leg WP that measurement error was described as being between 0.1 and 1.0%. Additionally, the authors conclude that measurement error should not be above 20 ml because that would not allow for detecting the effects of antidiuretic drugs, which can decrease lower leg volume by ca. 30 ml (Rabe *et al* 2010). However, average lower leg volume increases are expected to be greater than 100 ml or 3–5% after prolonged standing as has been shown in several previous studies (Hansen *et al* 1998, Belczak *et al* 2009).

Measured systematic error shown in Bland–Altman plots can be explained by an actual increase in lower leg volume from M1 to M2. One possible explanation could be that between M1 and M2, the subject's leg (of which volume was measured) was in a sloped position (as seen in figure 3) allowing an increase of lower leg's volume, which is known to occur during sitting (Chester *et al* 2002, Herold 2015). In addition, WP was performed immediately after arriving, getting the procedure explained and signing informed consent (only on day one). Another possibility is that this may have led to an underestimation of LLV due to the preceding activation of the muscular venous pump (by walking or biking). Solving these issues by standardising leg position in between measurements and including a seated resting period before M1 could have further improved reliability of WP.

Inter-rater reliability can be regarded as very good taking into account the ICC, which showed a nearly perfect agreement, and SEM values, which were only 4 ml apart.

Bioelectrical impedance. For the present study we used a measuring frequency of 370–372 Hz to mainly record extracellular fluid shifts (Kanai *et al* 1983). We assume that focusing on extracellular fluid is important since it is related to the pathophysiology of venous diseases. Lower leg volume increases directly after a posture shift from sitting/lying to standing due to an immediate gravitational fluid redistribution (Stick *et al* 1985). After a few minutes, orthostatic pressure induces an increase of extracellular fluid into capillaries and the lymphatic system. If lower leg muscle activity is insufficient (muscular venous pump), like it is the case in prolonged standing, venous pressure increases and leads to further stretching of vessels. This process can lead to sacculation (varicose veins) and venous insufficiency in the long term (Ganasegeran *et al* 2014, Herold 2015).

Test–retest reliability was found to be very good in previous studies both in healthy (Mally *et al* 2011) and lymphatic subjects (Czerniec *et al* 2009, Jain *et al* 2010) as well as

lower legs (Pichonnaz *et al* 2015) and forearms (Czerniec *et al* 2009, Jain *et al* 2010) using commercial BI devices. Although no comparable investigation could be found using the exact same measuring frequencies or same general setup. The SEMs of 1.75 (R1) and 1.59 μV (R2) correspond to approximately 5% of the measured BI values (see table 1). In previous studies, effects of prolonged standing on BI change of over 20% compared to baseline have been shown (Stick *et al* 1992, Sanders *et al* 2012). Therefore, the authors conclude that sufficient test–retest reliability is given for the conducted procedure. The same problem regarding systematic error as described for WP was found for BI from M1 to M2 and M2 to M3 as seen in Bland–Altman plots indicating a volume decrease from M1 up to M3 for both raters. This finding is in contrast to the results from the leg on which WP was conducted. The reason for that could be a fourth measurement procedure not described in the present publication. It was an explorative approach to investigate reliability of a force sense measurement procedure for which the leg had to be lifted in a mechanical device to about head level (while sitting) and at the same time actively contracting calf muscles. This could have led to an activation of the muscle venous pump and further to a lower leg volume decrease and thus to measured statistical difference. As mentioned in the WP discussion section, a standardised lower leg positioning in between measurements may improve SEM values further so that an underestimation of reliability is probable in this case.

Inter-rater reliability as calculated by ICC (2,1) was very low at 0.24. However, SEM values only differed minimally. This could be because R1 and R2 often measured very different absolute values comparing individual subjects. For example values recorded by R1 for subject 20 were 23.29, 27.73 and 29.63 μV and by R2 on a different day 42.29, 43.72 and 47.96 μV. The reason for these differences most probably is the electrode placement, which R1 and R2 conducted separately and can lead to a difference of inter-electrode distance of a few centimetres and further to different BI results. Therefore, ICC calculation may not be appropriate for BI measurement and, therefore, inter-rater reliability evaluation should be carried out by comparing SEM values alone.

Although water displacement is still regarded as the gold standard in measuring volume changes (Petersen *et al* 1999, Henschke *et al* 2006), plenty of other methods with specific pros and cons were used previously. Comparatively simple methods, requiring low costs, are circumference measurements that can lack precision if not conducted properly and often overestimate total volume depending on used model (Sander *et al* 2002, Taylor *et al* 2006). Other techniques like perometry, dual energy x-ray absorptiometry (DXA), BI or air plethysmography can also produce valid and reliable data measuring both healthy persons and patients with lymphedema. These methods require expensive devices and in the case of air plethysmography, cannot be used segmentally (Wagner and Heyward 1999, Deltombe *et al* 2007, Ridner *et al* 2007, Gjorup *et al* 2010, Newman *et al* 2013). The biggest advantage of BI measurements is the comparingly low required measuring time (in our case 20 s). For measuring lower leg oedema development in standing work, we wanted to include both the gold standard in volumetry and another less time consuming method and therefore chose waterplethysmography and bioelectrical impedance.

Muscle twitch force

There are no studies available investigating reliability of MTF known to the authors. However, MTF has previously been conducted in the triceps surae muscle during multiple hours of standing. Garcia *et al* (2015) found a force reduction after electrical stimulation compared to baseline of 30–40% after standing for more than 4 h. Calculated SEM values of 0.19 N for R1 and

0.23 N for R2 corresponding to about 11 and 13%, respectively, represent test-retest reliability and can, therefore, be described as sufficient for detecting measured effects after multiple hours of standing.

Measured statistically significant differences (systematic error) could indicate an influence of inter-cellular liquid distribution, changing the lower leg impedance (as described in previous section) due to measuring procedure and MTF. Further investigation to clarify such connection is needed. Additional SEM improvement may be achieved by methodological adaptation of the measuring procedure described for WP and BI.

Inter-rater reliability as calculated by an ICC of 0.71 is found to be moderate. However, in this case the problem is similar to the one described for BI data. Both raters conducted electrode placement separately leading to different absolute values for individual subjects. Furthermore, homogenous data with low values and low standard deviations will likely result in lower ICCs (Atkinson and Nevill 1998), which may be the case for present results. Comparing the SEMs of R1 and R2 (0.19 and 0.24) differences can be considered to be very low and therefore inter-rater reliability described as good.

Conclusions

All measurements conducted in present study showed satisfying test–retest- and inter-rater reliability for standing work evaluation of lower leg oedema (WP and BI) and muscle fatigue (MTF). Inter-rater reliability evaluated by calculating ICC has to be interpreted cautiously. The results of present investigation will be very helpful for interpretation of results measured during multiple hours of standing.

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References

Adamo D E, Khodaee M, Barringer S, Johnson P W and Martin B J 2009 Low mean level sustained and intermittent grip exertions: influence of age on fatigue and recovery *Ergonomics* **52** 1287–97

Adamo D E, Martin B J and Johnson P W 2002 Vibration-induced muscle fatigue, a possible contribution to musculoskeletal injury *Eur. J. Appl. Physiol.* **88** 134–40

Andersen J H, Haahr J P and Frost P 2007 Risk factors for more severe regional musculoskeletal symptoms: a two-year prospective study of a general working population *Arthritis Rheum* **56** 1355–64

Atkinson G and Nevill A M 1998 Statistical methods for assessing measurement error (reliability) in variables relevant to sports medicine *Sports Med.* **26** 217–38

Atsumi K, Kajiya F, Tsuji T and Tsujioka K (ed) 1987 *Medical Progress through Technology* (Berlin: Springer)

Bahk J W, Kim H, Jung-Choi K, Jung M-C and Lee I 2012 Relationship between prolonged standing and symptoms of varicose veins and nocturnal leg cramps among women and men *Ergonomics* **55** 133–9

Belczak C E Q, de Godoy J M P, Ramos R N, Oliveira M A D, Belczak S Q and Caffaro R A 2009 Rate of occupational leg swelling is greater in the morning than in the afternoon *Phlebol. Venous Forum R. Soc. Med.* **24** 21–5

Bland J and Altman D 1999 Measuring agreement in method comparison studies *Stat. Methods Med. Res.* **8** 135–60
Blangsted A K, Sjøgaard G, Madeleine P, Olsen H B and Søgaard K 2005 Voluntary low-force contraction elicits prolonged low-frequency fatigue and changes in surface electromyography and mechanomyography *J. Electromyogr. Kinesiol.* **15** 138–48
Brijker F, Heijdra Y F, Van Den Elshout F J, Bosch F H and Folgering H T 2000 Volumetric measurements of peripheral oedema in clinical conditions *Clin. Physiol.* **20** 56–61
Chester M R, Rys M J and Konz S A 2002 Leg swelling, comfort and fatigue when sitting, standing, and sit/standing *Int. J. Ind. Ergon.* **29** 289–96
Cole K S 1972 *Membranes, Ions and Impulses* (*Biophysics Series* vol 1) (Berkeley, CA: University of California Press)
Czerniec S A, Ward L C, Refshauge K M, Beith J, Lee M J, York S and Kilbreath S L 2009 Assessment of breast cancer-related arm lymphedema-comparison of physical measurement methods and self-report *Cancer Investig.* **28** 54–62
Deltombe T, Jamart J, Recloux S, Legrand C, Vandenbroeck N, Theys S and Hanson P 2007 Reliability and limits of agreement of circumferential, water displacement, and optoelectronic volumetry in the measurement of upper limb lymphedema *Lymphology* **40** 26–34
Ganasegeran K, Perianayagam W, Nagaraj P and Al-Dubai S A 2014 Psycho-behavioural risks of low back pain in railway workers *Occup. Med.* **64** 372–5
Garcia M-G, Läubli T and Martin B J 2015 Long-term muscle fatigue after standing work *Hum. Factors* **57** 1162–73
Gjorup C, Zerahn B and Hendel H W 2010 Assessment of volume measurement of breast cancer-related lymphedema by three methods: circumference measurement, water displacement, and dual energy x-ray absorptiometry *Lymphatic Res. Biol.* **8** 111–9
Goldie I F, Gunterberg B and Jacobsen C 1974 Foot volumetry as an objective test of the effect of antiphlogistic drugs in ankle sprains *Rheumatology* **13** 204–7
Hansen L, Winkel J and Jørgensen K 1998 Significance of mat and shoe softness during prolonged work in upright position: based on measurements of low back muscle EMG, foot volume changes, discomfort and ground force reactions *Appl. Ergon.* **29** 217–24
Hartmann S and Huch R 2005 Response of pregnancy leg edema to a single immersion exercise session *Acta Obstet. Gynecol. Scand.* **84** 1150–3
Henschke N, Boland R A and Adams R D 2006 Responsiveness of two methods for measuring foot and ankle volume *Foot Ankle Int.* **27** 826–32
Hermens H J 1999 *European Recommendations for Surface ElectroMyoGraphy: Results of the SENIAM Project* (*SENIAM* vol 8) (Enschede: Roessingh Research and Development)
Herold G (ed) 2015 *Innere Medizin 2015: Eine vorlesungsorientierte Darstellung; unter Berücksichtigung des Gegenstandskataloges für die Ärztliche Prüfung; mit ICD 10-Schlüssel im Text und Stichwortverzeichnis* (Köln: Selbstverl)
Hopkins W 2000 Measures of reliability in sports medicine and science *Sports Med.* **30** 1–15
Jaffrin M Y and Morel H 2008 Body fluid volumes measurements by impedance: a review of bioimpedance spectroscopy (BIS) and bioimpedance analysis (BIA) methods *Med. Eng. Phys.* **30** 1257–69
Jain M S, Danoff J V and Paul S M 2010 Correlation between bioelectrical spectroscopy and perometry in assessment of upper extremity swelling *Lymphology* **43** 85–94
Johnson P W, Ciriello V M, Kerin K J and Dennerlein J T 2013 Using electrical stimulation to measure physiological changes in the human extensor carpi ulnaris muscle after prolonged low-level repetitive ulnar deviation *Appl. Ergon.* **44** 35–41
Kanai H, Haeno M and Sakamoto K 1987 Electrical measurement of fluid distribution in legs and arms: medical progress through technology: medical engineering *Japan Research and Development* ed K Atsumi *et al* (Berlin: Springer) pp 159–70
Kanai H, Haeno M, Tagawa H and Sakamoto K 1988 Electrical measurement of fluid distribution in human legs and arms and its clinical application *Advances in Biomedical Measurement* ed E Carson *et al* (Berlin: Springer) pp 59–70
Kanai H, Sakamoto K and Haeno M 1983 Electrical measurement of fluid distribution in human legs: estimation of extra- and intra-cellular fluid volume *J. Microw. Power* **18** 233–43
Kim J H and Johnson P W 2014 Fatigue development in the finger flexor muscle differs between keyboard and mouse use *Eur. J. Appl. Physiol.* **114** 2469–82
Krijnen R, Boer E D, Adèr H and Bruynzeel D 1997 Venous insufficiency in male workers with a standing profession *Dermatology* **194** 111–20

Mally K, Trentmann J, Heller M and Dittmar M 2011 Reliability and accuracy of segmental bioelectrical impedance analysis for assessing muscle and fat mass in older Europeans: a comparison with dual-energy x-ray absorptiometry *Eur. J. Appl. Physiol.* **111** 1879–87

Man I O W, Lepar G S, Morrisey M C and Cywinsiki J K 2003 Effect of neuromuscular electrical stimulation on foot/ankle volume during standing *Med. Sci. Sports Exercise* **35** 630–4

McCulloch J 2002 Health risks associated with prolonged standing *Work* **19** 201–5

Mosti G and Partsch H 2013 Occupational leg oedema is more reduced by antigraduated than by graduated stockings *Eur. J. Vasc. Endovasc. Surg.* **45** 523–7

Newman A L, Rosenthall L, Towers A, Hodgson P, Shay C A, Tidhar D, Vigano A and Kilgour R D 2013 Determining the precision of dual energy x-ray absorptiometry and bioelectric impedance spectroscopy in the assessment of breast cancer-related lymphedema *Lymphatic Res. Biol.* **11** 104–9

Pensri P, Janwantanakul P and Chaikumarn M 2009 Prevalence of self-reported musculoskeletal symptoms in salespersons *Occup. Med.* **59** 499–501

Petersen E J, Irish S M, Lyons C L, Miklaski S F, Bryan J M, Henderson N E and Masullo L N 1999 Reliability of water volumetry and the figure of eight method on subjects with ankle joint swelling *J. Orthop. Sports Phys. Ther.* **29** 609–15

Pichonnaz C, Bassin J-P, Lécureux E, Currat D and Jolles B M 2015 Bioimpedance spectroscopy for swelling evaluation following total knee arthroplasty: a validation study *BMC Musculoskelet. Disord.* **16** 1088

Rabe E, Stücker M and Ottillinger B 2010 Water displacement leg volumetry in clinical studies—a discussion of error sources *BMC Med. Res. Methodol.* **10** 5

Ridner S H, Montgomery L D, Hepworth J T, Stewart B R and Armer J M 2007 Comparison of upper limb volume measurement techniques and arm symptoms between healthy volunteers and individuals with known lymphedema *Lymphology* **40** 35–46

Ringheim I, Austein H, Indahl A and Roeleveld K 2015 Postural strategy and trunk muscle activation during prolonged standing in chronic low back pain patients *Gait Posture* **42** 584–9

Sander A P, Hajer N M, Hemenway K and Miller A C 2002 Upper-extremity volume measurements in women with lymphedema: a comparison of measurements obtained via water displacement with geometrically determined volume *Phys. Ther.* **82** 1201–12

Sanders J E, Allyn K J, Harrison D S, Myers T R, Ciol M A and Tsai E C 2012 Preliminary investigation of residual-limb fluid volume changes within one day *J. Rehabil. Res. Dev.* **49** 1467–78

Seo A, Kakehashi M, Uda S, Tsuru S and Yoshinaga F 1995 Bioelectrical impedance measuring method for standing load evaluation *J. Occup. Health* **37** 83–7

Seo A, Rys M and Konz S 2001 Measuring lower leg swelling: optimum frequency for impedance method *Med. Biol. Eng. Comput.* **39** 185–9

Søgaard K, Blangsted A K, Jørgensen L V, Madeleine P and Sjøgaard G 2003 Evidence of long term muscle fatigue following prolonged intermittent contractions based on mechano- and electromyograms *J. Electromyogr. Kinesiol.* **13** 441–50

Stick C, Jaeger H and Witzleb E 1992 Measurements of volume changes and venous pressure in the human lower leg during walking and running *J. Appl. Physiol.* **72** 2063–8

Stick C, Stofen P and Witzleb E 1985 On physiological edema in man's lower extremity *Eur. J. Appl. Physiol. Occup. Physiol.* **54** 442–9

Taylor R, Jayasinghe U W, Koelmeyer L, Ung O and Boyages J 2006 Reliability and validity of arm volume measurements for assessment of lymphedema *Phys. Ther.* **86** 205–14

Tissot F, Messing K and Stock S 2005 Standing, sitting and associated working conditions in the Quebec population in 1998 *Ergonomics* **48** 249–69

Tomei F, Baccolo T P, Tomao E, Palmi S and Rosati M V 1999 Chronic venous disorders and occupation *Am. J. Ind. Med.* **36** 653–65

Tüchsen F, Krause N, Hannerz H, Burr H and Kristensen T S 2000 Standing at work and varicose veins *Scand. J. Work Environ. Health* **26** 414–20

Wagner D R and Heyward V H 1999 Techniques of body composition assessment: a review of laboratory and field methods *Res. Q. Exercise Sport* **70** 135–49

Werner R A, Gell N, Hartigan A, Wiggerman N and Keyserling W M 2010 Risk factors for plantar fasciitis among assembly plant workers *PM&R* **2** 110–6

Wittig P, Nöllenheidt C and Brenscheidt S 2013 *Grundauswertung der BIBB/BAuA-Erwerbstätigenbefragung 2012* (Dortmund/Berlin/Dresden: Selbstverl.) www.baua.de/dok/3666616 (Accessed: September 24 2016)

4.2 Research paper 2: Associations between lumbar movement, muscle activity and discomfort development during prolonged standing

One to two thirds of healthy, previously asymptomatic subjects develop LBP/ LBD when standing for two or more hours (Nelson-Wong *et al.*, 2008; Marshall *et al.*, 2011). The mechanisms behind LBD development are not well understood. In the second research paper it is tested whether movement patterns in the lower back or constant low-level lumbar muscle activity can be associated with the development of LBD during multiple hours of standing in an exploratory study.

The aims of research paper 2, relevant to this dissertation were:

- To investigate lumbar spine movement patterns during multiple hours of static standing comparing discomfort developers with asymptomatic subjects.
- To investigate if continuous low-level erector spinae muscle activity is present in discomfort developers and not in asymptomatic subjects.

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Associations between low back muscle activity, pelvic movement and low back discomfort development during prolonged standing – An exploratory laboratory study

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ABSTRACT

Low back discomfort (LBD) is common in long-term standing work. The aim of this study was to investigate whether development of LBD during standing is related to lumbar muscle activity and pelvic movement. In a secondary analysis we investigated whether age, gender, and standing work habituation moderates the above-mentioned relationship. Sixty subjects (15 young females, 15 young males, 15 older males, and 15 young males habituated to standing work) were included and had to stand for 4.5 h over three periods with two seated breaks. Surface electromyography, a gravimetrical position sensor, and a numeric rating scale were used to assess lumbar muscle activity, pelvic movement, and LBD, respectively. 22 of 55 analyzed subjects (40%) reported LBD and were assigned to the discomfort developer (DD) group. The remaining subjects (non-discomfort developer: NoDD) showed a statistically significant increase of medio-lateral pelvic movement in the progression of the three standing periods. Almost no differences occurred in lumbar muscle activity (except for the 5th percentile of surface electromyography, which was higher in NoDD). No influence of age, gender, or standing habituation was found. Increased pelvic movement may protect from LBD development during prolonged standing, although differences are very small and clinical relevance is unclear.

1. Introduction

Discomfort in the lower back region includes a broad spectrum of symptoms, of which pain is the most distinct and most investigated. Low back pain (LBP) is a widespread disorder (March et al., 2014). Although LBP seems to be a general epidemic with a one year prevalence up to 65% (Walker, 2000), it was found to be more common in certain occupations compared to the general working population (Punnett, 2014). Work-related physical factors that may cause LBP are whole body vibrations, repetitive tasks, lifting, pushing, pulling, and constrained trunk postures (Chen et al., 2004; da Costa and Vieira, 2010; Griffith et al., 2012; Lötters et al., 2003). Additionally, work-related psychosocial factors contribute to LBP development, such as high job demands and low social support (da Costa and Vieira, 2010; Lang et al., 2012). Further, the prevalence of LBP seems to increase with age, and is more common in women than in men (Dionne et al., 2006; Wong et al., 2017).

More recent studies found that occupational standing for a prolonged period of time was associated with LBP (Coenen et al., 2016; da Costa and Vieira, 2010; McCulloch, 2002). In this respect, it is suggested that transient LBP development during standing predicts future clinically relevant LBP in previously asymptomatic individuals (Nelson-Wong and Callaghan, 2014). Interestingly, several studies showed that the number of previously asymptomatic people who develop LBP during standing seems to be consistently between 32 and 70% (Aghazadeh et al., 2015; Marshall et al., 2011; Nelson-Wong et al., 2008, 2012; Nelson-Wong and Callaghan, 2010). Occupational standing is widespread within industrialized countries and across professions. In Germany and Canada, about 40–50% of the full-time working population are required to stand for the larger time of their shifts (Tissot et al., 2005; Wittig et al., 2013). Thus, the amount of people at a higher risk of developing musculoskeletal disorders in the lower back region compared to the general population is substantial (Andersen et al., 2007; Pensri et al., 2009; Werner et al., 2010).

A wide range of mechanisms for causal relationships between LBP/LBD and prolonged standing are discussed in the literature. Some

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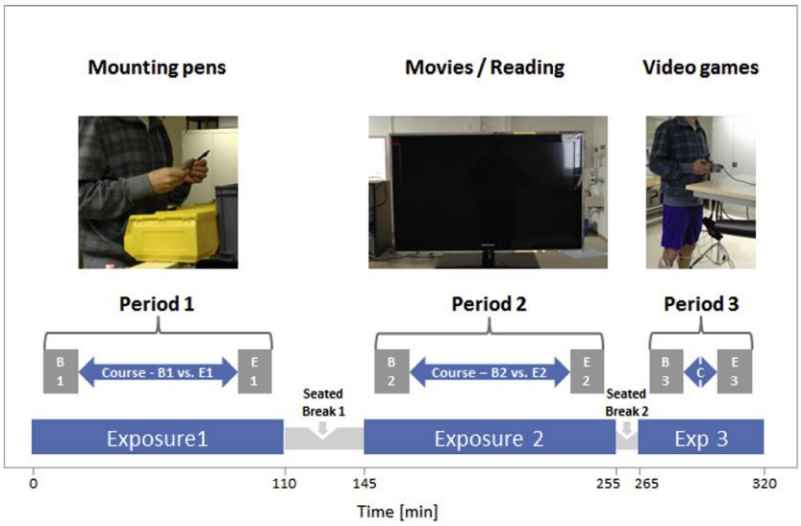

Fig. 1. Visualization of the experimental protocol. Each subject was exposed to three standing periods (Exposure 1–3; Exp.) with two seated breaks. Within each exposure, the first and last 20 min (excluding the first and last 5 min) were used for data analysis (B1-3: Beginning 1–3; E1-2: End 1–3). Different tasks were applied within each period.

authors found an influence of fatigue in the lumbar muscles (Antle and Côté, 2013; Balasubramanian et al., 2009), while others suggest that a lack of movement variation might be responsible for LBP development during static standing (Gallagher et al., 2011; Gregory and Callaghan, 2008). Additionally, some studies found reduced strength and endurance (Marshall et al., 2011), as well as increased co-contractions in the gluteus medius muscles (Aghazadeh et al., 2015; Nelson-Wong et al., 2008) in the LBP developer groups. It has also been suggested that neuromuscluar activity of the trunk musculature and kinematics of the lower back contribute to LBP (Behennah et al., 2018; Dankaerts et al., 2007). From a physiological perspective, it might be possible that developing LBP during standing has the same pathological origin as suggested for chronic myalgia in the trapezius muscle. Studies about chronic trapezius myalgia suggest that continuous static muscle activation of mostly type I muscle fibers induces metabolic overload of motor units that may cause pain (so-called Cinderella hypothesis) (Hägg, 1991; Visser and van Dieën, 2006; Zennaro et al., 2003). Associated with that, a lack of blood flow and thus an accumulation of metabolites in the muscle may contribute to LBP as well (Visser and van Dieën, 2006).

Therefore, the primary aim of this exploratory study was to investigate lumbar erector spinae muscle activation and pelvic movement during prolonged standing in subjects developing low back discomfort (LBD) compared to symptom-free persons. To include a broader spectrum of low back complaints, LBD was assessed instead of the more specific outcome LBP (Lee et al., 2018).

This study also investigated the influence of age, gender, and habituation to standing at work on the above-mentioned associations of LBD, lower back muscle activity, and pelvic movement. A deeper understanding of factors associated with LBD in standing work may help to develop concepts to prevent LBD/LBP in workers exposed to standing work.

2. Material and methods

2.1. Study population

Sixty healthy subjects from four subgroups were included in the present study to address the research aims. Subgroup 1: 15 females, age 18–35 years, not habituated to standing work (not habituated to standing is defined as standing less than 2 h per working shift); subgroup 2: 15 males, age 18–35 years, not habituated to standing work; subgroup 3: 15 men, age 45–67 years, not habituated to standing work; subgroup 4: 15 males, age 18–35 years, habituated workers who stand for at least 4 h per working shift, on at least four days per week, for at least one year prior to this study. Exclusion criteria were severe venous and musculoskeletal diseases (severe spine deformations, such as hyper lordosis or scoliosis), age lower than 18 or over 67, and medication including diuretics, venotonics, vasodilatators, antihypertensive drugs, or analgesics. The study was approved by the local ethics committee of the Medical Faculty, University of Tuebingen. All subjects signed informed consent prior to investigations and received financial compensation for their participation.

Full datasets were analyzed for 55 subjects (13 female, 42 male; age: 32.1 ± 12 years; weight: 74.8 ± 11 kg; height: 177 ± 9 cm). Two subjects did not complete the experimental protocol due to circulatory problems.Unrealistic SEMG or position sensor data occurred in three subjects, presumably due to electrode or sensor displacement during the seated breaks, which was not recognized during the measurements.

