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Characterization of lower limb joint moments during gait of Diabetes patients, with and without polyneuropathy

Dissertação apresentada com vista à obtenção do 2º ciclo em Atividade Física Adaptada, da Faculdade de Desporto da Universidade do Porto, ao abrigo do Decreto-Lei nº 74/2006, de 24 de março, na redação dada pelo Decreto-Lei nº 65/2018 de 16 de agosto.

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Abstract

Diabetes and diabetic polyneuropathy are associated with changes in the gait pattern, which increases the risk of foot ulcers and leads to higher morbidity and mortality. Despite the increased interest in the biomechanical gait analysis of diabetic individuals in the past decades, the conflicting results and the limited data on joint moments hamper the evidence of the effects of the disease on these parameters. The two studies described in this dissertation aimed at clarifying these findings. The first is a systematic review with meta-analysis on the joint moments in the gait of diabetic people, with and without polyneuropathy. The second consists of a sagittal and frontal plane biomechanical analysis of the joint moments during walking, comparing diabetic individuals, with and without polyneuropathy, with healthy subjects.

The first study aimed to examine the effects of diabetes and diabetic polyneuropathy on the ankle, knee and hip joint moments, during gait. A literature search was conducted, in line with the PRISMA guidelines, on PubMed, Scopus and Web of Science databases, for articles reporting joint moments in diabetics without polyneuropathy (DM), with diabetic polyneuropathy (DPN) and healthy ones (CONTROL), during gait. Meta-analyses were carried out on joint moment parameters reported by two or more studies. Ten articles were included in the review and meta-analysis were performed on eight joint moment parameters. A high level of heterogeneity was observed between studies. Meta analysis results suggested a higher ankle plantar flexion and knee flexion moments in CONTROL, when compared to DM and DPN groups, at a self-selected speed. No differences were observed in the hip joint moments. With an imposed speed of 1.2 m/s, evidence suggested higher ankle plantar flexion moments in the CONTROL group, when compared to the DM. No evidence of differences between DM and DPN was found in any of the reported joint moments.

The second study aimed to compare the joint moments at the ankle, knee and hip, in the sagittal and frontal planes, between DM, DPN and CONTROL subjects. Eight DM participants (age: 38.75 ± 18.09 years old; height: 1.68 ± 0.12 m; mass: 70.39 ± 16.46 kg; BMI: 24.70 ± 2.89 kg/cm^2), and eight DPN subjects

(age:64.63 ± 11.46 years old; height: 1.70 ± 0.13 m; mass: 87.14 ± 12.71 kg; BMI: 30.04 ± 2.65 kg/cm^2) participated in this study and were compared to the data of ten CONTROL individuals (age: 48.50 ± 7.75 years old; height: 1.73 ± 0.07 m; mass: 69.06 ± 13.52 kg; BMI: 22.86 ± 3.24 kg/cm^2) from a public multimodal database. The ankle, knee and hip joint moments, in the sagittal and frontal plane, were analyzed, at a self-selected gait speed. When compared to the DM group, the DPN group presented reduced ankle plantar flexion, ankle evertor, knee extension, knee flexion and hip flexion moments. The DM revealed increased knee flexion, knee extension and hip extensor moments, and reduced ankle evertor, knee valgus and hip abductor moments, when compared to CONTROL. The DPN presented higher knee flexion and knee varus moments, and reduced ankle evertor, ankle invertor and knee valgus moments, when compared to CONTROL.

These studies reveal that diabetes and diabetic polyneuropathy have more significant impact on these biomechanical parameters than previously reported, which may contribute to develop more effective interventions aiming at minoring the negative effects of diabetes and diabetic polyneuropathy.

Keywords: Biomechanics; Gait; Diabetes; Diabetic polyneuropathy; Joint moments; Systematic review; Meta-analysis.