2.2. Experimental design

Measurements started in the morning between 8 and 9 a.m. First, inclusion and exclusion criteria were controlled and previous musculoskeletal disorders in the lower back and leg regions were assessed using a questionnaire. In case of inclusion, subjects were prepared for experimental procedures. The experiment consisted of three standing periods (exposure 1–3) and two seated breaks: a 35 min break between exposures 1 and 2 - including standardized food - and a 10 min break between exposures 2 and 3. During exposure 1, subjects assembled and disassembled pens for 110 min. In exposure 2, participants either watched a movie or read for another 110 min. Exposure 3 included 55 min of mandatory playing of video games (Fig. 1). The content of the exposure periods was chosen to prevent boredom and for reasons of standardization. In total, each subject stood for 4 h and 35 min. The total standing duration was selected based on a previous study by our cooperation partners from the ETH Zurich (Garcia et al., 2015) for comparability.

2.3. Measurements and data analysis

2.3.1. Rating of discomfort

Subjects were asked to rate their perceived discomfort in different body regions including the lower back using a dichotomous question (no/yes) and a numeric rating scale (11 levels, 0 = no discomfort, 10 = highest imaginable discomfort) to assess discomfort intensity levels. Additionally, whenever discomfort was indicated, the study participants were asked to describe it in more detail (e.g. pain, burning, pulling, or tingling sensation, muscular tension). This short interview took place at the beginning, at the end, and every 27.5 min during exposures (13 times in total). Only ratings of perceived discomfort at the lower back region were included and analyzed, since LBD was the focus of the present paper.

2.3.2. Surface electromyography

Muscle activity was measured using bipolar SEMG. Two pre-gelled Ag/AgCl surface electrodes (Covidien™, Kendall™ ECG electrodes H93SG, distance between electrodes: 25 mm) were placed bilaterally on the lumbar erector spinae muscle, according to SENIAM (Hermens, 1999). Prior to electrode placement, the skin was cleaned and prepared with abrasive paste (Nupreb®, Weaver and Company) to improve SEMG signals and electrode adhesion. The bipolar SEMG signals were differentially amplified, analogue filtered (high pass filter, 4th order, −3 dB at 16 Hz; low pass filter, 10th order, −3 dB at 650 Hz) sampled at 2048 Hz, analyzed, and stored using a combined data analyzer and logger (PS11-UD®, THUMEDI GmbH & Co. KG, Thum, Germany; overall CMRR > 96 dB; overall effective noise < 0.8 μV RMS; linearity typ. ± 0.25 dB at 20–500 Hz). Data were real-time transformed by the device into the frequency domain (1024-point Fast Fourier Transformation using a Bartlett-window with 50% overlap), and digitally filtered (high-pass filter, 11th order, −3 dB at 16 Hz). Power line interference (50 Hz and its first seven harmonics) was removed by replacing it with the spectral values of a 2 Hz-wide band around its centre frequency by means of both spectral neighbors. Finally, the root-mean-square of the electrical activity (EA) was real-time calculated (250 m s moving window with 50% overlap) from the power spectrum and stored synchronously to the raw data and used for analysis. SEMG was measured continuously throughout the three standing periods.

In the present study with an intra-subject design, normalization is not necessarily required since electrodes were not reallocated; there is no comparison between different muscles of individuals (Burden, 2010). The purpose of this normalization procedure was to further reduce variance in the SEMG data due to inter-individual differences (e.g. thickness of subcutaneous fat tissue). In this respect a submaximal reference activation of the erector muscles was used to normalize surface electromyography (SEMG) data. To do this, a 10 kg weight attached to a rope, which was fastened to the subject's chest and ran through a trolley, was held for 20 s (Fig. 2). Shoulders and buttocks had contact to the wall. Subject's feet were positioned at a mark on the floor.

2.3.3. 3D gravimetrical position sensor

Pelvic movement in anterior/posterior and medio-lateral directions was measured by a three-dimensional position sensor (PS11-UD®, THUMEDI GmbH & Co. KG, Thum, Germany), which was placed on the first spinal process of the sacrum using adhesive tape. The sensor records position with respect to the absolute perpendicular gravitational axis, sampled at 8 Hz (resolution of 0.1°; max static error of 0.5° max repeatability error of 0.12° for temperatures between 18 and 32 °C). This allows insights in movement patterns of the pelvis, as well as the lower lumbar spine, because of the close anatomical connection of these structures. These position data were measured continuously throughout the three standing exposure periods.

2.3.4. Photo documentation

All measurements were documented by photographs taken randomly every 4–6 s by a common webcam and stored synchronously to the SEMG and position data by the measurement device (PS11 UD). Photos were used to check whether conspicuous data was caused by subject behavior (i.e. bending down).

Fig. 2. Normalization of M. erector spinae activity.

2.3.5. Supplemental data

Subjects' age, gender, body weight and height, occupational status, and musculoskeletal complaints during the last 12 months were recorded using the Nordic Questionnaire (Kuorinka et al., 1987).

2.3.6. Data preparation and statistical analyses

Post hoc, subjects were assigned to two LBD groups. Similar to the procedure described by Nelson-Wong and Callaghan, 2010, and adapted by Lee et al., (2018), all subjects that reported an increase of one or more for LBD intensity level during any of the three standing periods were included into the discomfort group (discomfort developer, DD). All other subjects were assigned to the non-discomfort group (non-discomfort developer, NoDD) (Lee et al., 2018; Nelson-Wong et al., 2008).

For the pelvic movement data in anterior/posterior and medio-lateral directions, interquartile ranges (25.-75. Quartile, IQR) were calculated to get information about both range of motion and frequency of position changes.

For erector muscle activity, the 5th, 50th, and 95th percentiles of the EA were calculated and given in percent of the reference EA. The reference EA was determined using the median activity of a stable 10 s period during the submaximal reference contraction described in the procedure section. The 5th percentile (p5-EA) represents low muscular activity, the median (p50-EA) represents the overall activity level, and the 95th percentile (p95-EA) gives an estimate about peaks in muscular activity (Lamotte et al., 1996).

Continuous data (erector activity and pelvic movement) were split into three exposure periods. The first and last 15 min of each exposure period were used for statistical analyses.

Data were visually inspected for extreme values. If extreme values were related to improper measurement or subjects' behavior (e.g. spontaneously picking up a pen from the floor despite interdiction to do so), they were removed from further analysis.

All continuous dependent variables (LBD intensity, erector activity, pelvic movement) were analyzed using mixed models. To better approximate a normal distribution of the data, all values were log-transformed for the statistical analysis based on linear mixed models containing the subject as a random effect. Effects of the following independent factors were tested: LBD group (DD, NoDD); subgroup (young females, young males, older males, and standing habituated young males); period (standing periods 1, 2, and 3), and progression (changes within the standing periods; begin vs. End). In case of a statistically significant main effect, we performed post-hoc tests with a Tukey HSD (Honestly Statistical Difference) test to compensate for multiple testing. We also tested whether there were significant two-way interactions between the independent variables.

Chi-square tests were applied to look for differences in the number of DD between the beginning and end of each standing period, and between the four subgroups. Alpha level to determine statistical significance was set to 0.05. Statistical analyses were conducted using JMP (JMP® 13.1.0) and SAS 9.4 (SAS Institute Inc.)

3. Results

3.1. Supplemental data

Nine of the 55 included subjects reported low back complaints in the previous 12 months and an additional four had lower back complaints during the past seven days, none of whom felt impeded in their regular jobs.

3.2. Rating of low back discomfort

Ratings of low back discomfort intensity ranged from 0 to 6 overall (10 = highest imaginable discomfort). The proportion of subjects developing LBD increased during exposure 1 from 1/55 (at 0 min) to 14/55 (at 82.5 min) and remained at that level until the end of the first exposure period. After the first break, the proportion of subjects with LBD decreased to 3/55 (at 0 min) and increased during exposure 2 to 18/55 (at 110 min). At the beginning of exposure 3, 8/55 subjects indicated LBD and this proportion increased to 16/55 after 55 min (Fig. 3).

In total, 22 of the 55 subjects (40%) indicated an increase of low back discomfort (at least 1 level of LBD intensity) during exposure periods 1–3 and were therefore assigned to the DD group. The number of identified DD and NoDD is shown in Table 1. Statistically significant increases of the number of subjects with LBD were observed (exposure 1: Chi2 19.2, $p = 0.0007$; exposure 2: Chi2 14.0, $p = 0.007$) within the first (n = 1 at 0 min to n = 14 at 110 min) and second (n = 3 at 0 min to n = 18 at 110 min) standing periods. The increase was not significant in the last period (n = 8 at 0 min to n = 16 at 55 min; Chi2 3.8, $p = 0.15$).

Fig. 5: Boxplots (Medians highlighted) of low back discomfort intensity ratings for all three standing periods (Exposure 1–3) in subjects with discomfort (n = 22).

Boxplots of the LBD ratings of the DD group are shown in Fig. 4. Within DD, discomfort intensity significantly increased with time ($F = 30.6$, $p < 0.001$) within each exposure period (exposure 1: median 0 to 2, exposure 2: median 0 to 2, exposure 3: median 0 to 2).

3.3. Lower back muscle (M. Erector spinae) activity

In general, muscular activity in the lower back was low, with a median activity less than 40% of the reference contraction (Fig. 5).

3.3.1. LBD groups

Data from p5-EA, p50-EA, and p95-EA for the left erector muscle for DD and NoDD are shown in Fig. 5. The only statistically significant main effect for the LBD groups was found for the p5-EA, which was higher in NoDD than in DD (11.7%$_{RVE}$ vs. 7.5%$_{RVE}$).

3.3.2. Exposure periods

The exposure period had a statistically significant association with low back muscle activity present in all SEMG variables (Table 2). Post hoc analysis indicated higher activities in exposure 1 compared to exposure 2 (left erector muscle: p5-EA = +2.5%$_{RVE}$, p50-EA = +5.7%$_{RVE}$, p95-EA = +9.6%$_{RVE}$; right erector muscle: p5-

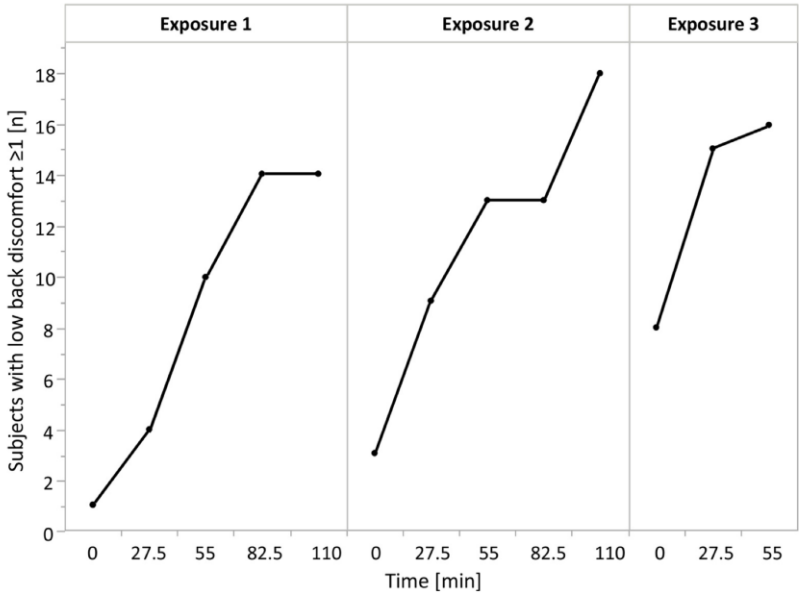

Fig. 3. Number of subjects with low back discomfort during Exposure 1 to 3 (n = 55).

Table 1
Number of subjects included in either 'discomfort developer' (DD) or 'non-discomfort developer' (NoDD) group based on their rating of lower back discomfort, separated by subgroups.

Subgroup	Younger female subjects < 35 years [n]	Younger male subjects < 35 years [n]	Older male subjects45 years [n]	Standing malesubjects (> 1 year of standing exposure at work) [n]	Total [n]
Discomfort developer	4 (31%)	3 (25%)	3 (25%)	8 (53%)	22 (40%)
Non-Discomfort Developer	9 (69%)	9 (75%)	9 (75%)	7 (47%)	33 (60%)
Total	13 (100%)	12 (100%)	12 (100%)	15 (100%)	55 (100%)

The distribution of DD and NoDD cases did not differ significantly between the four subgroups (Chi2 7.0, $p = 0.43$).

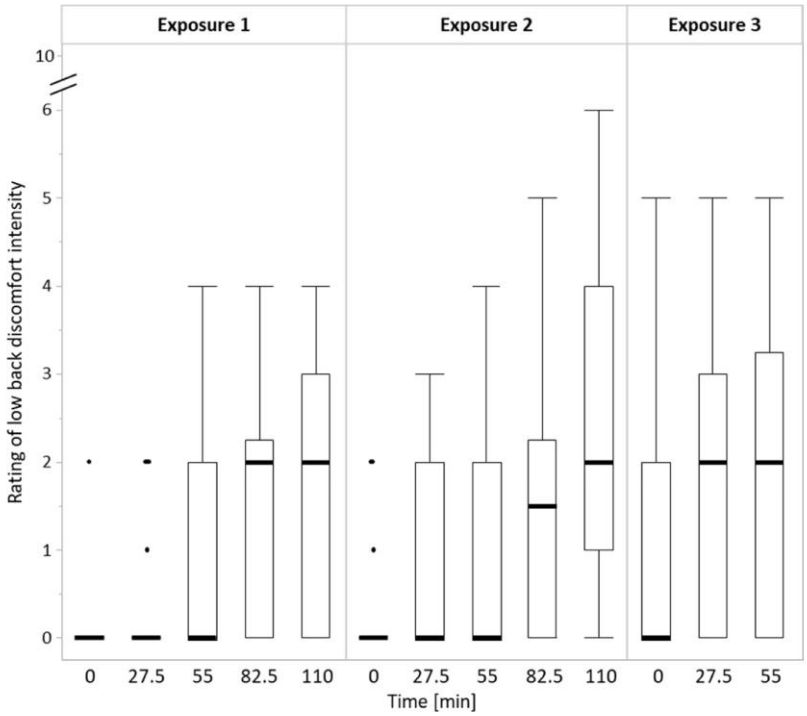

Fig. 4. Boxplots (Medians highlighted) of low back discomfort intensity ratings (0–10; 0 = no discomfort, 10 = highest imaginable discomfort) for all three standing periods (Exposure 1–3) in subjects with low back discomfort (n = 22).

EA = +1.4%$_{RVE}$, p50-EA = +6.6%$_{RVE}$, p95-EA = +9.2%$_{RVE}$). Additionally, EA was higher for all variables in exposure 1 than in exposure 3, except for the right p5-EA (left erector muscle: p5-EA = +2.8%$_{RVE}$, p50-EA = +7.3%$_{RVE}$, p95-EA = +25.5%$_{RVE}$; right erector muscle: p50-EA = +5.2%$_{RVE}$, p95-EA = +23.6%$_{RVE}$). These differences were statistically significant. Finally, p95-EA was 15.9%$_{RVE}$ and 14.4%$_{RVE}$ higher in the second exposure period compared to the third for the left and right erector muscles, respectively.

3.3.3. Progression within exposure periods

The progression within the exposure periods had a statistically significant main effect for p95-EA of the left and right erector muscles. It increased by 10.3%$_{RVE}$ and 9.6%$_{RVE}$ from the beginning to the end of an exposure period in the left and right erector muscles, respectively.

Neither subgroups, nor any interaction had further statistically significant impacts on muscle activation (Table 2).

3.3.3.1. Pelvic movement. Fig. 6 shows the interquartile ranges of pelvic movement in anterior/posterior and medio-lateral directions for NoDD and DD. Median interquartile ranges were between 3 and 5° for the anterior/posterior direction, and between 1 and 3° for the medio-lateral direction.

A statistically significant interaction was found between the LBD group and progression for the medio-lateral pelvic movement ($F = 7.4$, $p = 0.0009$). NoDD had a statistically significant increase in interquartile range from the beginning to the end of each period (difference 0.7°; $p < 0.0001$), which was not the case for DD (difference 0.2°; $p = 0.52$). No further statistically significant results were found with respect to the LBD groups.

Statistically significant main effects were found for the exposure period with smaller interquartile ranges of pelvic anterior/posterior movements in the first standing period than in the second (difference 0.7°; $p = 0.0003$), and the progression where the interquartile ranges at the beginning of each period were significantly lower than at the end for both anterior/posterior (difference 0.4°; $p = 0.0003$) and medio-lateral movements (difference 0.4°; $p < 0.0001$).

4. Discussion

The primary aim of this study was to investigate possible

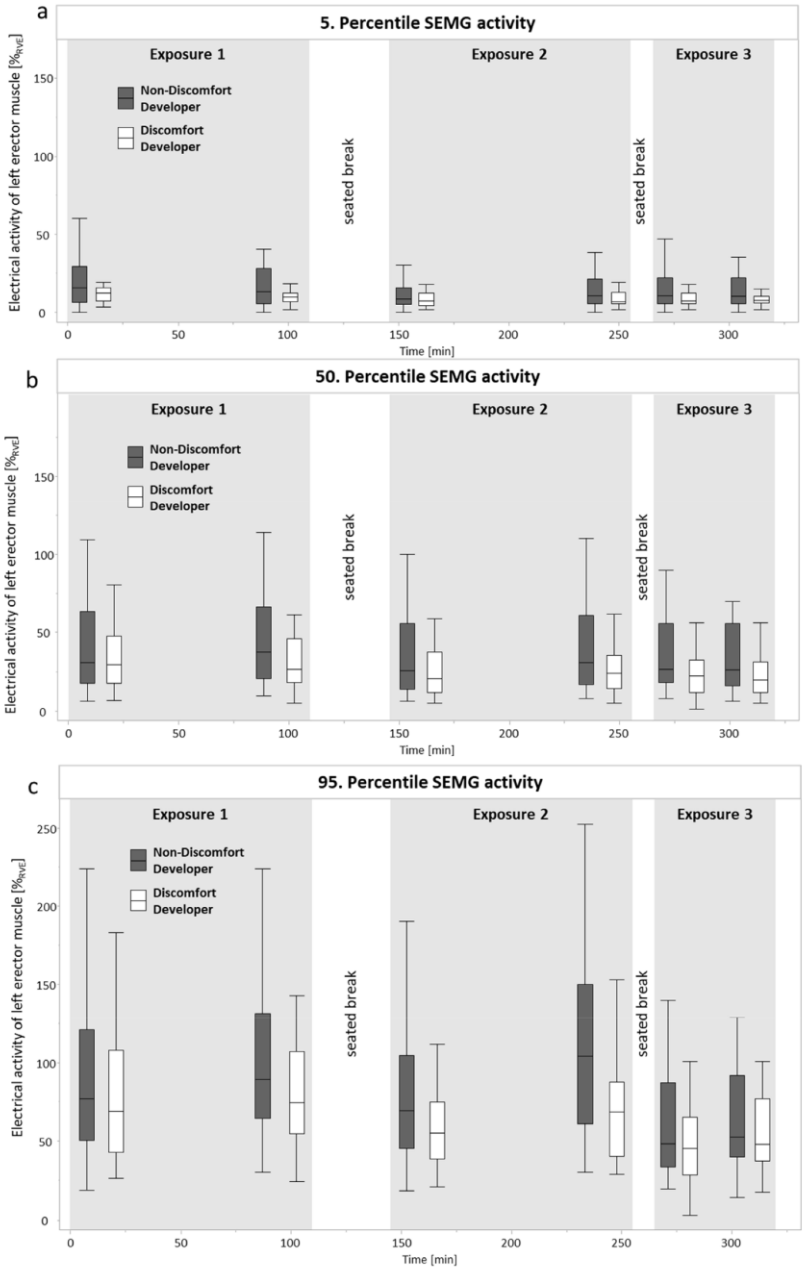

Figure 5. Boxplots of normalized ($\%_{RVE}$) 5th, 50^{th}, and 95th percentiles (p5-EA, p50-EA and p95EA) for left erector spinae muscle activity of the non-discomfort developer (a) and discomfort developer (b) at the beginning and end of each of the three standing periods (Exposure 1–3). RVE = reference voluntary electrical activation (n = 55).

associations between developing LBD during prolonged standing and low back muscle activity and pelvic movement in an exploratory approach. Our findings revealed that static standing for over 4 h induced LBD in 40% of the subjects who were subsequently considered discomfort developers. In this regard, the statistical analysis revealed an increase in low level back muscle activity (p5-EA) in the left erector muscle of about $4\%_{RVE}$ in NoDD compared to DD. Further, there was a statistically significant interaction between the factors LBD group and progression for pelvic medio-lateral movement, indicating a slight increase within the standing periods in NoDD compared to DD (about 0.5°

Table 2
F and p values for independent variables and interactions.

	LBD (yes/no)	Period	Progression	Subgroup	LBD x Progression	LBD x Subgroup	LBD x Period
Erector muscle activity (left)							
p5	**F = 5.1 p = 0.028**	**F = 14.8 p < 0.0001**	F = 1.4 p = 0.23	F = 1,8 p = 0.16	F = 1.4 p = 0.25	F = 0.2 p = 0.92	F = 0.4 p = 0.68
p50	F = 2.6 p = 0.11	**F = 19.5 p < 0.0001**	F = 0.7 p = 0.41	F = 2.5 p = 0.07	F = 2.0 p = 0.17	F = 0.8 p = 0.51	F = 1.1 p = 0.33
p95	F = 3.3 p = 0.08	**F = 33.1 p < 0.0001**	**F = 22.9 p < 0.0001**	F = 1.1 p = 0.35	F = 3.4 p = 0.07	F = 0.8 p = 0.48	F = 1.8 p = 0.18
Erector muscle activity (right)							
p5	F = 0.1 p = 0.77	**F = 4.2 p = 0.017**	F = 4.0 p = 0.051	F = 0.8 P = 0.48	F = 0.0 p = 0.87	F = 2.5 p = 0.07	F = 0.1 p = 0.87
p50	F = 0.0 p = 0.88	**F = 5.5 p = 0.005**	F = 1.5 p = 0.23	F = 0.6 P = 0.64	F = 1.3 p = 0.26	F = 1.3 p = 0.29	F = 0.1 p = 0.92
p95	F = 0.0 p = 0.91	**F = 24.3 p < 0.0001**	**F = 13.6 p = 0.0005**	F = 0.5 P = 0.69	F = 2.8 p = 0.1	F = 0.4 p = 0.78	F = 2.2 p = 0.11
Pelvic movement							
Interquartile range (posterior/anterior)	F = 1.4 p = 0.25	**F = 8.1 p = 0.0005**	**F = 10.9 p = 0.0017**	F = 0.5 p = 0.69	F = 3.7 p = 0.06	F = 0.4 p = 0.76	F = 1.0 p = 0.37
Interquartile range (medio-lateral)	F = 0.0 p = 0.85	F = 1.4 p = 0.26	**F = 23.6 p < 0.0001**	F = 0.5 p = 0.67	**F = 7.4 p = 0.009**	F = 0.1 p = 0.94	F = 0.9 p = 0.41

LBD = low back discomfort developers and non-discomfort developers; period = exposure period 1, 2, 3; progression = beginning and end of each exposure period; Subgroup = females younger than 35 years not habituated to standing (subgroup 1), males younger than 35 years not habituated to standing (subgroup 2), males between 45 and 67 years of age not habituated to standing (subgroup 3), males younger than 35 years habituated to standing (subgroup 4). P5 = 5th percentile normalized electrical activity; p50 = 50th percentile normalized electrical activity; p95 = 95th percentile normalized electrical activity.4.

higher interquartile range than in DD). In general, back muscle activity and pelvic movement were found to be rather low. Gender, age, or habituation to standing at work did not moderate these findings according to the subsample analysized in the present study.

In addition to these results, regardless of group, the standing period and the time progression within the standing period influenced several measures of lower back muscle activity and pelvic movement during 4.5 h of standing for all subgroups.

4.1. Low back discomfort

22 of our 55 subjects (40%) developed LBD while exposed to standing for four and a half hours. Only 15 subjects (out of 55, 27%) reported LBD in the first 110 min of standing. This is less than the number reported in previously conducted studies that exposed people to standing for 2 h or less and still had a percentage of 32–70% who developed low back pain (Aghazadeh et al., 2015; Nelson-Wong et al., 2008; Nelson-Wong and Callaghan, 2010). The main difference between those studies and our approach was how subjects were asked to rate discomfort/pain intensity levels. Nelson-Wong and collegues asked their subjects to draw a line on a 100 mm scale (Marshall et al., 2011; Nelson-Wong et al., 2008, 2012; Nelson-Wong and Callaghan, 2010, 2014, 2010), whereas we asked our subjects to rate their discomfort intensity verbally from zero to ten. Discomfort intensity levels may be different based on the rating method. In this regard, it was shown that these two approaches (VAS vs. NRS) lead to differences in absolute levels (Hasson and Arnetz, 2005; Menold and Bogner, 2016).

Although the statistical analysis revealed no significant differences between the DD to NoDD ratio in the four subgroups, our results indicate that the subgroups of young non-standing workers with a DD to NoDD ratio of 7 of 25 (28%; females: 4 of 13, 31%; males: 3 of 12, 25%) might have a lower risk of developing LBD compared to the older (8 of 15, 53%) and standing worker subgroups (7 of 15, 47%). Chronic LBP is considered to be more prevalent in females and older adults (Meucci et al., 2015). However, no gender differences occurred in our subsample of younger non-standing subjects (DD to No DD ration: younger male 31% vs. female 25%). The meta-analysis by Coenen et al. found that working in a standing position over 4 h per workday - which was the case for our standing worker subgroup – is associated with low back symptoms (Coenen et al., 2016). It is possible that occupational standing exposure already had an effect on these subjects, resulting in the tendency toward a higher proportion of DD compared to the younger non-standing worker subgroup (47% vs 28%), although both groups were previously symptom-free.

Discomfort intensity levels increased up to a median of two at the end of each of the three exposure periods, and decreased after the breaks back to a median of zero. This is similar to results for shorter standing periods in a previous study (Gallagher et al., 2014). DD may therefore benefit from short seated breaks during multiple hours of standing work, if they are implemented regularly. In their systematic review, Coenen et al. suggested refraining from standing for prolonged periods over 40 min (Coenen et al., 2017). In the present study, the number of subjects indicating LBD increased from four to ten between minute 27.5 and 55 in the first exposure period, which supports their hypothesis. Additionally, our study indicates that although seated breaks relieve LBD, LBD intensity increases more quickly after 110 and 220 min of static standing.

4.2. Low back muscle activity and pelvic movement in DD

The median erector spinae activity ranged from 20.9 to 39.1%$_{RVE}$ during the standing periods, and was similar between DD and NoDD. Low level muscle activity over long periods of time may lead to fatigue in type I muscle fibres due to a metabolic overload known as the 'Cinderalla hypothesis' (Hägg, 1991; Visser and van Dieën, 2006; Zennaro et al., 2003). A higher p5-EA of the lower back muscles during standing might indicate whether the muscles are at a higher risk of continuous activity without the possibility of rest, and therefore for LBD. However, this muscle activation profile was not found for the DD group. P5-EA levels were either similar (right erector muscle) or slightly higher (~4%RVE in the left erector muscle) in NoDD compared to DD ($F = 5.1$, $p = 0.028$).

Furthermore, an increase in p95-EA would indicate a greater range and more variability in muscle activity during standing, and thus a muscle activity profile preventing static muscle loading and blood flow restriction. Again, there was no difference between DD and NoDD.

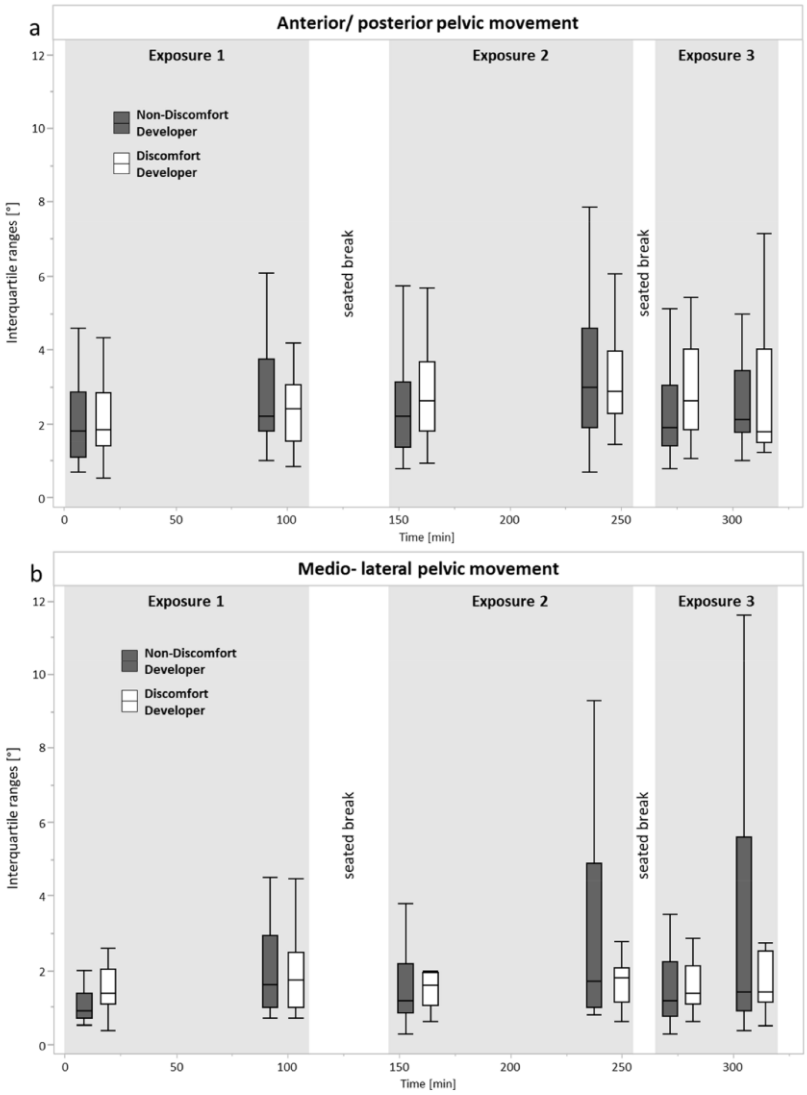

Fig. 6. Boxplots of interquartile ranges of the non-discomfort developers and discomfort developers in anterior/posterior (a) and medio-lateral pelvic (b) direction at the beginning and end of each of the three standing periods (Exposure 1–3; n = 55).

However, an increase in p95-EA (left and right erector muscles) and also in pelvic movements (both directions) occurred in both groups within the progression of the exposure periods. This increased muscle activity and movement may indicate that both groups followed the same strategy to reduce static posture, but that the DD group was somehow less effective than the NoDD group. This hypothesis is supported by the interaction between LBD group and progression, indicating an increase in pelvic movement (medio-lateral direction) for NoDD from the beginning to the end of the exposure periods, possibly protecting NoDD from developing LBD through more frequent and pronounced load changes from one leg to the other. This increased movement could be a strategy to reduce LBD similar to findings by Madeleine and Srinivasan and Mathiassen, 2012, who showed that increasing variation in repetitive movements can lower perceived discomfort for specific tasks (Madeleine, 2010; Srinivasan and Mathiassen, 2012). However, it is questionable whether dynamic, repetitive movements as analyzed in the mentioned studies can be compared with static standing. Furthermore, the difference in pelvic movement between the DD and NoDD was very small (0.5°), although this was well above the maximum repeatability error (0.12°) of the measuring device. However, this statistically significant difference must be interpreted carefully, since it is unclear whether such minor movement differences can be clinically relevant.

A different approach was taken by Nelson-Wong et al.,2008. They investigated co-contractions of trunk flexor-extensor muscles (lumbar erector spinae vs. internal/external oblique and rectus abdominis) and left vs. right gluteus medius muscles by calculating cross correlations of the SEMG activity. Trunk co-activation seemed to predispose pain

development in the first 30 min of standing with no significant differences between subjects with and without pain development in the following 90 min, whereas gluteus medius co-activation differed during the whole 2 h of standing (Nelson-Wong et al., 2008). The findings concerning gluteus medius co-activation were repeated in several subsequent studies from the same research group (Marshall et al., 2011; Nelson-Wong and Callaghan, 2010, 2014). Predicting pain or discomfort development is therefore more likely to be possible in altered muscle recruiting patterns for trunk and pelvis stabilization (left vs. right, agonist vs. antagonist) than in the investigated activity levels.

An important role in the development of low back pain has been attributed to structural (morphological) changes and adaptations of the activation patterns (Wong et al., 2014) of the deeper lumbar muscles (multifidus and transversus abdominis). However, these changes were shown for patients with existing LBP. It is unclear whether muscle adaptations can already be found in otherwise symptom-free individuals who develop LBD during prolonged standing, as in the present study.

Lower back kinematics were previously investigated in standing work using motion capture systems. Authors compared different footrest heights (Son et al., 2017), office workstations (Le and Marras, 2016), or sloped surfaces (Fewster et al., 2017; Gallagher et al., 2013; Gallagher and Callaghan, 2016). Further, Sorensen et al. investigated the connection between lumbar lordosis and subjects developing LBP during a 2 h standing period and found that the risk of developing LBP and its intensity increased with the angle of lumbar lordosis, which was evaluated prior to the standing exposure (Sorensen et al., 2015). Although lumbar lordosis angles were not specifically measured in the present study, they may have had an influence on the development of LBD.

4.3. Influence of gender, age, and habituation to standing work on low back muscle activity

No statistically significant differences between the four investigated subgroups were found. Neither gender in the younger subjects nor age or habituation to standing work in the male subjects had an influence on erector muscle activity or pelvic movements. Subgroup sizes may have been too small to show possible differences in the investigated variables.

4.4. Limitations

Several limitations of the present study have to be addressed. In this exploratory approach, comparisons between DD and NoDD, as well as the investigated subgroups, led to group sizes that may be too small to show possible associations. It may be possible to overcome this deficit in a subsequent study, where a sample size calculation with regard to meaningful effects would be possible based on the results of our present study. Further, the investigated sample only included young females and older males, which allowed comparisons regarding gender between the younger subgroups and regarding age in the male subgroups, only. Therefore, our findings are limited to those subgroups, which does not allow us to draw conclusions for older females or females habituated to standing work. The missing randomization of the tasks between the three periods might have led to order effects for which we cannot correct post-hoc. Finally, it is not possible to differentiate possible influences of the two breaks between exposures 1–3 and the tasks conducted within the standing periods.

5. Conclusion

Prolonged static standing led to LBD in about 40% of previously asymptomatic subjects. Further, our results indicate a small increase in medio-lateral pelvic movement in subjects that did not develop low back discomfort during 4.5 h of standing, which was not the case for the low back discomfort developer group. This might be a strategic starting point to help protect individuals from developing LBD. Interventions to increase pelvic movement may be beneficial to LBD developers. However, the clinical relevance of this finding needs further investigation due to the very small differences measured.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ergon.2019.07.001.

Declarations of interest

None.

References

Aghazadeh, J., Ghaderi, M., Azghani, M.-R., Khalkhali, H.-R., Allahyari, T., Mohebbi, I., 2015. Anti-fatigue mats, low back pain, and electromyography: an interventional study. Int. J. Occup. Med. Environ. Health 28 (2), 347–356. https://doi.org/10.13075/ijomeh.1896.00311.

Andersen, J.H., Haahr, J.P., Frost, P., 2007. Risk factors for more severe regional musculoskeletal symptoms: a two-year prospective study of a general working population. Arthritis Rheum. 56 (4), 1355–1364. https://doi.org/10.1002/art.22513.

Antle, D.M., Côté, J.N., 2013. Relationships between lower limb and trunk discomfort and vascular, muscular and kinetic outcomes during stationary standing work. Gait Posture 37 (4), 615–619. https://doi.org/10.1016/j.gaitpost.2012.10.004.

Balasubramanian, V., Adalarasu, K., Regulapati, R., 2009. Comparing dynamic and stationary standing postures in an assembly task. Int. J. Ind. Ergon. 39 (5), 649–654. https://doi.org/10.1016/j.ergon.2008.10.017.

Behennah, J., Conway, R., Fisher, J., Osborne, N., Steele, J., 2018. The relationship between balance performance, lumbar extension strength, trunk extension endurance, and pain in participants with chronic low back pain, and those without. Clin. Biomech. 53, 22–30. https://doi.org/10.1016/j.clinbiomech.2018.01.023.

Burden, A., 2010. How should we normalize electromyograms obtained from healthy participants? What we have learned from over 25 years of research. J. Electromyogr. Kinesiol. 20 (6), 1023–1035. https://doi.org/10.1016/j.jelekin.2010.07.004.

Chen, J.-C., Chang, W.-R., Shih, T.-S., Chen, C.-J., Chang, W.P., Dennerlein, J.T., Ryan, L.M., Christiani, D.C., 2004. Using exposure prediction rules for exposure assessment: an example on whole-body vibration in taxi drivers. Epidemiology 15 (3), 293–299.

Coenen, P., Parry, S., Willenberg, L., Shi, J.W., Romero, L., Blackwood, D.M., Healy, G.N., Dunstan, D.W., Straker, L.M., 2017. Associations of prolonged standing with musculoskeletal symptoms-A systematic review of laboratory studies. Gait Posture 58, 310–318. https://doi.org/10.1016/j.gaitpost.2017.08.024.

Coenen, P., Willenberg, L., Parry, S., Shi, J.W., Romero, L., Blackwood, D.M., Maher, C.G., Healy, G.N., Dunstan, D.W., Straker, L.M., 2016. Associations of occupational standing with musculoskeletal symptoms: a systematic review with meta-analysis. Br. J. Sports Med. https://doi.org/10.1136/bjsports-2016-096795. bjsports-2016-096795.

da Costa, B.R., Vieira, E.R., 2010. Risk factors for work-related musculoskeletal disorders: a systematic review of recent longitudinal studies. Am. J. Ind. Med. 53 (3), 285–323. https://doi.org/10.1002/ajim.20750.

Dankaerts, W., O'Sullivan, P.B., Burnett, A.F., Straker, L.M., 2007. The use of a mechanism-based classification system to evaluate and direct management of a patient with non-specific chronic low back pain and motor control impairment–a case report. Man. Ther. 12 (2), 181–191. https://doi.org/10.1016/j.math.2006.05.004.

Dionne, C.E., Dunn, K.M., Croft, P.R., 2006. Does back pain prevalence really decrease with increasing age? A systematic review. Age Ageing 35 (3), 229–234. https://doi.org/10.1093/ageing/afj055.

Fewster, K.M., Gallagher, K.M., Callaghan, J.P., 2017. The effect of standing interventions on acute low-back postures and muscle activation patterns. Appl. Ergon. 58, 281–286. https://doi.org/10.1016/j.apergo.2016.07.002.

Gallagher, K.M., Callaghan, J.P., 2016. Standing on a declining surface reduces transient prolonged standing induced low back pain development. Appl. Ergon. 56, 76–83. https://doi.org/10.1016/j.apergo.2016.03.014.

Gallagher, K.M., Campbell, T., Callaghan, J.P., 2014. The influence of a seated break on prolonged standing induced low back pain development. Ergonomics 57 (4),

555–562. https://doi.org/10.1080/00140139.2014.893027.
Gallagher, K.M., Nelson-Wong, E., Callaghan, J.P., 2011. Do individuals who develop transient low back pain exhibit different postural changes than non-pain developers during prolonged standing? Gait Posture 34 (4), 490–495. https://doi.org/10.1016/j.gaitpost.2011.06.025.
Gallagher, K.M., Wong, A., Callaghan, J.P., 2013. Possible mechanisms for the reduction of low back pain associated with standing on a sloped surface. Gait Posture 37 (3), 313–318. https://doi.org/10.1016/j.gaitpost.2012.07.020.
Garcia, M.-G., Läubli, T., Martin, B.J., 2015. Long-term muscle fatigue after standing work. Hum. Factors 57 (7), 1162–1173. https://doi.org/10.1177/0018720815590293.
Gregory, D.E., Callaghan, J.P., 2008. Prolonged standing as a precursor for the development of low back discomfort: an investigation of possible mechanisms. Gait Posture 28 (1), 86–92. https://doi.org/10.1016/j.gaitpost.2007.10.005.
Griffith, L.E., Shannon, H.S., Wells, R.P., Walter, S.D., Cole, D.C., Côté, P., Frank, J., Hogg-Johnson, S., Langlois, L.E., 2012. Individual participant data meta-analysis of mechanical workplace risk factors and low back pain. Am. J. Public Health 102 (2), 309–318. https://doi.org/10.2105/AJPH.2011.300343.
Hägg, G.M., 1991. Static Work Loads and Occupational Myalgia: A New Explanation Model - Part of Monograph.
Hasson, D., Arnetz, B., 2005. Validation and findings comparing VAS vs. Likert scales for psychosocial measurements. Int. Electron. J. Health Educ. 8.
Hermens, H.J., 1999. European Recommendations for Surface ElectroMyoGraphy: Results of the SENIAM Project. Roessingh Research and Development, Enschede, pp. 122.
Kuorinka, I., Jonsson, B., Kilbom, A., Vinterberg, H., Biering-Sørensen, F., Andersson, G., Jørgensen, K., 1987. Standardised Nordic questionnaires for the analysis of musculoskeletal symptoms. Appl. Ergon. 18 (3), 233–237.
Lamotte, T., Priez, A., Lepoivre, E., Duchêne, J., Tarrière, C., 1996. Surface electromyography as a tool to study the head rest comfort in cars. Ergonomics 39 (5), 781–796. https://doi.org/10.1080/00140139608964498.
Lang, J., Ochsmann, E., Kraus, T., Lang, J.W.B., 2012. Psychosocial work stressors as antecedents of musculoskeletal problems: a systematic review and meta-analysis of stability-adjusted longitudinal studies. Soc. Sci. Med. 75 (7), 1163–1174. https://doi.org/10.1016/j.socscimed.2012.04.015. 1982.
Le, P., Marras, W.S., 2016. Evaluating the low back biomechanics of three different office workstations: seated, standing, and perching. Appl. Ergon. 56, 170–178. https://doi.org/10.1016/j.apergo.2016.04.001.
Lee, J.Y., Baker, R., Coenen, P., Straker, L., 2018. Use of a footrest to reduce low back discomfort development due to prolonged standing. Appl. Ergon. 67, 218–224. https://doi.org/10.1016/j.apergo.2017.09.009.
Lötters, F., Burdorf, A., Kuiper, J., Miedema, H., 2003. Model for the work-relatedness of low-back pain. Scand. J. Work. Environ. Health 29 (6), 431–440.
Madeleine, P., 2010. On functional motor adaptations: from the quantification of motor strategies to the prevention of musculoskeletal disorders in the neck-shoulder region. Acta Physiol. 199 (Suppl. 679), 1–46. https://doi.org/10.1111/j.1748-1716.2010.02145.x.
March, L., Smith, E.U.R., Hoy, D.G., Cross, M.J., Sanchez-Riera, L., Blyth, F., Buchbinder, R., Vos, T., Woolf, A.D., 2014. Burden of disability due to musculoskeletal (MSK) disorders. Best practice & research. Clin. Rheumatol. 28 (3), 353–366. https://doi.org/10.1016/j.berh.2014.08.002.
Marshall, P.W.M., Patel, H., Callaghan, J.P., 2011. Gluteus medius strength, endurance, and co-activation in the development of low back pain during prolonged standing. Hum. Mov. Sci. 30 (1), 63–73. https://doi.org/10.1016/j.humov.2010.08.017.
McCulloch, J., 2002. Health risks associated with prolonged standing. Work 19 (2), 201–205.
Menold, N., Bogner, K., 2016. Design of Rating Scales in Questionnaires.
Meucci, R.D., Fassa, A.G., Faria, N.M.X., 2015. Prevalence of chronic low back pain: systematic review. Rev. Saude Publica 49. https://doi.org/10.1590/S0034-8910.2015049005874.
Nelson-Wong, E., Alex, B., Csepe, D., Lancaster, D., Callaghan, J.P., 2012. Altered muscle recruitment during extension from trunk flexion in low back pain developers. Clin. Biomech. 27 (10), 994–998. https://doi.org/10.1016/j.clinbiomech.2012.07.007.
Nelson-Wong, E., Callaghan, J.P., 2010. Is muscle co-activation a predisposing factor for low back pain development during standing? A multifactorial approach for early identification of at-risk individuals. J. Electromyogr. Kinesiol. 20 (2), 256–263. https://doi.org/10.1016/j.jelekin.2009.04.009.
Nelson-Wong, E., Callaghan, J.P., 2014. Transient low back pain development during standing predicts future clinical low back pain in previously asymptomatic individuals. Spine 39 (6), E379–E383. https://doi.org/10.1097/BRS.0000000000000191.
Nelson-Wong, E., Gregory, D.E., Winter, D.A., Callaghan, J.P., 2008. Gluteus medius muscle activation patterns as a predictor of low back pain during standing. Clin. Biomech. 23 (5), 545–553. https://doi.org/10.1016/j.clinbiomech.2008.01.002.
Pensri, P., Janwantanakul, P., Chaikumarn, M., 2009. Prevalence of self-reported musculoskeletal symptoms in salespersons. Occup. Med. (Oxf.) 59 (7), 499–501. https://doi.org/10.1093/occmed/kqp059.
Punnett, L., 2014. Musculoskeletal disorders and occupational exposures: how should we judge the evidence concerning the causal association? Scand. J. Publ. Health 42 (13 Suppl. l), 49–58. https://doi.org/10.1177/1403494813517324.
Son, J.-I., Yi, C.-H., Kwon, O.-Y., Cynn, H.-S., Lim, O.-B., Baek, Y.-J., Jung, Y.-J., 2017. Effects of footrest heights on muscle fatigue, kinematics, and kinetics during prolonged standing work. J. Back Musculoskelet. Rehabil. https://doi.org/10.3233/BMR-170798.
Sorensen, C.J., Norton, B.J., Callaghan, J.P., Hwang, C.-T., van Dillen, L.R., 2015. Is lumbar lordosis related to low back pain development during prolonged standing? Man. Ther. 20 (4), 553–557. https://doi.org/10.1016/j.math.2015.01.001.
Srinivasan, D., Mathiassen, S.E., 2012. Motor variability in occupational health and performance. Clin. Biomech. 27 (10), 979–993. https://doi.org/10.1016/j.clinbiomech.2012.08.007.
Tissot, F., Messing, K., Stock, S., 2005. Standing, sitting and associated working conditions in the Quebec population in 1998. Ergonomics 48 (3), 249–269. https://doi.org/10.1080/00140130512331326799.
Visser, B., van Dieën, J.H., 2006. Pathophysiology of upper extremity muscle disorders. J. Electromyogr. Kinesiol. 16 (1), 1–16. https://doi.org/10.1016/j.jelekin.2005.06.005.
Walker, B.F., 2000. The prevalence of low back pain: a systematic review of the literature from 1966 to 1998. J. Spinal Disord. 13 (3), 205–217.
Werner, R.A., Gell, N., Hartigan, A., Wiggerman, N., Keyserling, W.M., 2010. Risk factors for plantar fasciitis among assembly plant workers. PM&R 2 (2), 110–116.
Wittig, P., Nöllenheidt, C., Brenscheidt, S., 2013. Grundauswertung der BIBB/BAuA-Erwerbstätigenbefragung 2012: mit den Schwerpunkten Arbeitsbedingungen, Arbeitsbelastungen und gesundheitliche Beschwerden.
Wong, A.Y., Karppinen, J., Samartzis, D., 2017. Low back pain in older adults: risk factors, management options and future directions. Scoliosis Spinal Disord. 12, 14. https://doi.org/10.1186/s13013-017-0121-3.
Wong, A.Y.L., Parent, E.C., Funabashi, M., Kawchuk, G.N., 2014. Do changes in transversus abdominis and lumbar multifidus during conservative treatment explain changes in clinical outcomes related to nonspecific low back pain? A systematic review. J. Pain : Off. J. Am. Pain Soc. 15 (4). https://doi.org/10.1016/j.jpain.2013.10.008. 377.e1-35.
Zennaro, D., Läubli, T., Krebs, D., Klipstein, A., Krueger, H., 2003. Continuous, intermitted and sporadic motor unit activity in the trapezius muscle during prolonged computer work. J. Electromyogr. Kinesiol. 13 (2), 113–124.

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4.3 Research paper 3: Changes in lower leg oedema and gastrocnemius muscle activity during prolonged standing and walking considering age, gender and standing work experience

Prolonged standing leads to an orthostatic oedema increasing venous pressure which is a long-term risk factor for vascular diseases (Pfisterer *et al.*, 2014; Serralheiro *et al.*, 2017). Activating the muscle-venous pump can reduce swelling, but it is unknown to which extent this mechanism works when walking for multiple hours. Further, MSD of the lower legs might be due to continuous low-level activation of the calf muscles, leading to fatigue and thus complaints.

The third research paper investigates the effect of prolonged standing and walking on mentioned surrogate parameters.

The aims of research paper 3, relevant to this dissertation were:

- To investigate, if there is a difference between multiple hours of static standing and walking on lower leg oedema.
- To evaluate oedema progression during standing and walking.
- To examine if continuous low-level gastrocnemius muscle activity is present during multiple hours of standing and walking, as a possible explanation of lower leg muscle fatigue.

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ARTICLE

Physiological changes during prolonged standing and walking considering age, gender and standing work experience

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ABSTRACT

Occupational standing is associated with musculoskeletal and venous disorders. The aim was to investigate whether lower leg oedema and muscle fatigue development differ between standing and walking and whether age, gender and standing work habituation are factors to consider. Sixty participants (15 young females, 15 young males, 15 older males, and 15 young males habituated to standing work) were included and required to stand/walk for 4.5 hours in three periods with two seated breaks. Waterplethysmography/bioelectrical impedance, muscle twitch force and surface electromyography were used to assess lower leg swelling (LLS) and muscle fatigue as well as gastrocnemius muscle activity, respectively. While standing led to LLS and muscle fatigue, walking did not. Low-level medial gastrocnemius activity was not continuous during standing. No significant influence of age, gender and standing habituation was observed. Walking can be an effective prevention measure to counteract the detrimental effects of quasi-static standing.

Practitioner summary: Prolonged standing leads to lower leg oedema and muscle fatigue while walking does not. The primary cause of fatigue may be in other muscles than the medial gastrocnemius. Walking may be an effective prevention measure for health risks of occupational standing when included intermittently.

Abbreviation: BI: bioelectrical impedance; LLS: lower leg swelling; SEMG: surface electromyography; MTF: muscle twitch force; WP: waterplethysmography; Bsl: Baseline; L: Lunch; E: Evening; MTM: method times measurement; EA: electrical activity; IQR: interquartile range; p: percentile; M: mean; SE: standard error; Adj: adjusted

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KEYWORDS
Standing work; lower leg; surface electromyography; oedema; muscle twitch force; bioelectrical impedance

Background

Occupational standing is associated with a wide range of medical issues. Musculoskeletal complaints such as low back and lower leg pain, and venous disorders, such as varicosis or venous insufficiency have been associated with jobs requiring long hours of standing (Waters and Dick 2015; Coenen et al. 2017). About 50% of the workers in industrialised countries and across professions are required to stand for the larger part of their shift (Tissot, Messing, and Stock 2005; Wittig, Nöllenheidt, and Brenscheidt 2013; Graf et al. 2015). This provides an enormous potential for prevention measures to reduce the risk of the above-mentioned health impairments. The mechanisms behind lower leg musculoskeletal complaints during standing work are most probably related to restricted freedom of movement paralleled by continuous static muscle activity, which solicits primarily type I muscle fibres, and a decrease in blood flow over time, leading to muscle fatigue as previously shown for the upper extremities (Hägg 1991; Zennaro et al. 2003; Visser and van Dieën 2006). Several studies have evaluated muscle fatigue during prolonged standing work through measurements including muscle twitch force (Garcia, Läubli, and Martin 2015; Garcia et al. 2016) subjective perception of discomfort (Cham and Redfern 2001; Wiggermann and Keyserling 2013), and surface electromyography (Madeleine, Voigt, and Arendt-Nielsen 1998, Halim et al. 2012). Previous studies showed that muscle fatigue, and more specifically

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its long-lasting component, can be quantified by the decrease in amplitude and increase in duration of muscle twitch force induced by electrical stimulation at low frequency (Edwards et al. 1977; Adamo, Martin, and Johnson 2002; Adamo et al. 2009). Hence, the muscle twitch force (MTF) method applied at the ankle joint can serve to objectively measure muscle fatigue of the lower legs. Additionally, activity of a lower leg muscle (e.g. the gastrocnemius muscle) measured by surface electromyography (SEMG) would help to indicate whether its pattern of activation contributes to MTF changes.

Furthermore, an increase in lower leg oedema, which develops rapidly during static standing (Stick, Stofen, and Witzleb 1985), leads to an increase in circumferential stress of the venous walls (increased venous hypertension). This is believed to trigger pathophysiological remodelling processes (e.g. fibrosis and thickening of the venous wall, atrophy of elastic fibres) that can lead to varicose veins and chronic venous insufficiency (Segiet et al. 2015; Serralheiro et al. 2017; Mansilha and Sousa 2018). In addition, decreased hemodynamics can lead to pro-inflammatory responses, further contributing to venous wall remodelling (Pfisterer et al 2014, Mansilha and Sousa 2018). A commonly used surrogate measure for the development of venous diseases is the lower leg volume (Kanai, Haeno, and Sakamoto 1987; Hansen, Winkel, and Jørgensen 1998). The gold standard of volumetry is the so called waterplethysmography (WP) (Petersen et al. 1999; Henschke, Boland, and Adams 2006). However, this procedure is time consuming (Wall et al. 2017). Another approach uses the property of bioelectrical impedance (BI) which is based on frequency dependent electrical resistance changes due to variations in liquid quantity in the encompassed area (Kanai, Sakamoto, and Haeno 1983; Seo, Rys, and Konz 2001). The short measurement duration with this method allows estimation of the oedema progression over time.

Epidemiological data suggest an increase in risk of venous symptoms with age (Robertson et al. 2013) but data on gender differences are not conclusive. While some studies show a higher prevalence of venous disorders in females (Carpentier et al. 2004; Wrona et al. 2015), others found no differences (Evans et al. 1999; Robertson et al. 2013) or at least not for higher degrees of chronic venous insufficiency (Rabe et al. 2012).

Some studies have proposed walking as an intervention for prolonged standing work, as it may counteract the influence of pathophysiological pathways (Balasubramanian, Adalarasu, and Regulapati 2009; Garcia et al. 2016), mediating hemodynamic reduction and the increase in venous pressure. Continuous walking leads to an increase in lower leg blood flow and to an activation of the muscle-venous-pump, which to some extent counteracts the development of lower leg oedema (Stick, Grau, and Witzleb 1989). However, it is unclear whether walking can prevent the above-mentioned detrimental effects of static standing or aggravating/exacerbating effects associated with muscular fatigue and vascular outcomes. Other interventions, including sitting breaks (Gallagher, Campbell, and Callaghan 2014) and active breaks to alleviate muscle fatigue, discomfort and/or lower leg oedema induced by prolonged standing have been investigated (Balasubramanian, Adalarasu, and Regulapati 2009; Garcia, Laubli, and Martin 2018). In addition, studies related to prolonged standing work have not explored the potential difference between individuals habituated and not habituated to standing work and only a few have investigated age and gender differences during long hours of prolonged standing (e.g. Garcia, Läubli, and Martin 2015).

Hence, the present study attempted to address some gaps in the literature by testing the following questions in an explorative approach:

Primary question:

1. Can continuous slow pace walking on a treadmill and quasi-static standing be differentiated by lower leg oedema and muscle fatigue magnitudes?

Secondary questions:

2. Does habituation to prolonged standing work has an influence on oedema and muscle fatigue in the lower legs?
3. Are age and gender factors relevant in lower leg oedema and muscle fatigue development?
4. How high are the static and dynamic components and variability of gastrocnemius muscle activity during prolonged standing and walking?
5. Is there a correlation between muscle fatigue and static low-level gastrocnemius muscle activity?

Methods

Participants

Sixty healthy individuals participated in the present study. In order to investigate possible age and gender effects 15 young women, 15 young men and 15 older men who were non-standing workers (defined as: not required to stand for more than two hours per

working shift) were included. Another group of 15 male standing workers (defined as: required to stand for at least four hours per working shift, on at least four days per week, for at least one year) was also included to investigate possible habituation effects resulting from long term standing exposure. Exclusion criteria were: severe venous and musculoskeletal diseases (severe spine deformations such as hyperlordosis or scoliosis), age lower than 18 or higher than 67 and medication including diuretics, venotonics, vasodilatators, antihypertensive drugs or analgesics and pregnancy for females. Inclusion criteria were age range18–30 for the younger groups and 45–67 for the older group. The study was approved by the local ethics committee of the Medical Faculty, University of Tuebingen. All participants signed informed consent prior to investigations and received financial compensation for their participation.

Two participants did not complete the experiments due to circulatory problems. Further exclusions are mentioned in the respective measurement procedures. Anthropometric data of all included participants are shown in Table 1.

Procedure

All participants took part in both a standing and walking 'workday' in the laboratory (in randomised order), each including three different tasks (1: assembling pens, 110 min; 2: watching movies, 110 min; 3: playing video games, 55 min). The mandatory break between the two experimental conditions was two to seven days. Each workday included a 35 min seated lunch break between tasks 1 and 2, and a 10 min seated break between tasks 2 and 3. Hence, the total work time was 4 hours and 35 minutes, the complete workday duration was 5 hours and 20 min (Figure 1).

A sixty-minute seated recovery period was provided at the end of the workday after task 3. Task contents were selected to prevent boredom while avoiding significant upper limb exertion. Walking was conducted on a treadmill with speed determined as a function of height and gender using the methods-time measurement (MTM) approach (Britzke 2014). Since the MTM speed recommendation does not consider working while walking it was reduced by 50% to maintain participants task performance (MacEwen, MacDonald, and Burr 2015). Measurements started in the morning between 8 and 9 am. First, in- and exclusion criteria were assessed. Before the experiment, the lower leg side for measurements was randomly selected (BI, MTF and SEMG on one side, WP on the other side). A submaximal reference activation of the gastrocnemius muscle was used for normalisation of electromyographic data. For this reference contraction, the lower leg was fastened in a custom-designed restraining device equipped with a force sensor (Figure 2).

The participant was required to exert constant plantar flexion (push downward with the ball of the foot) of 25 N for 20 s. The median of the most stable 10 s period was used for SEMG normalisation. Visual force feedback was provided on a computer screen placed next to the foot.

Table 1. Anthropometric data of included participants for each of the four groups.

Group	Younger females $n=15$	Younger males $n=15$	Older males $n=15$	Standing worker males $n=15$
Age	24 ± 4 years	24 ± 3 years	52 ± 6 years	25 ± 4 years
Height	165 ± 6 cm	183 ± 4 cm	179 ± 8	182 ± 8 cm
Weight	59 ± 7 kg	76 ± 5	75 ± 7 kg	83 ± 11 kg

Figure 2. Reference contraction of the gastrocnemius muscle. The 25 N plantar flexion was maintained constant for 20 s. Force feedback was presented on a visual display next to the foot.

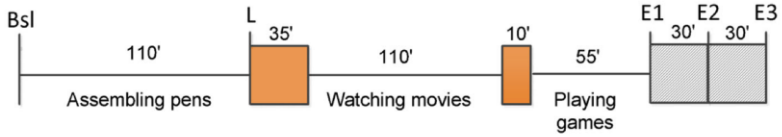

Figure 1. Workday schedule. The horizontal lines represent the working periods (standing or walking) with their respective tasks (1 = assembling pens, 2 = watching a movie or reading, and 3 = playing video games), and the boxes represent the rest breaks. Muscle twitch force and bioelectrical impedance metrics were obtained at times Bsl (baseline), L (beginning of lunch break), E1 (immediately after last work period), E2 (30 min after last work period), and E3 (1 hr after last work period). SEMG was measured continuously until E1 and waterplethysmography only at Bsl and E1.

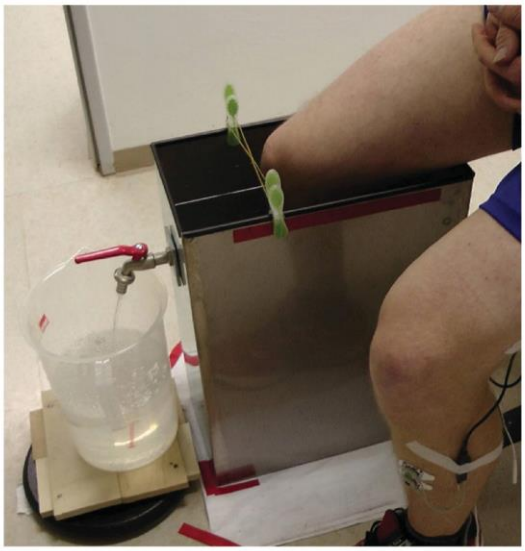

Figure 3. Experimental setup for waterplethysmography measures.

Measurements

Lower leg volume

Waterplethysmography

Waterplethysmography (WP), based on the Archimedean principle of water displacement, was used to measure the lower leg volume in ml. Figure 3 shows the water tank and leg posture. The setup and measurement procedure were validated in terms of test-retest reliability and inter-rater reliability and detailed in a previous study (Wall et al. 2017). The volume of the selected lower leg was measured immediately before the first and immediately after the last work periods (at Bsl and E1).

Bioelectrical impedance

Bioelectrical impedance (BI) measurements were conducted with a four-electrode setup as detailed in Wall et al. (2017). Two stimulation electrodes through which a constant low-intensity current (1 ms square pulse duration at a frequency of 13 Hz with a 300 µA intensity) was applied and two additional electrodes, which measured resulting voltage between stimulation electrodes (see Figure 4), were placed on the selected lower leg. An impedance decrease is related to a leg volume increase (oedema), which is measured by a decrease in voltage. The sampling frequency was 370–372 Hz which allows estimation of intercellular liquid distribution changes (Cole 1972; Kanai, Haeno, and Sakamoto 1987). In contrast to WP, BI

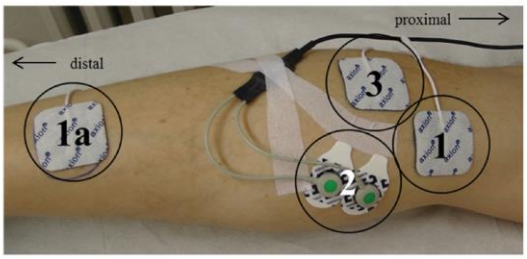

Figure 4. Electrodes setup for bioelectrical impedance (BI), muscle twitch force (MTF) and surface electromyography (SEMG) measures. 1 and 1a = stimulation electrodes for BI, 2 = measuring electrodes for BI and SEMG, 3 and 1a = Stimulation electrodes for MTF measurement.

measurements take only 20 s while participants sit relaxed on a chair. Details of this validated measurement procedure and data processing can be found in Wall et al. (2017). In comparison to WP, BI can be measured rapidly and without a change in posture. Hence, BI was measured before (Baseline, Bsl) and after (at Lunch, L) the first period, after the third period (Evening 1, E1), as well as 30 min (Evening 2, E2) and 60 min (Evening 3, E3) after the third work period (five measurements in total) to determine the course of oedema development (see Figure 1 for timeline). Changes in lower leg volume (LLV) are expressed in percent of the initial value measured at the baseline.

Gastrocnemius muscle twitch force and activation

Muscle twitch force

MTF was quantified in a seated relaxed posture by electrical stimulation of the gastrocnemius and soleus muscles (1 ms pulse, constant current ranging from 10 to 30 mA) at a frequency of 2 Hz through a Digimeter LTD stimulator (DS7A) and a pulse generator (DG2A). The procedure was detailed in previous work (Garcia, Läubli, and Martin 2015; Garcia et al. 2016; Garcia, Laubli, and Martin 2018). Briefly, the foot was positioned in a zero degree ankle dorsiflexion angle and resting on a fixed plate connected to a force sensor. The stimulation electrodes were placed in the area corresponding to the elicitation of the largest twitch force, the cathode close to the motor point (Botter et al. 2011) and anode over the upper part of the Achilles tendon. The stimulation intensity was selected individually for each participant based on the most tolerable discomfort with the largest twitch force and it remained constant for all measurements. The induced plantar flexion twitch force was measured by

the strain gauge placed under the foot pedal at the level of the distal part of the ball of the foot.

For each participant, the stimulated leg was randomly selected and strapped during the stimulation for isometric measurement. Twitch force amplitude and duration (contraction time + ½ relaxation time) were computed in real-time by a custom software based on LabVIEW (National Instruments Corp., USA). The force signal was sampled at 1000 Hz. MTF was quantified by the average over three series of 30 twitches with a coefficient of variation <3% obtained during the steady state period after electrically induced potentiation (Garcia et al. 2016; Kim and Johnson 2014). Each MTF measurement period lasted about 3 to 4 minutes.

Surface electromyography

A common method to assess muscle activity is bipolar SEMG. Two pre-gelled Ag/AgCl surface electrodes (Covidien™, Kendall™ ECG electrodes H93SG, inter-electrode distance: 25 mm) were placed, as recommended by SENIAM (Hermens 1999), on the medial gastrocnemius muscle of the selected leg. The SEMG signals were amplified, bandpass filtered (4th order high pass at 16 Hz; 10th order low pass at 650 Hz), sampled at 2048 Hz and recorded by a combined data analyser and logger (PS11-UD®, THUMEDI GmbH & Co. KG, Thum, Germany). Data were real-time transformed into the frequency domain (1024-point Fast Fourier Transform using a Bartlett-window with 50% overlap), and digitally high-pass filtered (11th order at 16 Hz); power line interference (50 Hz and first seven harmonics) was replaced by the spectral values of a 2 Hz wide band signal around its centre frequency corresponding to the means of both spectral neighbours. Finally, the root-mean-square of the EMG (EA, [μV]) was computed in real-time and stored synchronously to the raw data.

SEMG were recorded continuously throughout each workday (standing and walking) and split into three working periods (see Figure 1). Of each working period, the first and last 20 min (excluding the first and last 5 min of each period to avoid transients) were used for data analysis. The 5th and 95th (p5-EA and p95-EA) percentiles and the interquartile ranges (IQR) of the EA were calculated and expressed in a percent of the reference EA. The reference EA was determined by the median activity of a stable ten-second period during the submaximal reference contraction. p5-EA represents the static, low-level, muscle activity, while p95-EA represents the peak activity. The dynamic activity is represented by the IQR (Wall et al. 2019). These specific values were computed to contrast standing and walking muscle activity, and possible changes associated with muscle fatigue.

Statistical analyses

The MTF, WP, SEMG and BI dependent variables were analysed using mixed models in JMP 13 (SAS Inc. Cary, NC, USA) and SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Statistical significance was set to $\alpha = 0.05$. Since in standing 83 p5-EA values were negligible the values were dichotomised into 0 (no measurable activity) and 1 (some activity). Only one measurement corresponded to 0 in walking. Hence, the two conditions were separately analysed: a linear mixed model for standing and a mixed model based on logits for walking.

Data normal distributions were verified by rating histograms, skewness and kurtosis (Kim 2012; 2013). Not normally distributed data were log-transformed. Experimental condition (standing vs. walking), group [(a) young females, (b) young males, (c) old males (d) young males habituated to standing work] and time (only for MTF and BI; five measurements at B, L, E1, E2 and E3) were considered as fixed factors. Participants and day (within participant) were added as random factors in all cases. Two-way and three-way interactions were also tested for BI and MTF followed by Sidak *post-hoc* tests corrected for multiple comparisons. Measurements were graphically represented as a percentage of baseline only to facilitate visualisation of the results.

For the statistical analysis of the SEMG data, the p5-EA, p95-EA and IQR where computed for 15 min periods at the beginning and end of each standing and walking period (total of six values). The fixed factors of condition (standing or walking), group and time, and their interactions were calculated. As in the analysis of MTF, participants and day (within participant) were added as random factors.

Additionally, Spearman correlations between signs of fatigue (MTF amplitude) at E1 and p5_EA were separately calculated for the standing and walking conditions over the respective six periods. Correlations between fatigue (MTF) at E1 and mean IQR were also calculated.

Results

Lower leg oedema

Waterplethysmography

Fifty-seven participants were included in the analysis. Data were missing for two participants (one for each

condition). In addition, one subject was excluded due to movement induced water spillage.

The mixed model indicated a statistically significant effect of condition (standing vs. walking, $F = 173.7$, $p < .0001$). LLV increased from baseline to E1 by 3.6 % (~116 ml) after standing. However, the increase in LLV was only 0.03 % (~1 ml) after walking. Differences between age and gender groups were not statistically significant.

Bioelectrical impedance

Fifty full datasets (standing and walking) could be analysed. Additionally, four datasets included only data corresponding to the standing experiment and five included only data corresponding to walking. Exclusions were made due to signal corruptions identified by visual inspection. As it was not normally distributed, BI Data were log transformed for the statistical analysis (see Table 2).

Table 2. Mixed model for bioelectrical impedance including the factors Time (five measurements), Group (young male, young female, older male, young male habituated to standing), Condition (standing and walking) and their interactions.

Source	df	F ratio	*p*
Time	4	92.2	**<0.0001***
Group	3	0.6	0.6
Condition	1	53.8	**<0.0001***
Condition × Time	4	123.9	**<0.0001***
Group × Condition	3	3.9	**0.016***
Group × Time	12	1.9	**0.038***
Group × Condition × Time	12	2.4	**0.006***

Note. Bold font and *indicate significant values, $\alpha = 0.05$.

The only statistically significant interaction effect was observed for Condition × Group × Time ($p = 0.006$); which indicated that BI was only significantly lower ($p = 0.045$) at E3 than Bsl in the walking condition for young individuals habituated to standing.

For the standing condition, all two-way interactions were significant (Condition × Time; Group × Condition; Group × Time). Condition × Time revealed significant (L, E1-3; $p < 0.0001$) differences between baseline and all other measurement times. The Condition × Time interaction revealed significant ($p < 0.0001$) differences between baseline and L, E1, E2 and E3. Finally, *post-hoc* analysis showed no significant Group x Condition and Group × Time interaction. No significant effect was observed in the walking condition. Results corresponding to the two conditions are illustrated in Figure 5.

Lower leg muscle fatigue and activation

Muscle twitch force

The mixed model analysis (Table 3) revealed that the main effects of Time, Condition and Group were statistically significant for twitch amplitude and duration. The Condition × Time and Group × Time two-way interactions were significant for both measures, while the Group × Condition interaction was significant only for twitch duration. However, the three-way interaction, Group × Condition × Time, was not significant for either twitch amplitude or duration.

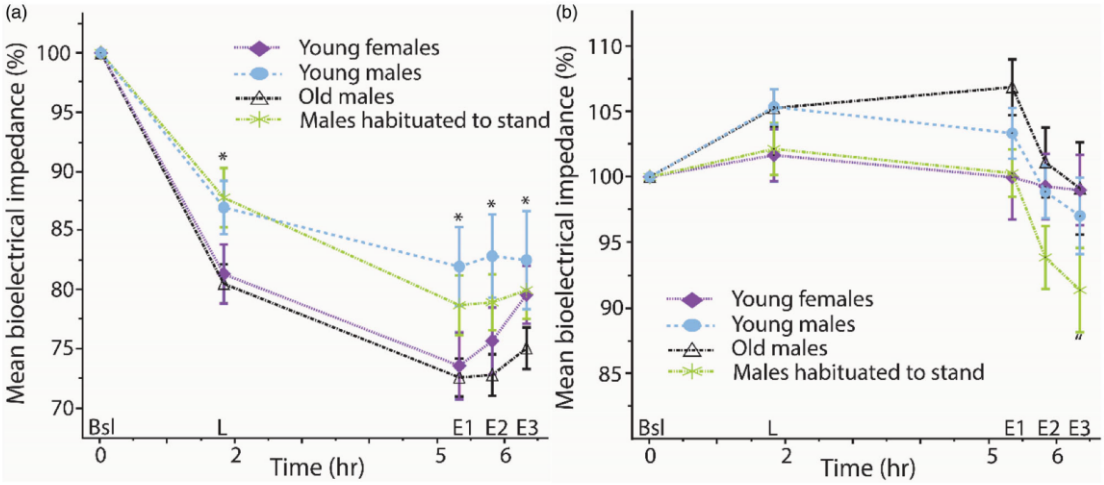

Figure 5. Changes in bioelectrical impedance for all groups relative (%) to baseline (Bsl) at lunch time (L), in the evening (E1) and after 30- and 60-min recovery (evening 2 and 3, E2 and E3) when (a) standing and (b) walking. Vertical bars indicate standard errors. *indicate a significant difference for all groups when compared with Bsl and quotation mark (") a significant difference for the corresponding group, when compared with Bsl.

Table 3. Mixed model for muscle twitch force (MTF) amplitude and duration with the factors Time (five measurements), Group (young male, young female, older male, young male habituated to standing), Condition (standing and walking) and their interactions.

	MTF amplitude			MTF duration		
Source	df	F ratio	*p*	df	F ratio	*p*
Time	4	74.9	**<0.0001***	4	142.1	**<0.0001***
Group	3	3.6	**0.013***	3	5.2	**0.002***
Condition	1	28.7	**<0.0001***	1	70.6	**<0.0001***
Condition × Time	4	19.5	**<0.0001***	4	16.5	**<0.0001***
Group × condition	3	0.6	0.62	3	3.5	**0.017***
Group × time	12	4.2	**<0.0001***	12	1.8	**0.048***
Group × condition × time	12	1.6	0.11	12	0.2	0.99

Note: Bold font and *indicate significant values, $\alpha = 0.05$.

MTF in standing condition

In the standing condition, *post-hoc* analysis revealed that twitch amplitude was significantly lower at E1, E2 and E3 than at baseline for young females, young males and older males, while it was only smaller at E2 and E3 than at baseline for males habituated to standing work (Table 4).

However, for all male groups twitch amplitude was significantly lower ($p = <0.0001$) at E1 than L. In this condition, twitch duration was significantly higher for all groups at E1, E2 and E3 when compared to baseline. However, at L the relative difference to Bsl was significant for all groups except the older males (Table 4). The corresponding results are illustrated in Figure 6.

MTF in walking condition

In the walking condition, *post-hoc* analysis revealed that twitch amplitude was significantly higher for older males at L and significantly lower for males habituated to standing work at E3 when compared to baseline (Table 5).

Moreover, for older males and males habituated to standing, twitch amplitude was significantly lower (Adj *p*-value <0.0001) at E2 and E3 when compared to L, while it was only lower at E3 for young males. Twitch duration was significantly higher at E3 for all groups, and at E2 for young females and young males, when compared to baseline (Table 5). Corresponding results are illustrated in Figure 7. Please note that scales are not identical in Figures 6 and 7 to preserve visual representation of significant effects.

Surface electromyography

Forty-nine full datasets (standing and walking) were analysed in the final model. Additionally, data available from five participants only for standing and from

Table 4. Change in twitch force over time during the standing condition for each group.

Standing condition: Mean (M) relative changes of muscle twitch force (MTF) measures (standard error, SE) over time given in % of baseline, including adjusted (Adj) *p*-value when compared to baseline

		L		E1		E2		E3	
MTF	Group	M(SE)%	Adj *p*-value	M(SE)%	Adj *p*-value	M(SE)%	Adj *p*-value	M(SE)%	Adj *p*-value
Amplitude	Young females	83.95 (6.9)	0.23	67.7 (6.9)	**0.0001***	67.1 (6.9)	**0.0001***	67.6 (6.9)	**0.0002***
	Young males	100.10 (5.83)	1	83.7 (5.8)	**0.02***	78.3 (5.8)	**0.002***	72.6 (6.0)	**<0.0001***
	Old males	113.85 (6.05)	1	62.5 (6.1)	**<0.0001***	54.6 (6.1)	**<0.0001***	49.8 (6.1)	**<0.0001***
	Young habituated to standing work	115.13 (5.64)	1	84.3 (5.6)	0.13	77.6 (5.6)	**0.003***	67.8 (5.6)	**<0.0001***
Duration	Young females	113.81 (2.81)	**0.005***	115.8 (2.8)	**0.0002***	121.7 (2.8)	**<0.0001***	125.5 (2.8)	**<0.0001***
	Young males	110.10 (2.38)	**0.003***	111.8 (2.4)	**0.004***	119.6 (2.4)	**<0.0001***	126.2 (2.5)	**<0.0001***
	Old males	106.25 (2.47)	0.72	108.5 (2.5)	**0.003***	115.7 (2.5)	**<0.0001***	124.6 (2.5)	**<0.0001***
	Young habituated to standing work	112.76 (2.29)	**0.0004***	111.1 (2.3)	**0.01***	116.0 (2.3)	**<0.0001***	123.6 (2.23)	**<0.0001***

Note. Bold font and *indicate significant values, $\alpha = 0.05$.

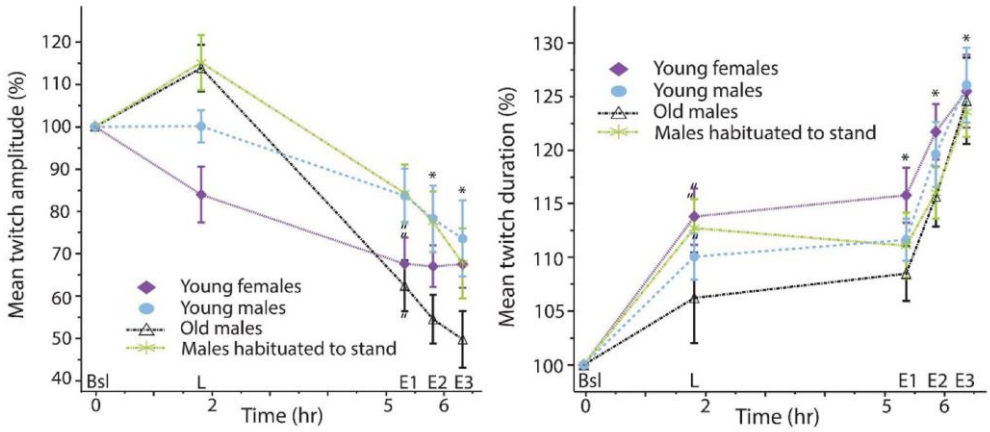

Figure 6. MTF in standing condition. Changes in muscle twitch force amplitude and duration (% baseline reference, Bsl) at lunch time (L), in the evening (E1) and after 30- and 60- min recovery (evening 2 and 3, E2 and E3). Vertical bars indicate standard errors. *indicates a significant difference for all groups, and quotation mark (") a significant difference for the corresponding group, when compared with Bsl.

three participants only for walking were included into the statistical model. Excluded outlying data were related to sensor displacement or contact loss (e.g. due to sweating). Data were log transformed due to non-normal distribution. As p5-EA was negligible for several participants a signed rank test was used to test for differences between standing and walking conditions.

All the SEMG parameters were significantly lower in the standing than the walking condition (p5-EA: $F = 446.5$, $p < 0.0001$; p95-EA: $F = 888.8$, $p < 0.0001$; IQR: $F = 1334.1$, $p < 0.0001$), as illustrated in Figure 8. The only statistically significant interaction, Condition × Time, was found for the p95-EA with lower activity at the beginning of the second standing period compared to the end of the first and the second period ($F = 2.5$, $p = 0.028$). Age and gender group differences were not statistically significant for any parameter (p5-EA standing: $F = 1.3$, $p = 0.27$; p5-EA walking: $F = 1.3$, $p = 0.29$; p95-EA: $F = 0.5$, $p = 0.72$; IQR: $F = 0.5$, $p = 0.68$).

Correlations between the p5-EA or the IQR and the MTF amplitude at E1 in both the standing (p5-EA: $r = 0.2$, $p = 0.17$; IQR: $r = 0.15$; $p = 0.31$ and walking (p5-EA: $r = -0.05$, $p = 0.73$; IQR: $r = 0.004$; $p = 0.98$) condition were not statistically significant.

Discussion

Lower leg oedema

Both WP and BI showed that lower leg oedema developed in the standing condition but not during the walking condition. This finding is in line with previous results obtained with similar measures (Belczak et al. 2009; Karimi et al. 2016; Garcia, Laubli, and Martin 2018). While WP measures the whole LLV including venous blood pooling, BI measures only intercellular liquid distribution, as a frequency spectrum below 1 kHz was used. According to the Cole model (Cole 1972; Kanai, Haeno, and Sakamoto 1987; Jaffrin and Morel 2008), in this frequency range current flows mainly through extra-cellular fluid due to the high impedance of cell membranes. However, the advantage of the corresponding quick measurement time allowed multiple measures during and after the end of the workday such that the oedema progression could be documented. As illustrated in Figure 6, oedema progression (BI decrease) is higher from Bsl to L (110 min of standing) than from L to E1 (165 min of standing). This shows a fast increase in LLV in the first two hours of standing which subsequently slows down. This profile corresponds to an exponential evolution of LLV in static standing.

Furthermore, the oedema persists at least one-hour post-work when remaining seated. The change from standing to sitting does not seem to be sufficient/efficient enough to reduce the orthostatic pressure and associated detrimental effects. This is similar to the development of oedema when remaining seated and epidemiological data indicating that not only prolonged standing but also sitting is associated with a higher risk for venous disorders, although to a lesser extent (Lacroix et al. 2003; Sudol-Szopinska et al. 2011).

Our result also shows that walking at a slow speed of 2.3 km/h max prevents the development of lower

Table 5. Change in twitch force over time during the walking condition for each group.

		Walking condition: Mean (M) relative changes of muscle twitch force (MTF) measures (standard error, SE) over time given in % of baseline, including adjusted (Adj) *p*-value when compared to baseline							
		L		E1		E2		E3	
MTF	Group	M(SE)%	Adj *p*-value	M(SE)%	Adj *p*-value	M(SE)%	Adj *p*-value	M(SE)%	Adj *p*-value
Amplitude	Young females	111.72 (6.9)	0.995	107.34 (6.9)	1	103.18 (6.9)	1	106.88 (6.9)	1
	Young males	109.70 (5.83)	0.995	105.38 (5.83)	1	95.26 (5.83)	0.999	88.82 (5.83)	0.942
	Old males	153.67 (6.24)	**0.0004***	131.31 (6.24)	0.224	107.18 (6.24)	1	90.48 (6.05)	0.999
	Young habituated to standing work	116.78 (5.64)	0.502	104.87 (5.64)	1	87.15 (5.64)	0.346	74.31 (5.64)	**0.0002***
Duration	Young females	101.35 (2.81)	1	103.67 (2.81)	1	110.74 (2.81)	**0.012***	115.41 (2.81)	**0.0006***
	Young males	97.08 (2.38)	0.994	97.72 (2.38)	1	109.24 (2.38)	**0.009***	117.95 (2.38)	**<0.0001***
	Old males	95.06 (2.55)	0.727	94.88 (2.55)	0.537	106.76 (2.55)	0.420	115.49 (2.47)	**<0.0001***
	Young habituated to standing work	98.78 (2.29)	1	98.49 (2.29)	1	106.85 (2.29)	0.214	116.63 (2.29)	**<0.0001***

Note. Bold font and *indicate significant values, $\alpha = 0.05$.

leg oedema (Figure 5), which is most likely due to the activation of the muscle-venous-pump. Voluntary dynamic activation of leg muscles appears to be more efficient than other interventions aimed at reducing leg oedema (and therefore venous hypertension) such as unstable support (Madeleine, Voigt, and Arendt-Nielsen 1997; Karimi et al. 2016), compression stockings (Partsch, Winiger, and Lun 2004; Mosti and Partsch 2013) or intermittent exercise (Uda, Seo, and Yoshinaga 1997). However, continuous walking is rarely applicable in occupational settings and may not be compatible with a number of work tasks. Therefore, it is necessary to investigate how insertion of short walking/dynamic periods between static standing periods influences LLV. Both the frequency and proportion of standing and walking alternations should be investigated to find the most effective pattern to reduce venous hypertension and increase blood flow in order to counteract pathophysiological mechanisms of venous disorders. This is of particular interest since walking may also contribute to the reduction of muscle fatigue, as observed here and in a previous study (Garcia et al. 2016).

No substantial influence of age, gender or standing habituation was found. The only significant effect was seen for the young males habituated to standing work, after the walking condition. They were the only group that showed a significant increase in LLV after one hour of seated rest following the walking condition. This may indicate disruption of the vascular system (e.g. weakened venous valves); whereas, walking may have attenuated the increase in LLV when compared to standing (Figure 5).

Lower leg muscle fatigue

In the standing condition, muscle fatigue indicated by the decrease in MTF amplitude and increase in duration was significant for all groups immediately after or within 30 min of prolonged standing work and persisted for at least an hour post-work. In the walking condition, the muscle fatigue stage is particularly noteworthy as the twitch amplitude decreases and/or duration increases only appear 30 min post-work, regardless of the groups characteristics (see Figures 6, 7). This delayed fatigue phenomenon has been previously observed and explained. Earlier studies showed that muscle fatigue can be evidenced by the decrease in amplitude and increase in duration of muscle twitch force induced by electrical stimulation at low frequency (Edwards et al. 1977; Adamo, Martin, and Johnson 2002; Adamo et al. 2009). However, before a

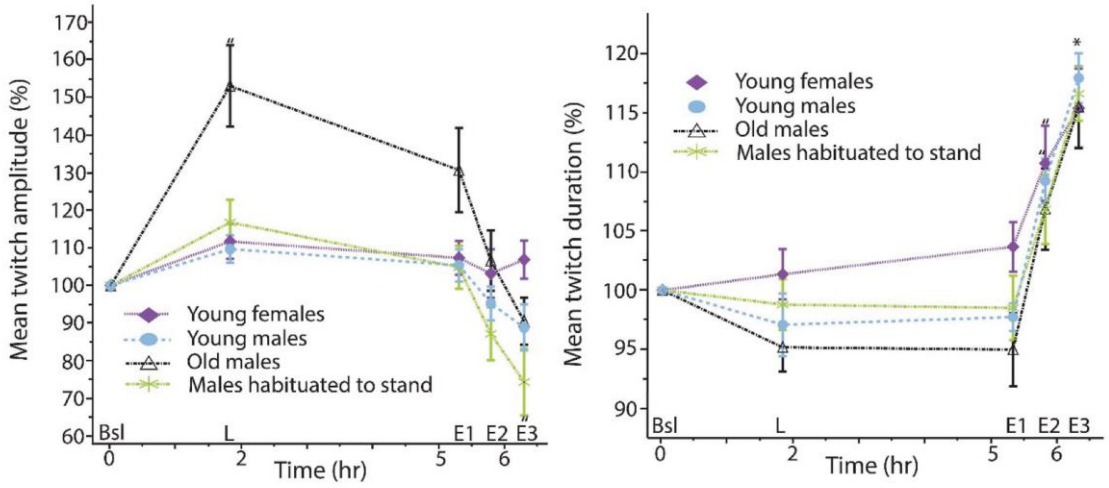

Figure 7. MTF in walking condition. Changes in muscle twitch force amplitude and duration (% of baseline reference, Bsl) at lunch time (L), in the evening (E1) and after 30- and 60-min recovery (evening 2 and 3, E2 and E3). Vertical bars indicate standard errors. Asterisk (*) indicates a significant difference for all groups and quotation mark (") a significant difference for the corresponding group, when compared with Bsl.

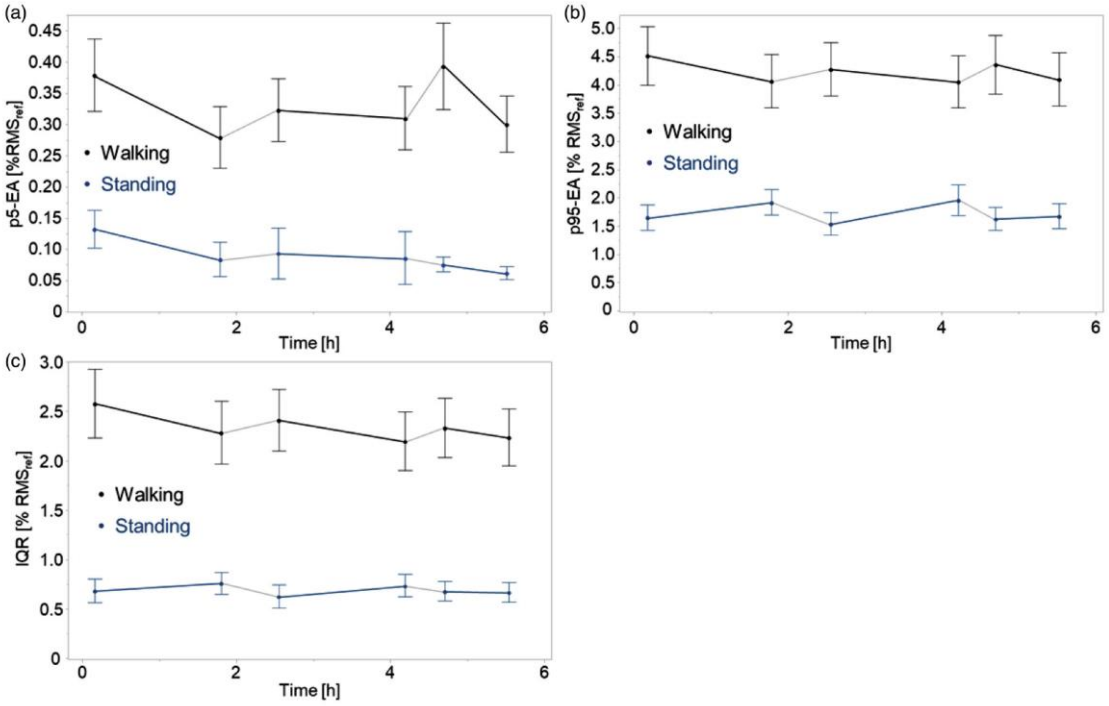

Figure 8. Means and standard errors of gastrocnemius muscle activity (a) 5th percentiles (p5-EA), (b) 95th percentiles (p95-EA) and (c) interquartile ranges (IQR), for the standing and walking condition at the beginning and end of each standing and walking period.

fatigue stage, the muscle can undergo a combined stage of potentiation and fatigue translated by an increase in both twitch amplitude and duration (Johnson et al. 2013; Kim and Johnson 2014; Garcia et al. 2016). This combined stage is clearly observed in all male groups during the standing condition at time L. It is also observed in the walking condition, where muscle twitch force amplitude and duration do not

change or tend to increase at L or E1. Overall, for all groups, regardless of condition (standing or walking) the fatigue stage becomes prominent 30 min post-work and continues to progress up to more than an hour post-work. However, fatigue appears less prominent after walking than quasi-static standing. These results are in agreement with our previous studies concerning the delayed onset, progression and persistence of muscle fatigue, in which age, gender and flooring characteristics do not influence the detrimental effect of prolonged standing work (Garcia, Läubli, and Martin 2015; Garcia et al. 2016). In addition, the meagre changes in twitch amplitude and duration after 110 min of standing work also corroborate our earlier suggestion that this standing duration is acceptable in terms of localised muscle fatigue (Garcia et al. 2016). This does not preclude that discomfort and/or pain could indicate other limits to consider during the work period.

Some differentiations between groups and conditions can be noted before the second post-work measure (E2). In the standing condition, the decrease in MTF amplitude relative to baseline is not significant until E2 for the young males habituated to standing, while the increase in twitch duration was already significant at time L (Figure 6). In addition, for this group, the decrease in twitch amplitude relative to L is significant immediately post-work (E1). Hence, these variations indicate an interaction between potentiation and fatigue during the work period (Garner, Hicks, and McComas 1989; Johnson et al. 2013; Kim and Johnson 2014; Garcia et al. 2016) that may be difficult to differentiate between groups. However, the difference between the young males habituated to standing and the other groups could be associated with a possible adaptation of motor unit recruitment strategy to fatigue (Singh and Latash 2011; Ortega-Auriol et al. 2018) that temporarily delays the onset of fatigue but does not prevent its development resulting from the prolonged standing exposure.

A potentiation-fatigue interaction (increase in MTF amplitude followed by a decrease, concomitant to an increase in duration) is also observed in the walking condition for the older male group (Figure 7). Walking at a slow pace appears to delay the onset of muscle fatigue when compared to standing, as in the former case the increase in twitch duration becomes significant only beyond 30 min post work. The discernible potentiation for the older participants may be explained in that older individuals tend to be less active / more sedentary and generally exhibit less muscle strength than younger individuals (see Francis et al. 2017 for a review), which likely leads to a larger recruitment of motor units to perform the same task, thereby favouring potentiation. This interpretation is supported by the trend in potentiation (at L) followed by a large decline in twitch force magnitude (at E1 and after) in the standing condition.

In sum, slow-paced walking may delay and reduce the negative effects of fatigue as corroborated in Garcia et al. (2016). However, walking should not be considered an ultimate solution, as long-lasting fatigue is still evident post-work. Moreover, habituation to standing work does not seem to add benefit to prolonged slow-paced walking, since MTF amplitude and duration show the clear presence of fatigue one-hour post-work.

Medial gastrocnemius activity

As expected, gastrocnemius muscle activation differs considerably between standing and walking. Muscle activity is lower and less variable during standing than walking. Despite the use of a highly sensitive EMG system, p5-EA was very low and no activity was measurable in several instances. However, p95-EA in standing was about one-third the value obtained in the walking condition, which may not be a negligible muscle activation. Hence, the contribution of this muscle to changes in MTF fatigue should not be excluded but it is likely to play a rather minor role. Other parts of the triceps surae muscle, such as the soleus, are suspected to be the major contributors to fatigue development as measured by MTF. This perspective is supported by the results of Dos Anjos et al. (2015) who found that the medial part of the soleus muscle is activated continuously during static standing rather than the medial gastrocnemius, which is activated intermittently. Another possible explanation may be that oedema interferes with MTF measures; however, there is no known evidence of such phenomenon. A recent paper argued that this effect is unlikely as the authors observed a decrease of lower leg volume after a resting period following prolonged standing work, but muscle twitch force remained the same (Garcia, Laubli, and Martin 2018).

Limitations

There are some limitations to the present study that must be addressed. The effect of the distribution of the standing and walking periods was not tested. The selected sequences may have led to a possible order effect. However, the present results agree with our previous results. Finally, we did not consider any parameters of task performance that would allow us to ensure

an equal task performance level during the walking condition. This should be kept in mind when considering walking periods as a workplace intervention.

Conclusions

When compared to prolonged static standing, continuous slow pace walking is beneficial, as it contributes to reduced lower leg oedema and muscle fatigue. Gender, age or habituation to standing did not influence the development of oedema when standing or the muscle-venous-pump function during walking. Muscle fatigue is evidenced by changes in MTF amplitude and duration. However, the medial gastrocnemius may not be the muscle primarily fatigued by static standing.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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References

Adamo, D. E., M. Khodaee, S. Barringer, P. W. Johnson, and B. J. Martin. 2009. "Low Mean Level Sustained and Intermittent Grip Exertions: influence of Age on Fatigue and Recovery." *Ergonomics* 52 (10): 1287–1297. doi:10.1080/00140130902984935..

Adamo, D. E., B. J. Martin, and P. W. Johnson. 2002. "Vibration-Induced Muscle Fatigue, a Possible Contribution to Musculoskeletal Injury." *European Journal of Applied Physiology* 88 (1–2): 134–140. doi:10.1007/s00421-002-0660-y.

Balasubramanian, V., K. Adalarasu, and R. Regulapati. 2009. "Comparing Dynamic and Stationary Standing Postures in an Assembly Task." *International Journal of Industrial Ergonomics* 39 (5): 649–654. doi:10.1016/j.ergon.2008.10.017.

Belczak, C. E. Q., J. M. P. de Godoy, R. N. Ramos, M. A. Oliveira, S. Q. de Belczak, and R. A. Caffaro. 2009. "Rate of Occupational Leg Swelling is Greater in the Morning than in the Afternoon." *Phlebology: The Journal of Venous Disease* 24 (1): 21–25. doi:10.1258/phleb.2008.008042.

Botter, A., G. Oprandi, F. Lanfranco, S. Allasia, N. A. Maffiuletti, and M. A. Minetto. 2011. "Atlas of the Muscle Motor Points for the Lower Limb: implications for Electrical Stimulation Procedures and Electrode Positioning." *European Journal of Applied Physiology* 111 (10): 2461–2471. doi:10.1007/s00421-011-2093-y.

Britzke, B. 2014. *MTM in Einer Globalisierten Wirtschaft: Arbeitsprozesse Systematisch Gestalten Und Optimieren*. München: mi-Wirtschaftsbuch.

Carpentier, P. H., H. R. Maricq, C. Biro, C. O. Ponçot-Makinen, and A. Franco. 2004. "Prevalence, Risk Factors, and Clinical Patterns of Chronic Venous Disorders of Lower Limbs: A Population-Based Study in France." *Journal of Vascular Surgery* 40 (4): 650–659. doi:10.1016/j.jvs.2004.07.025.

Cham, R., and M. S. Redfern. 2001. "Effect of Flooring on Standing Comfort and Fatigue." *Human Factors: The Journal of the Human Factors and Ergonomics Society* 43 (3): 381–391. doi:10.1518/001872001775898205.

Coenen, P., S. Parry, L. Willenberg, J. W. Shi, L. Romero, D. M. Blackwood, G. N. Healy, D. W. Dunstan, and L. M. Straker. 2017. "Associations of Prolonged Standing with Musculoskeletal symptoms-A Systematic Review of Laboratory Studies." *Gait and Posture* 58: 310–318. doi:10.1016/j.gaitpost.2017.08.024.

Cole, K. S. 1972. *Membranes, Ions and Impulses*. Vol 1. Berkeley and Cal: University of California Pr.

Dos Anjos, F. V., F. Fontanella, M. Gazzoni, and T. M. M. Vieira. 2015. "Does the Global Temporal Activation Differ in Triceps Surae During Standing Balance?" Conference proceedings: Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society." *Annual Conference*, pp. 3464–3467.

Edwards, R. H., D. K. Hill, D. A. Jones, and P. A. Merton. 1977. "Fatigue of Long Duration in Human Skeletal Muscle after Exercise." *The Journal of Physiology* 272 (3): 769–778. doi:10.1113/jphysiol.1977.sp012072.

Evans, C. J., F. G. Fowkes, C. V. Ruckley, and A. J. Lee. 1999. "Prevalence of Varicose Veins and Chronic Venous Insufficiency in Men and Women in the General Population: Edinburgh Vein Study." *Journal of Epidemiology and Community Health* 53: 149–153. doi:10.1136/jech.53.3.149.

Francis, P., M. Lyons, M. Piasecki, J. Mc Phee, K. Hind, and P. Jakeman. 2017. "Measurement of Muscle Health in Aging." *Biogerontology* 18 (6): 901–911. doi:10.1007/s10522-017-9697-5.

Gallagher, K. M., T. Campbell, and J. P. Callaghan. 2014. "The Influence of a Seated Break on Prolonged Standing Induced Low Back Pain Development." *Ergonomics* 57 (4): 555–562. doi:10.1080/00140139.2014.893027.

Garcia, M-G., T. Läubli, and B. J. Martin. 2015. "Long-Term Muscle Fatigue after Standing Work." *Human Factors: The Journal of the Human Factors and Ergonomics Society* 57 (7): 1162–1173. doi:10.1177/0018720815590293.

Garcia, M-G., T. Laubli, and B. J. Martin. 2018. "Muscular and Vascular Issues Induced by Prolonged Standing With Different Work-Rest Cycles With Active or Passive Breaks." *Human Factors* 60 (6): 806–821.

Garcia, M-G., R. Wall, B. Steinhilber, T. Läubli, and B. J. Martin. 2016. "Long-Lasting Changes in Muscle Twitch Force during Simulated Work While Standing or Walking."

Human Factors: The Journal of the Human Factors and Ergonomics Society 58 (8): 1117–1127. doi:10.1177/0018720816669444.

Garner, S. H., A. L. Hicks, and A. J. McComas. 1989. "Prolongation of Twitch Potentiating Mechanism throughout Muscle Fatigue and Recovery." *Experimental Neurology* 103 (3): 277–281. doi:10.1016/0014-4886(89)90051-4.

Graf, M., R. Krieger, T. Läubli, and B. J. Martin. 2015. "Should we Recommend People to Stand More Than Sit at Work?" Paper presented at the 19th Triennial Congress of the International Ergonomics Association, Melbourne, Australia.

Hägg, G. M. 1991. Static Work Loads and Occupational Myalgia: A New Explanation Model – Part of Monograph. In Elektromyographical kinesiology, Anderson PA, Hobart DJ, Danhoff JV (Eds.,). Elsevier, Amsterdam, pp 141–144.

Halim, I., A. R. Omar, A. M. Saman, and I. Othman. 2012. "Assessment of Muscle Fatigue Associated with Prolonged Standing in the Workplace." *Safety and Health at Work* 3 (1): 31–42. doi:10.5491/SHAW.2012.3.1.31.

Hansen, L., J. Winkel, and K. Jørgensen. 1998. "Significance of Mat and Shoe Softness during Prolonged Work in Upright Position: based on Measurements of Low Back Muscle EMG, Foot Volume Changes, Discomfort and Ground Force Reactions." *Applied Ergonomics* 29 (3): 217–224. doi:10.1016/S0003-6870(97)00062-8..

Henschke, N., R. A. Boland, and R. D. Adams. 2006. "Responsiveness of Two Methods for Measuring Foot and Ankle Volume." *Foot and Ankle International* 27: 826–832. doi:10.1177/107110070602701013.

Hermens, H. J. 1999. *European Recommendations for Surface ElectroMyoGraphy: Results of the SENIAM Project*. Vol 8. Enschede: Roessingh Research and Development.

Jaffrin, M. Y., and H. Morel. 2008. "Body Fluid Volumes Measurements by Impedance: A Review of Bioimpedance Spectroscopy (BIS) and Bioimpedance Analysis (BIA) Methods." *Medical Engineering and Physics* 30: 1257–1269. doi:10.1016/j.medengphy.2008.06.009.

Johnson, P. W., V. M. Ciriello, K. J. Kerin, and J. T. Dennerlein. 2013. "Using Electrical Stimulation to Measure Physiological Changes in the Human Extensor Carpi Ulnaris Muscle after Prolonged Low-Level Repetitive Ulnar Deviation." *Applied Ergonomics* 44 (1): 35–41. doi:10.1016/j.apergo.2012.04.007.

Kanai, H., M. Haeno, K. Sakamoto. 1987. "Electrical Measurement of Fluid Distribution in Legs and Arms: Medical Progress through Technology." In *Medical Engineering in Japan – Research and Development*, edited by K. Atsumi, 159–170. Dordrecht: Springer Netherlands.

Kanai, H., K. Sakamoto, and M. Haeno. 1983. "Electrical Measurement of Fluid Distribution in Human Legs: Estimation of Extra- and Intra-Cellular Fluid Volume." *Journal of Microwave Power* 18 (3): 233–243. doi:10.1080/16070658.1983.11689328.

Karimi, Z., T. Allahyari, M. R. Azghani, and H. Khalkhali. 2016. "Influence of Unstable Footwear on Lower Leg Muscle Activity, Volume Change and Subjective Discomfort during Prolonged Standing." *Applied Ergonomics* 53 (Pt A): 95–102. doi:10.1016/j.apergo.2015.09.003.

Kim, H-Y. 2012. "Statistical Notes for Clinical Researchers: Assessing Normal Distribution (1)." *Restorative Dentistry and Endodontics* 37: 245–248. doi:10.5395/rde.2012.37.4.245.

Kim, H-Y. 2013. "Statistical Notes for Clinical Researchers: Assessing Normal Distribution (2) Using Skewness and Kurtosis." *Restorative Dentistry and Endodontics* 38: 52–54. doi:10.5395/rde.2013.38.1.52.

Kim, J. H., and P. W. Johnson. 2014. "Fatigue Development in the Finger Flexor Muscle Differs between Keyboard and Mouse Use." *European Journal of Applied Physiology* 114 (12): 2469–2482. doi:10.1007/s00421-014-2974-y.

Lacroix, P., V. Aboyans, P. M. Preux, M. B. Houlès, and M. Laskar. 2003. "Epidemiology of Venous Insufficiency in an Occupational Population." *International Angiology* 22 (2): 172–176.

MacEwen, B. T., D. J. MacDonald, and J. F. Burr. 2015. "A Systematic Review of Standing and Treadmill Desks in the Workplace." *Preventive Medicine* 70: 50–58. doi:10.1016/j.ypmed.2014.11.011.

Madeleine, P., M. Voigt, and L. Arendt-Nielsen. 1997. "Subjective, Physiological and Biomechanical Responses to Prolonged Manual Work Performed Standing on Hard and Soft Surfaces." *European Journal of Applied Physiology* 77 (1–2): 1–9. doi:10.1007/s004210050292.

Mansilha, A., and J. Sousa. 2018. "Pathophysiological Mechanisms of Chronic Venous Disease and Implications for Venoactive Drug Therapy." *International Journal of Molecular Sciences* 19 (6): 1669. doi:10.3390/ijms19061669.

Mosti, G., and H. Partsch. 2013. "Occupational Leg Oedema is More Reduced by Antigraduated than by Graduated Stockings." *European Journal of Vascular and Endovascular Surgery* 45 (5): 523–527. doi:10.1016/j.ejvs.2013.01.032.

Ortega-Auriol, P. A., T. F. Besier, W. D. Byblow, and A. J. C. McMorland. 2018. "Fatigue Influences the Recruitment, but Not Structure, of Muscle Synergies." *Frontiers in Human Neuroscience* 12: 217. doi:10.3389/fnhum.2018.00217.

Partsch, H., J. Winiger, and B. Lun. 2004. "Compression Stockings Reduce Occupational Leg Swelling Dermatol Surg." 30: 737–743. doi:10.1111/j.1524-4725.2004.30204.x.

Petersen, E. J., S. M. Irish, C. L. Lyons, S. F. Miklaski, J. M. Bryan, N. E. Henderson, and L. N. Masullo. 1999. "Reliability of Water Volumetry and the Figure of Eight Method on Subjects with Ankle Joint Swelling." *Journal of Orthopaedic* and *Sports Physical Therapy* 29 (10): 609–615. doi:10.2519/jospt.1999.29.10.609.

Pfisterer, L., G. Konig, M. Hecker, and T. Korff. 2014. "Pathogenesis of Varicose Veins - Lessons from Biomechanics VASA." *Vasa* 43 (2): 88–99. doi:10.1024/0301-1526/a000335.

Rabe, E., Guex, J. J., Puskas, A., Scuderi, A., Fernandez Quesada F., VCP Coordinators. 2012. "Epidemiology of Chronic Venous Disorders in Geographically Diverse Populations: Results from the Vein Consult Program." *International Angiology* 31 (2): 105–115.

Robertson, L., A. J. Lee, C. J. Evans, S. Boghossian, P. L. Allan, C. V. Ruckley, and F. G. R. Fowkes. 2013. "Incidence of Chronic Venous Disease in the Edinburgh Vein Study Journal of Vascular." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 1 (1): 59–67. doi:10.1016/j.jvsv.2012.05.006.

Segiet, O. A., M. Brzozowa-Zasada, A. Piecuch, D. Dudek, E. Reichman-Warmusz, and R. Wojnicz. 2015. "Biomolecular Mechanisms in Varicose Veins Development." *Annals of*

Vascular Surgery 29 (2): 377–384. doi:10.1016/j.avsg.2014.10.009.

Seo, A., M. Rys, and S. Konz. 2001. "Measuring Lower Leg Swelling: Optimum Frequency for Impedance Method." *Medical* and *Biological Engineering* and *Computing* 39 (2): 185–189. doi:10.1007/BF02344802.

Serralheiro, P., A. Soares, C. M. Costa Almeida, and I. Verde. 2017. "TGF-β1 in Vascular Wall Pathology: Unraveling Chronic Venous Insufficiency Pathophysiology." *International Journal of Molecular Sciences* 18 (12): 2534. doi:10.3390/ijms18122534.

Singh, T., and M. L. Latash. 2011. "Effects of Muscle Fatigue on Multi-Muscle Synergies." *Experimental Brain Research* 214 (3): 335–350. doi:10.1007/s00221-011-2831-8.

Stick, C., H. Grau, and E. Witzleb. 1989. "On the Edema-Preventing Effect of the Calf Muscle Pump." *European Journal of Applied Physiology and Occupational Physiology* 59 (1–2): 39–47. doi:10.1007/BF02396578.

Stick, C., P. Stofen, and E. Witzleb. 1985. "On Physiological Edema in Man's Lower Extremity." *European Journal of Applied Physiology and Occupational Physiology* 54 (4): 442–449. doi:10.1007/BF02337192.

Sudol-Szopinska, I., A. Bogdan, T. Szopinski, A K. Panorska, and M. Kolodziejczak. 2011. "Prevalence of Chronic Venous Disorders among Employees Working in Prolonged Sitting and Standing Postures." *International Journal of Occupational Safety and Ergonomics: Ergonomics* 17: 165–173. doi:10.1080/10803548.2011.11076887.

Tissot, F., K. Messing, and S. Stock. 2005. "Standing, Sitting and Associated Working Conditions in the Quebec Population in 1998." *Ergonomics* 48 (3): 249–269. doi:10.1080/00140130512331326799.

Uda, S., A. Seo, and F. Yoshinaga. 1997. "Swell-Preventing Effect of Intermittent Exercise on Lower Leg during Standing Work." *Industrial Health* 35 (1): 36–40. doi:10.2486/indhealth.35.36.

Visser, B., and J. H. van Dieën. 2006. "Pathophysiology of Upper Extremity Muscle Disorders." *Journal of Electromyography and Kinesiology* 16 (1): 1–16. doi:10.1016/j.jelekin.2005.06.005.

Wall, R., T. Läubli, R. Seibt, M. A. Rieger, and B. Steinhilber. 2019. "Associations between Low Back Muscle Activity, Pelvic Movement and Low Back Discomfort Development during Prolonged Standing – an Exploratory Laboratory Study." *International Journal of Industrial Ergonomics* 72: 380–389. doi:10.1016/j.ergon.2019.07.001.

Wall, R., O. Lips, R. Seibt, M. Rieger, and B. Steinhilber. 2017. "Intra- and Inter-Rater Reliability of Lower Leg Waterplethysmography, Bioelectrical Impedance and Muscle Twitch Force for the Use in Standing Work Evaluation." *Physiological Measurement* 38 (5): 701–714. doi:10.1088/1361-6579/aa6711.

Waters, T. R., and R. B. Dick. 2015. "Evidence of Health Risks Associated with Prolonged Standing at Work and Intervention Effectiveness." *Rehabilitation Nursing* 40 (3): 148–165. doi:10.1002/rnj.166.

Wiggermann, N., and W. M. Keyserling. 2013. "Effects of anti-Fatigue Mats on Perceived Discomfort and Weight-Shifting during Prolonged Standing." *Human Factors: The Journal of the Human Factors and Ergonomics Society* 55 (4): 764–775. doi:10.1177/0018720812466672.

Wittig, P., C. Nöllenheidt, and S. Brenscheidt. 2013. Grundauswertung der BIBB/BAuA-Erwerbstätigenbefragung 2012: mit den Schwerpunkten Arbeitsbedingungen, Arbeitsbelastungen und gesundheitliche Beschwerden. http://www.baua.de/de/Publikationen/Fachbeitraege/Gd73.html;jsessionid=73081D9CDE1D057BF965E21107D3B503.1_cid323.

Wrona, M., K-H. Jöckel, F. Pannier, E. Bock, B. Hoffmann, and E. Rabe. 2015. "Association of Venous Disorders with Leg Symptoms: Results from the Bonn Vein Study 1." *European Journal of Vascular and Endovascular Surgery: Surgery* 50 (3): 360–367. doi:10.1016/j.ejvs.2015.05.013..

Zennaro, D., T. Läubli, D. Krebs, A. Klipstein, and H. Krueger. 2003. "Continuous, Intermitted and Sporadic Motor Unit Activity in the Trapezius Muscle during Prolonged Computer Work." *Journal of Electromyograpphy Kinesiology* 13 (2): 113–124. doi:10.1016/S1050-6411(02)00066-4.

5 Discussion

The third chapter of this doctoral thesis includes a comprehensive and supplementary discussion. Important aspects of the discussions already provided in the three research papers will only be mentioned but not discussed in detail again. Additionally, broader supplementary aspects that have not been included in the research papers are reviewed in this chapter. Finally, results from a follow-up study (only published in conference proceedings, yet) are mentioned and argued.

5.1 WP and BI measurements

Generally, good inter- and intra-rater reliability of the self-developed procedures in WP and BI measurements were found in study 1. Both methods can appropriately detect lower leg volume changes in standing work, with standard error of measurement (SEM) values of 23/ 27 ml (ca. 0.9%) for WP and 3.8/ 3.4 Ω (ca. 5%) for BI, because expected volume increases are over 100 ml (3-5 % WP/ ca. 20% BI; (Hansen *et al.*, 1998; Belczak *et al.*, 2009; Stick *et al.*, 1992; Sanders *et al.*, 2012). The necessity for good standardization of leg placement can be seen in the systematic error that was present between M1 and M2 in both WP and BI and between M2 and M3 only in BI. Regarding that, especially in WP an increase in lower leg volume from M1 to M2 was found, whereas in BI a decrease was measured from M1 to M3. The reason for this discrepancy is that WP and BI were measured on different legs which were placed differently between measurements. Subjects were seated with the WP leg in a downward position and BI leg was elevated for another exploratory measurement not mentioned in the publication. This situation led to an increased volume in the WP leg and a decreased volume in the BI leg. Taking all that into account, it can be assumed that reproducibility for both volume measurement procedures is further improvable, if leg placement is standardized. Lastly, for future standing work evaluation it seems to be very important to consider the subject's baseline value as they won't travel similarly to the laboratory. Arriving after a car or bus ride could result in a beginning oedema compared to subjects that arrive by foot or bike, activating their muscle-venous pump. Therefore, it might be sensible to try to reset lower leg

volume prior to the measurements by elevating legs in a supine position and additionally activating the muscle-venous pump by intermittently moving feet in full range of motion in dorsiflexion and plantarflexion for 15-20 minutes.

5.2 Movement as a prevention measure

Both publications 2 and 3 showed that movement can be beneficial in the prevention of MSD and VD during prolonged standing. However, the statistically significant differences in lateral movement in publication 2 have to be interpreted carefully. The measured differences are very low with 0.7° of increase in interquartile ranges from the beginning to the end of the standing periods for the NoDD and 0.2° for the DD. It is unclear, if such low movement ranges can influence blood flow or muscle activation. No differences in the assessed erector spinae muscle activity were found in the same publication. It might be that deeper lumbar muscles like multifidi and transversus abdominis are more relevant than the measured erector spinae muscles. It was shown that these deeper lumbar muscles undergo morphological changes and adaptations in activation patterns in the development of LBP (Wong *et al.*, 2014). These changes were only shown in patients with existing LBP and might therefore be a result of LBP and not a precursor. However, it is thinkable that measured low range movements might have a bigger influence on the deeper and smaller multifidi muscles than on the superficial erector spinae, influencing low back discomfort development in healthy subjects during prolonged standing. Further research is necessary to verify this idea.

Other factors that were found to differ between PD/ DD and NPD/ NoDD are trunk and gluteus medius muscle co-activations and lumbar lordosis angle (Nelson-Wong *et al.*, 2008; Sorensen *et al.*, 2015). PD/ DD are suggested to have an increased muscle co-activation compared to symptom free subjects. The increased simultaneous activation of antagonist muscle groups might be another indication of a more rigid posture during prolonged standing, leading to pain/ discomfort development. In case of lumbar lordosis, it was shown that PD had a significantly larger lordosis angle than the NPD. Further, pain intensity increased

with lordosis angle. It is hypothesized that an increased lordotic posture causes a higher compressive loading of dorsal spinal structures (Sorensen *et al.*, 2015).

A very clear positive effect of movement was shown on lower leg oedema development in publication 3. The attributed venous risks can be prevented completely by continuous slow pace walking. Furthermore, data from the same study show similar effects on subjective ratings of discomfort of the lower legs and the lower back region. These results were only published as a conference paper yet (Steinhilber *et al.*, 2016).

Continuous walking is rather rare in an occupational setting. Most standing workplaces require walking and standing. Therefore, it is very interesting to investigate the preventive effect of walking in more detail. Both frequency of changes and proportion of standing and walking should be considered to find a setup that is feasible for workplaces and also effective in preventing MSD and VD.

The only studies that investigated the effect of muscle-venous pump activation on lower leg oedema development did not use walking as their intervention. Uda et al. compared different leg movement exercises (1 min each 10 min of standing): knee-bending, foot-stepping, stationary walking and heel-raising. They found that knee-bending was the most effective way of oedema prevention because of the simultaneous use of thigh and calf muscles (Uda *et al.*, 1997). Stick et al. were effective in reducing an orthostatic oedema by cycling (Stick *et al.*, 1989). However, both of these measures are more difficult to implement in actual standing workplaces than intermittent walking.

A similar approach of preventing standing work risks by intermittent walking bouts were conducted in two publications by Balasubramanian et al. They investigated the difference of short walking bouts (walking from one station to the other) and stationary standing in a 60 min assembly task on discomfort, lower leg and back muscle fatigue. They found that intermittent walking was effective in reducing both discomfort and muscle fatigue of the lower legs (Balasubramanian *et al.*, 2009). In the second publication subjects conducted the same protocol but only for 25 min. Again, the intermittent walking showed positive effects on subjective ratings of lower extremity discomfort (Balasubramanian *et al.*, 2008). However,

these studies only included nine and eleven subjects, respectively, who conducted the experiment barefoot, which makes the results at least questionable. Furthermore, fatigue by means of continuous low-level activation is unlikely to occur in the gastrocnemius medius muscle (measured in research paper 3). It might be that other parts of the triceps surea muscle are at risk of fatigue, as suggested by several studies (Balasubramanian *et al.*, 2009; Garcia *et al.*, 2015; Garcia *et al.*, 2016). The measured changes in muscle twitch force might also be a consequence of lower leg oedema and a resulting water deposit in the muscle fibres, leading to a disruption of the action potential provoked during MTF measurements. This is also a reasonable explanation for the unchanged MTF during walking with an indication of muscular fatigue (decrease of twitch amplitude and increase of twitch duration) during 60 min sitting after the walking experiment (see figure 8 in research paper 3). In the same measuring period lower leg oedema is validated by BI (see figure 6 in research paper 3). Again, walking is preventing lower leg oedema rather than fatigue.

The subgroup analyses in research papers 2 and 3 showed no statistically significant differences in any of the investigated parameters for age and gender. Unfortunately, no studies were found investigating age or gender related influences of static standing or continuous walking on physiological parameters. Lower leg oedema and discomfort seem to develop independently of these factors in a healthy population. Recommendations of workplace design or intervention measures can be suggested without differentiation of age and gender, until new studies with possible larger sample sizes show otherwise.

5.3 Outlook and further research for standing work recommendations

In a follow-up study to the standing and walking evaluation on which publication 2 and 3 are based on, the Institute of Occupational Medicine, Social Medicine and Health Services Research in Tübingen investigated two different standing/ walking cycles. Subjects were thus measured on four different days for two hours respectively. Additionally to the two hours of only standing (100% standing) and only walking (0% standing), two cyclic changes from standing to walking once

every ten minutes were conducted. Both cycles started with standing changing to walking after 3.5 minutes in one of the measuring days (35% standing) and after 6.5 minutes on the other day (65% standing). Again, subjective ratings of discomfort of the lower back and lower extremities as well as BI and WP (amongst others) were measured equally to the previous study. First results showed that discomfort ratings were reduced substantially comparing 100% standing to 65% standing with a decrease of the number of subjects developing low back discomfort from 17 when only standing, to 5 when changing from standing to walking every 6.5 minutes (Wall *et al.*, 2018).

Regarding oedema development a model with the parameters exposure time, standing proportion and oedema variation (resulting from changes between standing and walking) was developed (Seibt *et al.*, 2018). This model is able to predict lower leg oedema when the parameters exposure time, standing proportion and frequency of changes between standing and walking (oedema variation) are known. Relative oedema increase itself is not sufficient to predict venous health risks. The next steps towards a risk assessment is a 'translation' of oedema development into a health risk using epidemiological data. If studies can be found that show specific risk increases (e.g. by means of odds ratios or hazard ratios) in defined standing work (known or good estimation of standing time and proportion etc.), the model could be used to predict venous health risk.

There are some limitations of the described risk assessment model that should be addressed in future research. To date, it is not possible to include sitting into the risk evaluation, as it was not part of the underlying measurements. Other factors that might contribute to venous and musculoskeletal risks, like predisposition, gender and age are not implemented yet either.

Coenen et al. concluded in their systematic review, that the exposure limit for continuous static standing is at ca. 40 min. This number is based on dose-response relationships of standing time and LBP/ LBD intensity ratings of laboratory studies (Coenen *et al.*, 2017). The threshold was set for the assumed clinically relevant increase in LBP/ LBD intensity of 9 mm on a 100 mm visual analogue scale (Kelly, 1998). This limit was exceeded after 42 min, cumulating the results

of every included laboratory study. The LBD intensity rating results from research paper 2 showed an increase in the number of subjects with LBD from 4 after 27.5 min to 10 after 55 min and a considerable increase in LBD intensity from minute 27.5 to minute 82.5 (see figure 3 and figure 4 of research paper 2), confirming Coenen et al. results to some extent. However, it is unknown how long a break from static standing should be included and how it should look like (sitting or walking). Additionally, our results indicate that the 40 min limit is not necessarily valid after two, four or six hours of total standing time. This can be seen by the faster increase in LBD intensity and by the number of subjects with LBD after the first and second seated break (see figure 3 of research paper 2), which was also shown in another publication (Gallagher *et al.*, 2014). While the recommendation for an initial standing exposure might be valid, it is not possible to give advice for a whole standing work shift, based on the present findings concerning LBP/ LBD prevention.

Based on the SEMG results regarding the lower extremities of research paper 3, no profound recommendations for exposure limits can be given. The model in the follow-up study, described in the beginning of this chapter, can also be adapted to lower leg discomfort. This might be a first step towards recommendations for preventing lower leg musculoskeletal complaints, if they are not related to lower leg oedema, as hypothesized by some authors (Coenen *et al.*, 2017; Friden *et al.*, 1986).

Continuous walking can be safely recommended for the prevention of lower leg oedema and thus the risk of VD. However, this is rarely or never applicable in existing workplaces. The follow-up study from which yet no results have been published in a peer-reviewed journal, is the first step towards concrete statements for workplace design and risk assessments concerning VD. The developed model can be used as the basis for recommending specific standing and walking schedules for workplaces where work in seated positions is not allowed.

5.4 Limitations

Several limitations apply to the research papers 2 and 3. The tasks within the standing and walking periods were not conducted in a randomized order. This

might have led to order effects which are impossible to correct for, post-hoc. Additionally, the influence of the tasks within the periods and the seated breaks on measured outcomes cannot be differentiated. The sample size in research paper 2 and research paper 3 was comparatively high with 60 included subjects. However, by forming subgroups for the analysis of an age, gender and standing habituation effect, the resulting group sizes might have been too small to show possible associations. Sample size calculations could avoid this issue in future studies. Finally, the described oedema model should be validated in a subsequent study in order to confirm or adapt the calculated risks for VD in specific occupational settings.

5.5 Conclusions

Lower leg volume changes (lower leg oedema) can be reliably measured by the described procedures of the waterplethysmography and bioelectrical impedance methods (see research paper 1), independent of the investigator (if a minimum of fifty measurements were conducted previously). The standard error of measurement is satisfactory low, so that expected lower leg volume changes during standing work can be measured sufficiently as a surrogate parameter for an increased venous health risk. Adaptations concerning standardization procedures (reset of oedema before baseline measurement) should be implemented for upcoming studies to further improve reliability.

Previously asymptomatic people might develop LBD because of less movement in the lower back region during prolonged standing compared to those who are symptom free. This mechanism is most probably not connected to continuous low-level erector muscle activity, but rather to deeper trunk stabilizing musculature like the multifidi and transversus abdominis. This hypothesis has to be investigated in future research. Other factors like trunk and gluteus muscle co-activation and increased lumbar lordosis might also be contributing to LBD development. A previously suggested threshold of 40 min for continuous static standing to prevent LBP/ LBD can be confirmed by the findings in research paper 2. This limit may only be applicable in the first standing period of a working shift, because

the increase in LBP/ LBD intensity is faster after seated breaks with increasing standing time.

Lower leg discomfort is unlikely to occur due to gastrocnemius muscle fatigue during prolonged standing. The measured activity levels were very low and not present continuously. Based on the ‘Cinderella Hypothesis’ muscular fatigue can therefore not be concluded. Either other parts of the triceps surea muscle, like the soleus, or the increasing stress on passive structures due to lower leg oedema are the reason for lower leg discomfort.

Generally, continuous slow pace walking was found to be an effective intervention to prevent LBD and lower leg oedema. Further research might include modelling of oedema and discomfort progression during standing and walking to develop an objective risk assessment method for future workplace design.

6 Abstract

Background

Prolonged standing is required in many of today's workplaces. Epidemiological studies show that continuous static standing is associated with multiple adverse health outcomes, like musculoskeletal and venous disorders (MSD and VD). Pain and discomfort in the lower leg and lower back regions are common among standing workers. They increase with age and are more common in females. Several laboratory studies showed that standing for two or more hours alone can initiate low back pain/ discomfort (LBP/ LBD) in 30% to 70% of the participants. The mechanisms behind this are not fully understood. Most hypothesis assume that continuous static posture is playing a major role in the development of complaints of both the lower legs and the lower back. In this regard, the 'Cinderella Hypothesis' might be a reasonable explanation. Here, it is assumed that fatigue of type I muscle fibres through prolonged low-level activation, leads to a metabolic overload and thus pain or discomfort. Regarding venous diseases, continuous circumferential stress of the venous wall (increased venous pressure) and decreased blood flow, resulting from static standing, facilitate pathophysiological mechanisms, leading to pro-inflammatory responses. The result of these mechanisms is venous wall remodelling with fibrosis, thickening of the venous walls and atrophy of elastic fibres, making veins susceptible to varicosis and consequential damages. Increasing movement seems to be a reasonable prevention mechanism for both MSD and VD by reducing static posture and activation of muscle-venous pump function. Surrogate parameters for an increased risk of MSD and VD measure subjective rating of discomfort (via numeric rating scale, NRS), muscle activity (via surface electromyography, SEMG), lower back movement (via position sensor, PS) and lower leg oedema (via waterplethysmography and bioelectrical impedance, WP and BI). The latter two are measured with self-developed procedures and devices and were therefore tested for reproducibility.

Methods

The first study investigated the intra- and inter-rater reliability of WP and BI measurements (M) in 20 healthy subjects. Each method was measured three times by two different raters on two separate days. As the main outcome for reproducibility the standard error of measurement (SEM) was used. In the second paper 60 healthy subjects were included and had to stand for five hours (including two seated breaks after 110 and 220 minutes) in three periods. The participants were asked to rate their lower back discomfort periodically during standing via NRS. SEMG was measured bilaterally on the erector muscle. Additionally, a PS was placed at the sacrum (S1) to measure lower back movement in lateral and anterior/ posterior direction. Post hoc, a discomfort developer (DD) and a non-discomfort developer (NoDD) group was separated based on NRS ratings. A linear mixed model was calculated to find possible differences in muscle activation and movement patterns between DD and NoDD. The third publication also included 60 healthy subjects that had to stand and walk for approximately five hours (including two seated breaks after 110 min and 220 min) in three periods. Lower leg oedema was measured using BI and WP. SEMG was measured to see if continuous low-level activation in the gastrocnemius muscle was present. Again, a linear mixed model was calculated in order to find differences between the two conditions (standing and walking) and the course of the experiments. Further, it was tested if gender and age moderate tested surrogate parameters.

Results

The SEM for WP and BI were 27 ml and 3.8 Ω for rater 1 and 23 ml and 3.4 Ω for rater 2. Statistically significant increases of WP and BI from M1 to M2 were detected. Additionally, BI increased further from M2 to M3. The second study showed that there was a statistically significant increase in lateral lower back movement for NoDD from the beginning to the end of each standing period, which was not the case for the DD. No further statistically significant differences between the DD and NoDD were found. The third paper showed that lower leg volume increased significantly during standing (3.6% average) and resulted in a 0.3% average change after walking. The oedema increased rapidly in the first 110 min with a subsequent flattening in the rest of the experiment. All the SEMG values were statistically significantly lower in standing than in walking. During

standing several subjects had no activity (shown by means of 5th percentile) in the gastrocnemius muscle. No statistically significant differences were found for older and female subjects.

Discussion

Generally, SEM values showed good reproducibility of WP and BI. Both methods are suitable for detecting lower leg volume changes during standing, reliably. The increase in WP and BI values from M1 to M2 and M2 to M3 in BI can be explained by the lack of standardization prior to the first measurement after the subjects arrived in the laboratory and the positioning of the leg between the measurements. This resulted in an actual change in lower leg volume. Better standardization (resting period before the first measurement and horizontal leg placement between measurements) can therefore lead to a further increase in reproducibility of WP and BI. The second study showed that DD moved less in the course of the standing exposure than the NoDD. This may indicate that more movement in the lower back region (e.g. via walking) could protect from developing LBD. The third paper revealed that even slow pace walking can protect oedema progression completely by activating the muscle-venous pump. The progression of oedema during standing seems to follow an exponential curve with an initial fast increase and a subsequent lower development of oedema. Gastrocnemius muscle fatigue by means of the ‘Cinderella Hypothesis’ seems unlikely during walking (because of high variability in activation) and standing because the activation level is rather low but not continuous, indicated by the frequent non-activation. Either other parts of the triceps surae (soleus) muscle are activated continuously or other mechanisms (like lower leg oedema) are the reasons for MSD in the lower legs. No moderating effect of gender and age was found in either of the publications.

7 Zusammenfassung

Hintergrund

Viele Arbeitsplätze in der heutigen Wirtschaft erfordern langandauerndes Stehen. Epidemiologische Studien zeigen, dass kontinuierliches, statisches Stehen mit diversen gesundheitlichen Folgen, wie Muskelskelett Beschwerden (MSD) des unteren Rückens und der unteren Extremitäten sowie venösen Erkrankungen (VD) assoziiert werden. Beschwerden der unteren Extremitäten und des lumbalen Rückens treten gehäuft bei Menschen in Stehberufen, in steigendem Alter und bei Frauen auf. Einige Laborstudien zeigten zudem, dass zweistündiges Stehen allein dazu führen kann, dass bei 30% bis 70% der Studienteilnehmer Rückenbeschwerden (LBP) entstehen. Die Mechanismen dahinter sind noch nicht vollständig geklärt. Die meisten Hypothesen gehen davon aus, dass eine kontinuierliche, statische Haltung eine wichtige Rolle in der Entstehung von MSD in den Beinen und dem lumbalen Rücken spielen. Diesbezüglich könnte die „Cinderella Hypothese“ eine sinnvolle Erklärung bieten. Sie geht davon aus, dass es zu einer Ermüdung von Typ I Muskelfasern aufgrund von langanhaltender, niedriger Aktivierung kommt, die in der Folge zu einer metabolischen Überlastung und schließlich zu Schmerzen/ Beschwerden führt. Bezüglich venöser Erkrankungen geht man davon aus, dass eine kontinuierliche Dehnungsbelastung der Venenwände (erhöhter venöser Druck) und ein verringerter Blutfluss, aufgrund von statischem Stehen, pathophysiologische Mechanismen in Gang setzen, die zu entzündungsfördernden Vorgängen führen. Das Resultat dieser Vorgänge ist ein Umbau der Venenwände mit Fibrosierung, Verdickung und Atrophie elastischer Fasern. Diese Prozesse machen Venen anfällig für Varikosen und Folgeschäden. Vermehrte Bewegung scheint ein vielversprechender Ansatz für die Prävention von MSD und VD zu sein, indem man statische Haltungen reduziert und die Muskel-Venen Pumpe aktiviert. Surrogatparameter für ein erhöhtes Risiko von MSD und VD beinhalten subjektive Beschwerdeangaben (via einer numerischen rating Skala, NRS), Bewegung im unteren Rücken (via Lagesensor, PS), muskuläre Aktivität (Oberflächen Elektromyographie, SEMG) und das Unterschenkelödem (via Wasserplethysmographie und bioelektrischer Impedanz,

WP und BI). Die letzten beiden Messverfahren und -durchführungen sind teilweise selbst entwickelt und müssen daher auf ihre Reproduzierbarkeit hin überprüft werden.

Methoden

Die erste Studie untersuchte die intra- und inter-rater Reliabilität der WP und BI Messungen (M) an 20 gesunden Versuchspersonen. Jedes Messverfahren wurde dreimal von zwei unterschiedlichen Ratern an zwei separaten Tagen durchgeführt. Der Hauptkennwert zur Einschätzung der Reproduzierbarkeit war der „standard error of measurment“ (SEM). In der zweiten Studie wurden 60 gesunde Studienteilnehmer eingeschlossen, die ca. fünf Stunden (inklusive zwei Pausen im Sitzen, nach 110 min und 220 min) aufgeteilt in drei Perioden gestanden sind. In regelmäßigen Abständen wurden die Beschwerden des unteren Rückens mittels NRS abgefragt. SEMG wurde beidseits am M. erector spinae gemessen. Zusätzlich wurde ein Lagesensor am Sakrum (Höhe S1) befestigt, um die Bewegung der Lendenwirbelsäule in lateraler und anterior- posteriorer Richtung zu messen. Post hoc wurden zwei Gruppen – Beschwerdeentwickler (DD) und nicht- Beschwerdeentwickler (NoDD) – auf Grundlage der NRS Angaben gebildet. Es wurde ein lineares gemischtes Modell („linear mixed model“) berechnet, um mögliche Unterschiede im Bewegungsverhalten und der Aktivierung des M. erector spinae zwischen DD und NoDD zu finden. In der dritten Publikation wurden ebenfalls 60 gesunde Personen eingeschlossen die ca. fünf Stunden (inklusive zwei Pausen im Sitzen, nach 110 und 220 min) aufgeteilt in drei Perioden gestanden und gegangen sind. Das orthostatische Ödem wurde mittel WP und BI gemessen. SEMG wurde gemessen, um festzustellen, ob eine kontinuierliche, niedrige Aktivierung des M. gastrocnemius vorlag. Es wurde wiederum ein lineares gemischtes Modell berechnet, um Unterschiede zwischen den Versuchstagen (Stehen und Gehen), sowie dem Verlauf innerhalb der Versuchstage festzustellen. Zudem wurde überprüft, ob ein moderierender Einfluss von Geschlecht und Alter auf die getesteten Surrogatparameter besteht.

Ergebnisse

Der SEM für die WP und BI Messung lag bei 27 ml und 3,8 Ω für Rater 1 und bei 23 ml und 3,4 Ω bei Rater 2. Es wurde ein statistisch signifikanter Anstieg der WP und der BI zwischen M1 und M2 und zwischen M2 und M3 nur bei der BI bei beiden Ratern festgestellt. Die zweite Untersuchung zeigte, dass ein statistisch signifikanter Anstieg bei der lateralen Bewegung im unteren Rücken von Beginn bis zum Ende jeder Stehphase bei den NoDD vorlag. Dieser Anstieg zeigte sich bei den DD nicht. Es wurden keine weiteren statistisch signifikanten Unterschiede zwischen den zwei Gruppen festgestellt. Die dritte Publikation zeigte, dass beim Stehen ein signifikanter Anstieg des Unterschenkelvolumens stattfindet (3,6% im Mittel). Beim Gehen zeigte sich eine Änderung von 0,3% im Mittel. Das Ödem stieg während der ersten 110 min stark an und flachte in der Folge ab. Alle SEMG Kennwerte waren statistisch signifikant geringer beim Stehen als beim Gehen. Während dem Stehen zeigten einige Probanden keine Aktivität (anhand des 5. Perzentils) im M. gastrocnemius. Es konnte kein statistisch signifikanter Einfluss von Geschlecht und Alter in sämtlichen Parametern von Publikation 2 und 3 festgestellt werden.

Diskussion

Grundsätzlich zeigten die SEM Werte, dass eine gute Reproduzierbarkeit der WP und BI Messungen vorliegt. Beide Methoden sind gut geeignet, um Änderungen im Unterschenkelvolumen beim Stehen zuverlässig feststellen zu können. Der Anstieg der WP und BI Kennwerte von M1 und M2 kann auf eine mangelnde Standardisierung des Vorgehens vor der ersten Messung und auf die Haltung des Unterschenkels zwischen der ersten und zweiten Messung zurückgeführt werden. Eine verbesserte Standardisierung (z.B. eine Ruheperiode vor der ersten Messung und die Beine in horizontaler Lage zwischen den Messungen) könnte deswegen zu einer weiteren Verbesserung der Reproduzierbarkeit der WP und BI führen. Die zweite Studie zeigte, dass DD weniger Bewegung im Lumbalbereich im Verlauf der Stehexposition zeigten als die NoDD. Das könnte darauf hindeuten, dass mehr Bewegung (z.B. mittels Gehen) Schutz gegenüber der Beschwerdeentwicklung bieten könnte. In der dritten Studie wurde festgestellt, dass auch langsames Gehen und damit die Aktivierung der Muskel-Venen-Pumpe, die Entwicklung eines orthostatischen Ödems vollständig verhindern

kann. Die Ödementwicklung über die Zeit scheint einem exponentiellen Verlauf zu folgen, mit einem starken Anstieg zu Beginn und einem Abflachen der Kurve in der Folge. Eine Ermüdung des M. gastrocnemius nach der „Cinderella Hypothese“ scheint sowohl für das Gehen (aufgrund von hoher Variabilität der Aktivierung), als auch das Stehen (aufgrund der zwar niedrigen aber nicht konstanten Aktivierung) unwahrscheinlich. Entweder es sind andere Teile des M. triceps surae (z.B. M. soleus) den beschriebenen Mechanismen ausgesetzt oder es sind andere Vorgänge (z.B. das Unterschenkelödem) für die Beschwerden in den unteren Extremitäten verantwortlich. Alter und Geschlecht scheinen keinen Einfluss auf die untersuchten Parameter zu haben.

8 References

Aghazadeh, J., Ghaderi, M., Azghani, M.-R., Khalkhali, H.-R., Allahyari, T. and Mohebbi, I. (2015), “Anti-fatigue mats, low back pain, and electromyography: An interventional study”, *International journal of occupational medicine and environmental health*, Vol. 28 No. 2, pp. 347–356.

Allegra, C., Antignani, P.L., Will, K. and Allaert, F. (2014), “Acceptance, compliance and effects of compression stockings on venous functional symptoms and quality of life of Italian pregnant women”, *International angiology a journal of the International Union of Angiology*, Vol. 33 No. 4, pp. 357–364.

Antle, D.M. and Côté, J.N. (2013), “Relationships between lower limb and trunk discomfort and vascular, muscular and kinetic outcomes during stationary standing work”, *Gait & Posture*, Vol. 37 No. 4, pp. 615–619.

Aravind, B., Saunders, B., Navin, T., Sandison, A., Monaco, C., Paleolog, E.M. and Davies, A.H. (2010), “Inhibitory effect of TIMP influences the morphology of varicose veins”, *European journal of vascular and endovascular surgery the official journal of the European Society for Vascular Surgery*, Vol. 40 No. 6, pp. 754–765.

Balagué, F., Mannion, A.F., Pellisé, F. and Cedraschi, C. (2012), “Non-specific low back pain”, *Lancet (London, England)*, Vol. 379 No. 9814, pp. 482–491.

Balasubramanian, V., Adalarasu, K. and Regulapati, R. (2008), “Comparing stationary standing with an intermittent walking posture during assembly operations”, *Human Factors and Ergonomics in Manufacturing*, Vol. 18 No. 6, pp. 666–677.

Balasubramanian, V., Adalarasu, K. and Regulapati, R. (2009), “Comparing dynamic and stationary standing postures in an assembly task”, *International Journal of Industrial Ergonomics*, Vol. 39 No. 5, pp. 649–654.

Belczak, C.E.Q., de Godoy, J M P, Ramos, R.N., Oliveira, M.A. de, Belczak, S.Q. and Caffaro, R.A. (2009), “Rate of occupational leg swelling is greater in the morning than in the afternoon”, *Phlebology / Venous Forum of the Royal Society of Medicine*, Vol. 24 No. 1, pp. 21–25.

Bergan, J. (2007), “Molecular mechanisms in chronic venous insufficiency”, *Annals of vascular surgery*, Vol. 21 No. 3, pp. 260–266.

Berger, H., Caffier, G., Schultz, K. and Trippler, D. (2009), “Bewegungsergonomische Gestaltung von andauernder Steharbeit. Eine Handlungsanleitung zur Beurteilung der Arbeitsbedingungen”, available at: http://lasi.osha.de/docs/lv50.pdf.

Brijker, F., Heijdra, Y.F., Van Den Elshout, F J, Bosch, F.H. and Folgering, H.T. (2000), “Volumetric measurements of peripheral oedema in clinical conditions”, *Clinical physiology (Oxford, England)*, Vol. 20 No. 1, pp. 56–61.

Bromen, K., Pannier-Fischer, F., Stang, A., Rabe, E., Bock, E. and Jöckel, K.-H. (2004), “Lassen sich geschlechtsspezifische Unterschiede bei Venenerkrankungen durch Schwangerschaften und Hormoneinnahme erklären?”, *Gesundheitswesen (Bundesverband der Arzte des Offentlichen Gesundheitsdienstes (Germany))*, Vol. 66 No. 3, pp. 170–174.

Bussey, M.D., Kennedy, J.E. and Kennedy, G. (2016), “Gluteus medius coactivation response in field hockey players with and without low back pain”, *Physical therapy in sport official journal of the Association of Chartered Physiotherapists in Sports Medicine*, Vol. 17, pp. 24–29.

Carpentier, P.H., Maricq, H.R., Biro, C., Ponçot-Makinen, C.O. and Franco, A. (2004), “Prevalence, risk factors, and clinical patterns of chronic venous disorders of lower limbs. A population-based study in France”, *Journal of vascular surgery*, Vol. 40 No. 4, pp. 650–659.

CCOHS (2018), “Basic information on Standing at work”, available at: https://www.ccohs.ca/oshanswers/ergonomics/standing/standing_basic.html (accessed 27 November 2018).

Cham, R. and Redfern, M.S. (2001), “Effect of flooring on standing comfort and fatigue”, *Human factors*, Vol. 43 No. 3, pp. 381–391.

Chee, H.L., Rampal, K.G. and Chandrasakaran, A. (2004), “Ergonomic risk factors of work processes in the semiconductor industry in Peninsular Malaysia”, *Industrial health*, Vol. 42 No. 3, pp. 373–381.

Chester, M.R., Rys, M.J. and Konz, S.A. (2002), “Leg swelling, comfort and fatigue when sitting, standing, and sit/standing”, *International Journal of Industrial Ergonomics*, Vol. 29 No. 5, pp. 289–296.

Coenen, P., Parry, S., Willenberg, L., Shi, J.W., Romero, L., Blackwood, D.M., Healy, G.N., Dunstan, D.W. and Straker, L.M. (2017), “Associations of prolonged standing with musculoskeletal symptoms-A systematic review of laboratory studies”, *Gait & Posture*, Vol. 58, pp. 310–318.

Coenen, P., Willenberg, L., Parry, S., Shi, J.W., Romero, L., Blackwood, D.M., Maher, C.G., Healy, G.N., Dunstan, D.W. and Straker, L.M. (2016), “Associations of occupational standing with musculoskeletal symptoms: a systematic review with meta-analysis”, *British Journal of Sports Medicine*, bjsports-2016-096795.

da Costa, B.R. and Vieira, E.R. (2010), “Risk factors for work-related musculoskeletal disorders. A systematic review of recent longitudinal studies”, *American Journal of Industrial Medicine*, Vol. 53 No. 3, pp. 285–323.

Davies, A.H. (2019), “The Seriousness of Chronic Venous Disease: A Review of Real-World Evidence”, *Advances in therapy*, Vol. 36 No. Suppl 1, pp. 5–12.

Dicke, W. (2008), *Stehend K.O.? Wenn Arbeit durchgestanden werden muss .,* 2nd ed., Bundesanst. für Arbeitsschutz und Arbeitsmedizin; [Initiative Neue Qualität der Arbeit c/o Bundesanst. für Arbeitsschutz und Arbeitsmedizin] [Vertrieb], Dortmund-Dorstfeld, [Dortmund].

Dionne, C.E., Dunn, K.M. and Croft, P.R. (2006), “Does back pain prevalence really decrease with increasing age? A systematic review”, *Age and ageing*, Vol. 35 No. 3, pp. 229–234.

DOSH (2002), *Guidelines on occupational safety and health for standing at work*, Malaysia [Kuala Lumpur].

Ebben, J.M. (2003), “Improved ergonomics for standing work”, *Occupational health & safety (Waco, Tex.)*, Vol. 72 No. 4, pp. 72–76.

Eklöf, B., Rutherford, R.B., Bergan, J.J., Carpentier, P.H., Gloviczki, P., Kistner, R.L., Meissner, M.H., Moneta, G.L., Myers, K., Padberg, F.T., Perrin, M., Ruckley, C.V., Smith, P.C. and Wakefield, T.W. (2004), “Revision of the CEAP

classification for chronic venous disorders. Consensus statement", *Journal of vascular surgery*, Vol. 40 No. 6, pp. 1248–1252.

Ema Quilici Belczak, C., Pereira De Godoy, J.M., Quilici Belzack, S., Andréia De Moraes Silva, M. and Caffaro, R.A. (2012), "Compression stockings have a synergistic effect with walking in the late afternoon to reduce edema of the lower limbs", *International angiology a journal of the International Union of Angiology*, Vol. 31 No. 5, pp. 490–493.

Evans, C.J., Fowkes, F.G., Ruckley, C.V. and Lee, A.J. (1999), "Prevalence of varicose veins and chronic venous insufficiency in men and women in the general population. Edinburgh Vein Study", *Journal of Epidemiology & Community Health*, Vol. 53 No. 3, pp. 149–153.

Feldner, A., Otto, H., Rewerk, S., Hecker, M. and Korff, T. (2011), "Experimental hypertension triggers varicosis-like maladaptive venous remodeling through activator protein-1", *FASEB journal official publication of the Federation of American Societies for Experimental Biology*, Vol. 25 No. 10, pp. 3613–3621.

Fewster, K.M., Gallagher, K.M. and Callaghan, J.P. (2017), "The effect of standing interventions on acute low-back postures and muscle activation patterns", *Applied ergonomics*, Vol. 58, pp. 281–286.

Friden, J., Sfakianos, P.N. and Hargens, A.R. (1986), "Muscle soreness and intramuscular fluid pressure: comparison between eccentric and concentric load", *Journal of Applied Physiology*, Vol. 61 No. 6, pp. 2175–2179.

Gallagher, K.M. and Callaghan, J.P. (2015), "Early static standing is associated with prolonged standing induced low back pain", *Human Movement Science*, Vol. 44, pp. 111–121.

Gallagher, K.M. and Callaghan, J.P. (2016), "Standing on a declining surface reduces transient prolonged standing induced low back pain development", *Applied ergonomics*, Vol. 56, pp. 76–83.

Gallagher, K.M., Campbell, T. and Callaghan, J.P. (2014), "The influence of a seated break on prolonged standing induced low back pain development", *Ergonomics*, Vol. 57 No. 4, pp. 555–562.

Gallagher, K.M., Nelson-Wong, E. and Callaghan, J.P. (2011), "Do individuals who develop transient low back pain exhibit different postural changes than

non-pain developers during prolonged standing?", *Gait & Posture*, Vol. 34 No. 4, pp. 490–495.

Gallagher, K.M., Wong, A. and Callaghan, J.P. (2013), "Possible mechanisms for the reduction of low back pain associated with standing on a sloped surface", *Gait & Posture*, Vol. 37 No. 3, pp. 313–318.

Garcia, M.-G., Laubli, T. and Martin, B.J. (2018), "Muscular and Vascular Issues Induced by Prolonged Standing With Different Work-Rest Cycles With Active or Passive Breaks", *Human factors*, 18720818769261.

Garcia, M.-G., Läubli, T. and Martin, B.J. (2015), "Long-Term Muscle Fatigue After Standing Work", *Human factors*, Vol. 57 No. 7, pp. 1162–1173.

Garcia, M.-G., Wall, R., Steinhilber, B., Läubli, T. and Martin, B.J. (2016), "Long-Lasting Changes in Muscle Twitch Force During Simulated Work While Standing or Walking", *Human factors*, Vol. 58 No. 8, pp. 1117–1127.

Graf, M.K.R.L.T.&M.B.J. (2015), *Should we recommend people to stand more than sit at work?*, Paper presented at the 19th Triennial Congress of the International Ergonomics Association, Melbourne, Australia.

Gregory, D.E. and Callaghan, J.P. (2008), "Prolonged standing as a precursor for the development of low back discomfort: An investigation of possible mechanisms", *Gait & Posture*, Vol. 28 No. 1, pp. 86–92.

Griffith, L.E., Shannon, H.S., Wells, R.P., Walter, S.D., Cole, D.C., Côté, P., Frank, J., Hogg-Johnson, S. and Langlois, L.E. (2012), "Individual participant data meta-analysis of mechanical workplace risk factors and low back pain", *American journal of public health*, Vol. 102 No. 2, pp. 309–318.

Grobe, T., Steinmann, S. and Gerr, J. (2018), "Gesundheitsreport 2018. Fit oder fertig? Erwerbsbiografien in Deutschland", available at: https://www.tk.de/resource/blob/2035612/168c6d8c6e4a6a2919450f0281a03474/gesundheitsreport-2018-data.pdf (accessed 26 November 2018).

Hägg, G.M. (1991), *Static work loads and occupational myalgia: A new explanation model - Part of monograph*.

Halim, I. and Omar, A.R. (2012), "Development of prolonged standing strain index to quantify risk levels of standing jobs", *International journal of occupational safety and ergonomics JOSE*, Vol. 18 No. 1, pp. 85–96.

Halim, I., Omar, A.R., Saman, A.M. and Othman, I. (2012), “Assessment of muscle fatigue associated with prolonged standing in the workplace”, *Safety and health at work*, Vol. 3 No. 1, pp. 31–42.

Hansen, L., Winkel, J. and Jørgensen, K. (1998), “Significance of mat and shoe softness during prolonged work in upright position: based on measurements of low back muscle EMG, foot volume changes, discomfort and ground force reactions”, *Applied Ergonomics*, Vol. 29 No. 3, pp. 217–224.

Henschke, N., Boland, R.A. and Adams, R.D. (2006), “Responsiveness of Two Methods for Measuring Foot and Ankle Volume”, *Foot & Ankle International*, Vol. 27 No. 10, pp. 826–832.

Ismail, L., Normahani, P., Standfield, N.J. and Jaffer, U. (2016), “A systematic review and meta-analysis of the risk for development of varicose veins in women with a history of pregnancy”, *Journal of vascular surgery. Venous and lymphatic disorders*, Vol. 4 No. 4, 518-524.e1.

Kanai, H., Haeno, M. and Sakamoto, K. (1987), “Electrical measurement of fluid distribution in legs and arms. Medical Progress through Technology: Medical engineering in Japan Research and development”, in Atsumi, K., Kajiya, F., Tsuji, T. and Tsujioka, K. (Eds.), Springer Netherlands, Dordrecht, pp. 159–170.

Kanai, H., Haeno, M., Tagawa, H. and Sakamoto, K. (1988), “Electrical Measurement of Fluid Distribution in Human Legs and Arms and Its Clinical Application”, in Carson, E., Kneppo, P. and Krekule, I. (Eds.), *Advances in Biomedical Measurement*, Springer US, pp. 59–70.

Kanai, H., Sakamoto, K. and Haeno, M. (1983), “Electrical measurement of fluid distribution in human legs: estimation of extra- and intra-cellular fluid volume”, *The Journal of microwave power*, Vol. 18 No. 3, pp. 233–243.

Kankam, H.K.N., Lim, C.S., Fiorentino, F., Davies, A.H. and Gohel, M.S. (2018), “A Summation Analysis of Compliance and Complications of Compression Hosiery for Patients with Chronic Venous Disease or Post-thrombotic Syndrome”, *European journal of vascular and endovascular surgery the official journal of the European Society for Vascular Surgery*, Vol. 55 No. 3, pp. 406–416.

Karimi, Z., Allahyari, T., Azghani, M.R. and Khalkhali, H. (2016), “Influence of unstable footwear on lower leg muscle activity, volume change and subjective discomfort during prolonged standing”, *Applied Ergonomics*, 53 Pt A, pp. 95–102.

Kelly, A.M. (1998), “Does the clinically significant difference in visual analog scale pain scores vary with gender, age, or cause of pain?”, *Academic emergency medicine official journal of the Society for Academic Emergency Medicine*, Vol. 5 No. 11, pp. 1086–1090.

Krijnen, R., Boer, E.M. de and Ader, H.J. (1997), “Compression Stockings and Rubber Floor Mats: Do They Benefit Workers With Chronic Venous Insufficiency and a Standing Profession?”, *Journal of Occupational & Environmental Medicine*, Vol. 39 No. 9, pp. 889–894.

Lacroix, P., Aboyans, V., Preux, P.M., Houlès, M.B. and Laskar, M. (2003), “Epidemiology of venous insufficiency in an occupational population”, *International angiology a journal of the International Union of Angiology*, Vol. 22 No. 2, pp. 172–176.

Lang, J., Ochsmann, E., Kraus, T. and Lang, J.W.B. (2012), “Psychosocial work stressors as antecedents of musculoskeletal problems. A systematic review and meta-analysis of stability-adjusted longitudinal studies”, *Social science & medicine (1982)*, Vol. 75 No. 7, pp. 1163–1174.

Leboeuf-Yde, C., Fejer, R., Nielsen, J., Kyvik, K.O. and Hartvigsen, J. (2011), “Consequences of spinal pain: do age and gender matter? A Danish cross-sectional population-based study of 34,902 individuals 20-71 years of age”, *BMC musculoskeletal disorders*, Vol. 12, p. 39.

Lötters, F., Burdorf, A., Kuiper, J. and Miedema, H. (2003), “Model for the work-relatedness of low-back pain”, *Scandinavian journal of work, environment & health*, Vol. 29 No. 6, pp. 431–440.

MacColl, E. and Khalil, R.A. (2015), “Matrix Metalloproteinases as Regulators of Vein Structure and Function. Implications in Chronic Venous Disease”, *The Journal of pharmacology and experimental therapeutics*, Vol. 355 No. 3, pp. 410–428.

Madeleine, P., Voigt, M. and Arendt-Nielsen, L. (1998), “Subjective, physiological and biomechanical responses to prolonged manual work performed standing on hard and soft surfaces”, *European journal of applied physiology and occupational physiology*, Vol. 77 No. 1-2, pp. 1–9.

Mannello, F., Ligi, D., Canale, M. and Raffetto, J.D. (2014), “Omics profiles in chronic venous ulcer wound fluid. Innovative applications for translational medicine”, *Expert review of molecular diagnostics*, Vol. 14 No. 6, pp. 737–762.

Mansilha, A. and Sousa, J. (2018), “Pathophysiological Mechanisms of Chronic Venous Disease and Implications for Venoactive Drug Therapy”, *International journal of molecular sciences*, Vol. 19 No. 6.

March, L., Smith, E.U.R., Hoy, D.G., Cross, M.J., Sanchez-Riera, L., Blyth, F., Buchbinder, R., Vos, T. and Woolf, A.D. (2014), “Burden of disability due to musculoskeletal (MSK) disorders”, *Best practice & research. Clinical rheumatology*, Vol. 28 No. 3, pp. 353–366.

Marschall, J., Hildebrandt, S., Sydow, H. and Nolting, H.-D. (2017), *Gesundheitsreport 2017: Analyse der Arbeitsunfähigkeitsdaten. Update: Schlafstörungen, Beiträge zur Gesundheitsökonomie und Versorgungsforschung*, Vol. 16, 1. Auflage, medhochzwei Verlag, Heidelberg, Neckar.

Marshall, P.W.M., Patel, H. and Callaghan, J.P. (2011), “Gluteus medius strength, endurance, and co-activation in the development of low back pain during prolonged standing”, *Human Movement Science*, Vol. 30 No. 1, pp. 63–73.

McCulloch, J. (2002), “Health risks associated with prolonged standing”, *Work (Reading, Mass.)*, Vol. 19 No. 2, pp. 201–205.

Mosti, G. and Partsch, H. (2013), “Occupational Leg Oedema is More Reduced by Antigraduated than by Graduated Stockings”, *European Journal of Vascular and Endovascular Surgery*, Vol. 45 No. 5, pp. 523–527.

Munch Nielsen, C., Gupta, N., Knudsen, L.E. and Holtermann, A. (2017), “Association of objectively measured occupational walking and standing still with low back pain. A cross-sectional study”, *Ergonomics*, Vol. 60 No. 1, pp. 118–126.

Nelson-Wong, E. and Callaghan, J.P. (2010a), “Is muscle co-activation a predisposing factor for low back pain development during standing? A multifactorial approach for early identification of at-risk individuals”, *Journal of electromyography and kinesiology official journal of the International Society of Electrophysiological Kinesiology*, Vol. 20 No. 2, pp. 256–263.

Nelson-Wong, E. and Callaghan, J.P. (2010b), “The impact of a sloped surface on low back pain during prolonged standing work: a biomechanical analysis”, *Applied Ergonomics*, Vol. 41 No. 6, pp. 787–795.

Nelson-Wong, E., Gregory, D.E., Winter, D.A. and Callaghan, J.P. (2008), “Gluteus medius muscle activation patterns as a predictor of low back pain during standing”, *Clinical biomechanics (Bristol, Avon)*, Vol. 23 No. 5, pp. 545–553.

O'Callaghan, C.J. and Williams, B. (2000), “Mechanical strain-induced extracellular matrix production by human vascular smooth muscle cells. Role of TGF-beta(1)”, *Hypertension (Dallas, Tex. 1979)*, Vol. 36 No. 3, pp. 319–324.

Palacios-Ceña, D., Alonso-Blanco, C., Hernández-Barrera, V., Carrasco-Garrido, P., Jiménez-García, R. and Fernández-de-las-Peñas, C. (2015), “Prevalence of neck and low back pain in community-dwelling adults in Spain: an updated population-based national study (2009/10-2011/12)”, *European spine journal official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, Vol. 24 No. 3, pp. 482–492.

Palmer, K.T., Bonzini, M., Harris, E.C., Linaker, C. and Bonde, J.P. (2013), “Work activities and risk of prematurity, low birth weight and pre-eclampsia: an updated review with meta-analysis”, *Occupational and environmental medicine*, Vol. 70 No. 4, pp. 213–222.

Parent-Thirion, A., G. Vermeylen, G. van Houten, M. Lyly-Yrjänäinen, I. Biletta and J. Cabrita. (op. 2012), *Fifth European working conditions survey*, Publications Office of the European Union, Luxembourg.

Partsch, H., Winiger, J. and Lun, B. (2004), “Compression stockings reduce occupational leg swelling”, *Dermatologic surgery official publication for American Society for Dermatologic Surgery [et al.]*, Vol. 30 No. 5, 737-43; discussion 743.

Pensri, P., Janwantanakul, P. and Chaikumarn, M. (2009), “Prevalence of self-reported musculoskeletal symptoms in salespersons”, *Occupational medicine (Oxford, England)*, Vol. 59 No. 7, pp. 499–501.

Petersen, E.J., Irish, S.M., Lyons, C.L., Miklaski, S.F., Bryan, J.M., Henderson, N.E. and Masullo, L.N. (1999), “Reliability of Water Volumetry and the Figure of Eight Method on Subjects With Ankle Joint Swelling”, *J Orthop Sports Phys Ther*, Vol. 29 No. 10, pp. 609–615.

Pfisterer, L., Konig, G., Hecker, M. and Korff, T. (2014), “Pathogenesis of varicose veins - lessons from biomechanics”, *VASA. Zeitschrift fur Gefasskrankheiten*, Vol. 43 No. 2, pp. 88–99.

Rabe, E., Guex, J.J., Puskas, A., Scuderi, A. and Fernandez Quesada, F. (2012), “Epidemiology of chronic venous disorders in geographically diverse populations. Results from the Vein Consult Program”, *International angiology a journal of the International Union of Angiology*, Vol. 31 No. 2, pp. 105–115.

Rabe, E. and Pannier, F. (2010), “Societal costs of chronic venous disease in CEAP C4, C5, C6 disease”, *Phlebology*, 25 Suppl 1, pp. 64–67.

Rabe, E., Stücker, M. and Ottillinger, B. (2010), “Water displacement leg volumetry in clinical studies - A discussion of error sources”, *BMC Medical Research Methodology*, Vol. 10 No. 1, p. 5.

Raftry, S.M. and Marshall, P.W.M. (2012), “Does a 'tight' hamstring predict low back pain reporting during prolonged standing?”, *Journal of electromyography and kinesiology official journal of the International Society of Electrophysiological Kinesiology*, Vol. 22 No. 3, pp. 407–411.

Robertson, L., Lee, A.J., Evans, C.J., Boghossian, S., Allan, P.L., Ruckley, C.V. and Fowkes, F.G.R. (2013), “Incidence of chronic venous disease in the Edinburgh Vein Study”, *Journal of vascular surgery. Venous and lymphatic disorders*, Vol. 1 No. 1, pp. 59–67.

Safe Work Australia (2011), *National hazard exposure worker surveillance: exposure to biomechanical demands, pain and fatigue symptoms and the provision of controls in Australian workplaces.*, Canberra, Australia.

Saito, S., Trovato, M.J., You, R., Lal, B.K., Fasehun, F., Padberg, F.T., Hobson, R.W., Durán, W.N. and Pappas, P.J. (2001), “Role of matrix

metalloproteinases 1, 2, and 9 and tissue inhibitor of matrix metalloproteinase-1 in chronic venous insufficiency", *Journal of vascular surgery*, Vol. 34 No. 5, pp. 930–938.

Sanders, J.E., Allyn, K.J., Harrison, D.S., Myers, T.R., Ciol, M.A. and Tsai, E.C. (2012), "Preliminary investigation of residual-limb fluid volume changes within one day", *Journal of rehabilitation research and development*, Vol. 49 No. 10, pp. 1467–1478.

Segiet, O.A., Brzozowa-Zasada, M., Piecuch, A., Dudek, D., Reichman-Warmusz, E. and Wojnicz, R. (2015), "Biomolecular mechanisms in varicose veins development", *Annals of vascular surgery*, Vol. 29 No. 2, pp. 377–384.

Seibt, R., Wall, R., Rieger, M.A. and Steinhilber, B. (2018), "Modellierung der Ödembildung in den unteren Extremitäten bei Steharbeit", in *ARBEIT(S).WISSEN.SCHAF(F)T Grundlage für Management & Kompetenzentwicklung: 64. Kongress der Gesellschaft für Arbeitswissenschaft FOM Hochschule für Oekonomie & Management, 21.-23. Februar 2018*, GfA-Press, Dortmund.

Seo, A., Kakehashi, M., Uda, S., Tsuru, S. and Yoshinaga, F. (1995), "Bioelectrical impedance measuring method for standing load evaluation", *Sangyō eiseigaku zasshi = Journal of occupational health*, Vol. 37 No. 2, pp. 83–87.

Seo, A., Rys, M. and Konz, S. (2001), "Measuring lower leg swelling: Optimum frequency for impedance method", *Medical & Biological Engineering & Computing*, Vol. 39 No. 2, pp. 185–189.

Serralheiro, P., Soares, A., Costa Almeida, C.M. and Verde, I. (2017), "TGF-β1 in Vascular Wall Pathology. Unraveling Chronic Venous Insufficiency Pathophysiology", *International journal of molecular sciences*, Vol. 18 No. 12.

Sorensen, C.J., Norton, B.J., Callaghan, J.P., Hwang, C.-T. and van Dillen, L.R. (2015), "Is lumbar lordosis related to low back pain development during prolonged standing?", *Manual therapy*, Vol. 20 No. 4, pp. 553–557.

Speed, G., Harris, K. and Keegel, T. (2018), "The effect of cushioning materials on musculoskeletal discomfort and fatigue during prolonged standing at work. A systematic review", *Applied ergonomics*, Vol. 70, pp. 300–314.

Statistisches Bundesamt (Destatis) (2018), “Krankheitskosten in Mio. € für Deutschland”, available at: https://bit.ly/2DTUyvc (accessed 23 November 2018).

Steinhilber, B., Enghofer, A., Wall, R., Lips, O., Seibt, R., Schmeltzpfenning, T. and Rieger, M.A. (2017), “Reduktion des Unterschenkelvolumens während einer Stehexposition durch Kompressionsstrümpfe - Einfluss der Kompressionsklasse”, in Harth, V. and Heidrich, J. (Eds.), *Dokumentation der Vorträge und Poster, Hamburg, 15.-17. März 2017*, Geschäftsstelle der Deutschen Gesellschaft für Arbeitsmedizin und Umweltmedizin e. V, München.

Steinhilber, B., Seibt, R., Wall, R. and Rieger, M.A. (2016), “Welche Effekte hat mehrstündiges Stehen? Einfluss von Alter, Geschlecht und beruflicher Vorerfahrung auf subjektive und objektive Parameter.”, in Schmitz-Spanke, S. (Ed.), *Dokumentation der Vorträge und Poster, München, 09.-11. März 2016*, Geschäftsstelle der Deutschen Gesellschaft für Arbeitsmedizin und Umweltmedizin e. V, München.

Stewart Williams, J., Ng, N., Peltzer, K., Yawson, A., Biritwum, R., Maximova, T., Wu, F., Arokiasamy, P., Kowal, P. and Chatterji, S. (2015), “Risk Factors and Disability Associated with Low Back Pain in Older Adults in Low- and Middle-Income Countries. Results from the WHO Study on Global AGEing and Adult Health (SAGE)”, *PloS one*, Vol. 10 No. 6, e0127880.

Stick, C., Grau, H. and Witzleb, E. (1989), “On the edema-preventing effect of the calf muscle pump”, *European journal of applied physiology and occupational physiology*, Vol. 59 No. 1, pp. 39–47.

Stick, C., Jaeger, H. and Witzleb, E. (1992), “Measurements of volume changes and venous pressure in the human lower leg during walking and running”, *Journal of applied physiology (Bethesda, Md. 1985)*, Vol. 72 No. 6, pp. 2063–2068.

Stick, C., Stofen, P. and Witzleb, E. (1985), “On physiological edema in man's lower extremity”, *European journal of applied physiology and occupational physiology*, Vol. 54 No. 4, pp. 442–449.

Suva (2014), “Sitzen oder stehen? Ergonomische Gestaltung von Arbeitsplätzen”, available at: https://goo.gl/kYfq9g (accessed 8 June 2015).

Tabatabaeifar, S., Frost, P., Andersen, J.H., Jensen, L.D., Thomsen, J.F. and Svendsen, S.W. (2015), “Varicose veins in the lower extremities in relation to occupational mechanical exposures: a longitudinal study”, *Occupational and environmental medicine*, Vol. 72 No. 5, pp. 330–337.

Takase, S., Pascarella, L., Lerond, L., Bergan, J.J. and Schmid-Schönbein, G.W. (2004), “Venous hypertension, inflammation and valve remodeling”, *European Journal of Vascular and Endovascular Surgery*, Vol. 28 No. 5, pp. 484–493.

Tissot, F., Messing, K. and Stock, S. (2005), “Standing, sitting and associated working conditions in the Quebec population in 1998”, *Ergonomics*, Vol. 48 No. 3, pp. 249–269.

Tomei, F., Baccolo, T.P., Tomao, E., Palmi, S. and Rosati, M.V. (1999), “Chronic venous disorders and occupation”, *American Journal of Industrial Medicine*, Vol. 36 No. 6, pp. 653–665.

Tüchsen, F., Hannerz, H., Burr, H. and Krause, N. (2005), “Prolonged standing at work and hospitalisation due to varicose veins: a 12 year prospective study of the Danish population”, *Occupational and environmental medicine*, Vol. 62 No. 12, pp. 847–850.

Tüchsen, F., Krause, N., Hannerz, H., Burr, H. and Kristensen, T.S. (2000), “Standing at work and varicose veins”, *Scandinavian journal of work, environment & health*, Vol. 26 No. 5, pp. 414–420.

Uda, S., Seo, A. and Yoshinaga, F. (1997), “Swell-preventing effect of intermittent exercise on lower leg during standing work”, *Industrial health*, Vol. 35 No. 1, pp. 36–40.

Urbich, C., Mallat, Z., Tedgui, A., Clauss, M., Zeiher, A.M. and Dimmeler, S. (2001), “Upregulation of TRAF-3 by shear stress blocks CD40-mediated endothelial activation”, *The Journal of clinical investigation*, Vol. 108 No. 10, pp. 1451–1458.

van Beukering, M., van Melick, M., Mol, B., Frings-Dresen, M. and Hulshof, C.T.J. (2014), “Physically demanding work and preterm delivery: a systematic review and meta-analysis”, *International archives of occupational and environmental health*, Vol. 87 No. 8, pp. 809–834.

Visser, B. and van Dieën, J.H. (2006), “Pathophysiology of upper extremity muscle disorders”, *Journal of electromyography and kinesiology official journal of the International Society of Electrophysiological Kinesiology*, Vol. 16 No. 1, pp. 1–16.

Walker, B.F. (2000), “The prevalence of low back pain. A systematic review of the literature from 1966 to 1998”, *Journal of spinal disorders*, Vol. 13 No. 3, pp. 205–217.

Wall, R., Götte, N., Seibt, R., Rieger, M.A. and Steinhilber, B. (2018), “Rückenbeschwerden bei Steharbeit - Welche Bedeutung haben Aktivierungsmuster der Becken stabilisierenden Muskulatur und Aktivie-rungsphasen durch Gehen.”, in *ARBEIT(S).WISSEN.SCHAF(F)T Grundlage für Management & Kompetenzentwicklung: 64. Kongress der Gesellschaft für Arbeitswissenschaft FOM Hochschule für Oekonomie & Management, 21.-23. Februar 2018*, GfA-Press, Dortmund.

Wiggermann, N. and Keyserling, W.M. (2013), “Effects of anti-fatigue mats on perceived discomfort and weight-shifting during prolonged standing”, *Human factors*, Vol. 55 No. 4, pp. 764–775.

Wittig, P., Nöllenheidt, C. and Brenscheidt, S. (2013), “Grundauswertung der BIBB/BAuA-Erwerbstätigenbefragung 2012. mit den Schwerpunkten Arbeitsbedingungen, Arbeitsbelastungen und gesundheitliche Beschwerden”.

Wong, A.Y., Karppinen, J. and Samartzis, D. (2017), “Low back pain in older adults. Risk factors, management options and future directions”, *Scoliosis and spinal disorders*, Vol. 12, p. 14.

Wong, A.Y.L., Parent, E.C., Funabashi, M. and Kawchuk, G.N. (2014), “Do changes in transversus abdominis and lumbar multifidus during conservative treatment explain changes in clinical outcomes related to nonspecific low back pain? A systematic review”, *The journal of pain official journal of the American Pain Society*, Vol. 15 No. 4, 377.e1-35.

Woodside, K.J., Hu, M., Burke, A., Murakami, M., Pounds, L.L., Killewich, L.A., Daller, J.A. and Hunter, G.C. (2003), “Morphologic characteristics of varicose veins. Possible role of metalloproteinases”, *Journal of vascular surgery*, Vol. 38 No. 1, pp. 162–169.

Wrona, M., Jöckel, K.-H., Pannier, F., Bock, E., Hoffmann, B. and Rabe, E. (2015), “Association of Venous Disorders with Leg Symptoms. Results from the Bonn Vein Study 1”, *European journal of vascular and endovascular surgery the official journal of the European Society for Vascular Surgery*, Vol. 50 No. 3, pp. 360–367.

Yasim, A., Kilinc, M., Aral, M., Oksuz, H., Kabalci, M., Eroglu, E. and Imrek, S. (2008), “Serum concentration of procoagulant, endothelial and oxidative stress markers in early primary varicose veins”, *Phlebology*, Vol. 23 No. 1, pp. 15–20.

Zennaro, D., Läubli, T., Krebs, D., Klipstein, A. and Krueger, H. (2003), “Continuous, intermitted and sporadic motor unit activity in the trapezius muscle during prolonged computer work”, *Journal of electromyography and kinesiology official journal of the International Society of Electrophysiological Kinesiology*, Vol. 13 No. 2, pp. 113–124.

9 Declaration of own contribution

Publication 1

The concept and design of the study was done in collaboration with Dr. Benjamin Steinhilber and Robert Seibt.

All of the experiments were conducted by Oliwia Lips and myself (Rater 1: Oliwia Lips; Rater 2: Rudolf Wall). The statistical evaluation was done by me (according to Dr. Benjamin Steinhilber's instructions).

I declare that I have written the manuscript independently and that I have not used any sources other than those specified by me. After review by Dr. Benjamin Steinhilber, Prof. Monika A. Rieger and Robert Seibt, I have included all their changes in the final manuscript.

Publication 2

The concept and design of the study was done in collaboration with Dr. Benjamin Steinhilber, Prof. Monika A. Rieger, Dr. Thomas Läubli and Robert Seibt.

Most of the experiments were conducted by myself (or under my supervision) in collaboration with Tabea Pomes, Oliwia Lips, Amko Groeneveld and Valerie Dieter. The statistical evaluation was done by me (after consulting the Institute for Clinical Epidemiology and Applied Biometry and according to Dr. Benjamin Steinhilber's and Dr. Thomas Läubli's instructions).

I declare that I have written the manuscript independently and that I have not used any sources other than those specified by me. After review by Dr. Benjamin Steinhilber, Prof. Monika A. Rieger, Dr. Thomas Läubli and Robert Seibt, I have included all their changes in the final manuscript.

Publication 3

The concept and design of the study was done in collaboration with Dr. Benjamin Steinhilber, Prof. Monika A. Rieger, Dr. Thomas Läubli, Dr. Maria Gabriela Garcia Rodriguez and Robert Seibt.

Most of the experiments were conducted by myself (or under my supervision) in collaboration with Tabea Pomes, Oliwia Lips, Amko Groeneveld and Valerie Dieter. The ‘Muscle Twitch Force’ (MTF) measurements were conducted by Dr. Maria Gabriela Garcia Rodriguez and myself according to Dr. Garcia’s instructions. The statistical evaluation of the surface electromyography, waterplethysmography and bioelectrical impedance data was done by me (after consulting the Institute of Biometry and according to Dr. Benjamin Steinhilber's and Dr. Thomas Läubli’s instructions). Statistical analysis, figures and tables concerning MTF data was done by Dr. Maria Gabriela Garcia Rodriguez.

I declare that I have written the surface electromyography, waterplethysmography and bioelectrical impedance parts of the manuscript independently and that I have not used any sources other than those specified by me. All the MTF parts were written by Dr. Maria Gabriela Garcia Rodriguez. After review by Dr. Maria Gabriela Garcia Rodriguez, Dr. Benjamin Steinhilber, Prof. Monika A. Rieger, Dr. Thomas Läubli, Prof. Bernard Martin and Robert Seibt, I have included all their changes in the final manuscript.

Dissertation

This work was conducted in the Institute of Occupational Medicine, Social Medicine and Health Services Research under supervision of Prof. Dr. Monika A. Rieger and Dr. Benjamin Steinhilber.

The experiments and the statistical analysis were conducted according to the declarations of own contributions of the three included papers.

I declare that I have written the manuscript independently and that I have not used any sources other than those specified by me.

10 Theses resulting from the two studies of the dissertation

The theses mentioned below resulted from the two studies of the dissertation. The data used in those theses were not part of the publications in this dissertation except for minor parts of the doctoral thesis of Oliwia Lips as mentioned in the declaration of own contribution of paper 1.

Amko Gröneveld, Bachelor of Arts (B.A.) Medizintechnik:

> Effekte einer mehrstündigen Steh- und Gehexposition auf die Umfangsänderung der unteren Extremitäten - Modell zur zeitlichen Entwicklung des Ödems.

Oliwia Lips, Dr. med.:

> Reliabilität der Wasserplethysmographie zur Quantifizierung des Unterschenkelvolumens und Effekte einer Anti-Ermüdungsmatte auf das Unterschenkelvolumen sowie subjektive Beschwerdewahrnehmung bei mehrstündiger Stehexposition.

Jannika Salzmann, Bachelor of Arts (B.A.) Medizintechnik:

> Entwicklung geeigneter Kenngrößen zur Kraftsinnmessung bei Steharbeit.

Johanna Elisabeth Bollerey, Bachelor of Arts (B.A.) Medizintechnik:

> Kenngrößen der Kraftsinnmessung: Aspekte der Intratages-Reliabilität und Auswirkungen von statischer Muskelermüdung.

Verena Kunz, Bachelor of Arts (B.A.) Medizintechnik:

> Haltungsanalyse im Bereich der Lendenwirbelsäule bei mehrstündigen Steh-und Gehexposition: Ergebnisse einer explorativen Untersuchung.

11 List of scientific publications

11.1 Scientific journal contributions

Wall, R., Garcia, G., Läubli, T., Seibt, R., Rieger, M.A., Martin, B. and Steinhilber, B. (2020), “Physiological changes during prolonged standing and walking considering age, gender and standing work experience”, *Ergonomics*, Vol. 63 No. 5, pp. 579–592. DOI: 10.1080/00140139.2020.1725145.

Wall, R., Läubli, T., Seibt, R., Rieger, M.A. and Steinhilber, B. (2019), “Associations between low back muscle activity, pelvic movement and low back discomfort development during prolonged standing – An exploratory laboratory study”, *International Journal of Industrial Ergonomics*, Vol. 72, pp. 380–389. DOI: 10.1016/j.ergon.2019.07.001.

Wall, R.; Lips, O.; Seibt, R.; Rieger, M.; Steinhilber, B. (2017), “Intra- and inter-rater reliability of lower leg waterplethysmography, bioelectrical impedance and muscle twitch force for the use in standing work evaluation”, *Physiological Measurement*. DOI: 10.1088/1361-6579/aa6711.

Garcia, M.G, **Wall, R.**, Steinhilber, B., Läubli, T. & Martin, B.J. (2016), “Long-Lasting Changes in Muscle Twitch Force During Simulated Work While Standing or Walking”, *Human Factors*, Vol. 58 No. 8, pp. 1117–1127. DOI: 10.1177/0018720816669444

Wall, R., Seibt, R., & Steinhilber, B. (2016), ”Steharbeit – Risiken und Lösungsansätze mittels quantitativer Methoden”, *Eingeladener Beitrag bei der Zeitschrift: Medizinisch Orthopädische Technik,* 1, S. 12-17

11.2 Congress*/* conference contributions

Wall, R.; Läubli, T.; Klussmann, A.; Seibt, R.; Rieger, M.A., Steinhilber B. (2018), “Prolonged standing, lumbar spine movements and low back pain – a laboratory study”. *Oral presentation at the “20th Congress of the International Ergonomics Association (IEA)”* 2018 in Florence, Italy.

Wall, R.; Seibt, R.; Läubli, T.; Rieger, M.A., Steinhilber B. (2017), „Einfluss von Gehphasen auf das Unterschenkelvolumen bei mehrstündigem Stehen – Entwicklung eines Modells“. *Oral presentation at the „21.Symposium Arbeitsmedizin und Arbeitswissenschaft für Nachwuchswissenschaftler und Nachwuchswissenschaftlerinnen des Forums Arbeitsphysiologie*“ 2017 in Bad Münder, Germany.

Wall, R.; Seibt, R.; Klussmann, A.; Läubli, T.; Rieger, M.A., Steinhilber B. (2017), „Objektive Ermüdungszeichen der lumbalen Rückenmuskulatur bei mehrstündigem Stehen und Gehen“. *Poster presentation at the „Nachwuchssymposium der Deutschen Gesellschaft für Arbeits- und Umweltmedizin (DGAUM)“* 2017 in Hamburg, Germany.

Wall, R.; Seibt, R.; Klussmann, A.; Läubli, T.; Rieger, M.A., Steinhilber B. (2017), „Effekte mehrstündigen Stehens auf die Ödembildung der unteren Extremitäten sowie muskuläre Beanspruchung der LWS- und Unterschenkelmuskulatur. *Oral presentation at the „63. Frühjahrskongress der Gesellschaft für Arbeitswissenschaft e.V.“* 2017 in Brugg-Windisch and Zurich, Switzerland.

Wall, R.; Seibt, R.; Klussmann, A.; Läubli, T.; Rieger, M.A., Steinhilber B. (2016), „Effekte einer mehrstündigen Steh- und Gehexposition auf Zeichen muskulärer Ermüdung der lumbalen Rückenmuskulatur“. *Oral presentation at the „20. Symposium Arbeitsmedizin und Arbeitswissenschaft für Nachwuchswissenschaftler und Nachwuchswissenschaftlerinnen des Forums Arbeitsphysiologie von DGAUM und GfA“*, 2016 in Freiburg, Germany.

Wall, R.; Seibt, R.; Garcia, G.; Klussmann, A.; Läubli, T.; Martin, B.; Rieger, M.A., Steinhilber B. (2016), “Determining lower leg edema in standing work: Reliability of a modified Waterplethysmography and effects of prolonged standing exposure”. *Oral presentation at the at the “9th International Scientific Conference on the Prevention of Work-Related Musculoskeletal Disorders” (PREMUS)* 2016 in Toronto, Canada.

Wall, R., Lips, O., Seibt, R., Rieger, M.A., Steinhilber, B. (2016), „Testgütekriterien einer modifizierten Wasserplethysmographie: Test-Retest-Reliabilität und Interrater-Reliabilität bei der Erfassung des Unterschenkelvolumens“. *Oral*

presentation at the „Doktoranden-Werkstatt der Frühjahrskonferenz der Gesellschaft für Arbeitsmedizin (GfA)“ 2016 in Aachen, Germany.

Wall, R.; Seibt, R.; Garcia, G.; Klussmann, A.; Läubli, T.; Martin, B.; Rieger, M.A., Steinhilber B. (2016), „Erfassung des Ödems bei Steharbeit: Testgüte einer modifizierten Wasserplethysmographie und Effekte durch eine mehrstündige Stehexposition“. *Poster presentation at the „Nachwuchssymposium der Deutschen Gesellschaft für Arbeits- und Umweltmedizin (DGAUM)“* 2016 in Munich, Germany.

Wall, R.; Seibt, R.; Garcia, M.-G.; Klussmann, A.; Läubli, T.; Martin, B.; Rieger, M.A., Steinhilber B. (2015), „Effekte einer mehrstündigen Stehexposition auf ausgewählte Messgrößen physiologischer Beanspruchung“. *Poster presentation at the „22. Erfurter Tage“* 2015 in Erfurt, Germany.

Wall, R.; Seibt, R.; Garcia, M.-G.; Klussmann, A.; Läubli, T.; Martin, B.; Rieger, M.A., Steinhilber B. (2015), „Effekte einer mehrstündigen Stehexposition auf ausgewählte Messgrößen physiologischer Beanspruchung“. *Oral presentation at the „Nachwuchssymposium des Forum Arbeitsphysiologie (FAP)“* 2015 in Rostock, Germany.

Wall, R.; Seibt, R.; Garcia, M.-G.; Klussmann, A.; Läubli, T.; Martin, B.; Rieger, M.A., Steinhilber B. (2015), „Effekte einer mehrstündigen Stehexposition auf ausgewählte Messgrößen physiologischer und subjektiver Beanspruchung“. *Poster presentation at the* „Nachwuchssymposium der Deutschen Gesellschaft für Arbeits- und Umweltmedizin (DGAUM)“ 2015 in Munich, Germany.

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