Resumo

A diabetes e a polineuropatia diabética estão associadas a mudanças no padrão de marcha, o que aumenta o risco de ulceração, levando ao aumento da morbilidade e mortalidade. Nas últimas décadas, a análise biomecânica da marcha em sujeitos com diabetes tem sido alvo de um interesse crescente. Contudo, a par da escassez de estudos neste domínio, os resultados obtidos nos mesmos configuram-se como contraditórios, o que dificulta a compreensão dos efeitos da patologia nos momentos articulares. Os dois estudos descritos nesta dissertação têm como objetivo clarificar estes resultados. O primeiro é uma revisão sistemática da literatura com meta-análise dos momentos articulares na marcha de sujeitos com diabetes, com e sem polineuropatia. O segundo consiste numa análise biomecânica dos momentos articulares, durante a marcha, nos planos sagital e frontal, em sujeitos com diabetes, com e sem polineuropatia, e sujeitos saudáveis.

O primeiro estudo teve como objetivo avaliar os efeitos da diabetes e da polineuropatia diabética, nos momentos articulares do tornozelo, joelho e anca, durante a marcha. Foi realizada uma pesquisa bibliográfica, de acordo com as diretrizes PRISMA, nas bases de dados PubMed, Scopus e Web of Science, considerando os artigos que reportavam momentos articulares na marcha de sujeitos diabéticos sem polineuropatia (DM), em sujeitos diabéticos com polineuropatia (DPN) e sujeitos saudáveis (CONTROL). Foi conduzida uma meta-análise em momentos articulares reportados em, pelo menos, dois artigos. Foram incluídos, nesta revisão, dez artigos, tendo sido realizada uma meta-análise com oito parâmetros dos momentos articulares. Observou-se uma elevada heterogeneidade entre estudos. Os resultados da meta-análise apontam para momentos de flexão plantar do tornozelo e flexor do joelho aumentados no CONTROL, quando comparados com DM e DPN, a uma velocidade autoselecionada. Não foram observadas diferenças nos momentos articulares da anca.

O segundo estudo teve como objetivo comparar os momentos articulares do tornozelo, joelho e anca, nos planos sagital e frontal, entre sujeitos DM, DPN

e CONTROL. Oito sujeitos do grupo DM (idade: 38.75 ± 18.09 anos; altura: 1.68 ± 0.12 m; massa: 70.39 ± 16.46 kg; IMC: 24.70 ± 2.89 kg/m^2), e oito do grupo DPN (idade:64.63 ± 11.46 anos; altura: 1.70 ± 0.13 m; massa: 87.14 ± 12.71 kg; IMC: 30.04 ± 2.65 kg/m^2) participaram neste estudo, tendo sido comparados com os dados de dez sujeitos do grupo CONTROL (idade: 48.50 ± 7.75 anos; altura: 1.73 ± 0.07 m; massa: 69.06 ± 13.52 kg; IMC: 22.86 ± 3.24 kg/m^2) provenientes de uma base de dados multimodal pública. Os momentos articulares do tornozelo, joelho e anca, nos planos sagital e frontal, foram analisados a uma velocidade autoselecionada. Quando comparado com o grupo DM, o grupo DPN apresentou momentos de flexão plantar e inversor do tornozelo, extensor e flexor do joelho, e flexor da anca reduzidos. O grupo DM exibiu momentos flexor e extensor do joelho e extensor da anca aumentados, a par de momentos eversor do tornozelo, valgo do joelho e abdutor da anca reduzidos, comparativamente com o CONTROL. Foram observados valores mais elevados nos momentos flexor e varo do joelho e mais reduzidos nos momentos eversor e inversor do tornozelo e valgo do joelho no DPN, quando comparados com o CONTROL.

Estes estudos mostram que a diabetes e a polineuropatia diabética podem ter um impacto mais significativo nestes parâmetros biomecânicos do que a investigação tem mostrado, o que pode contribuir para o desenvolvimento de intervenções direcionadas para a redução dos efeitos negativos da diabetes e da polineuropatia diabética.

Palavras-chave: Biomecânica; Marcha; Diabetes; Polineuropatia diabética; Momentos articulares; Revisão sistemática; Meta-análise

1. General Introduction

Diabetes is a worldwide chronic metabolic disease with important implications for individuals, not only for their health, but also because of the potential social stigma and economic burden (World Health Organization, 2019).

One of the most common long-term complications of the disease is the development of a length-dependent polyneuropathy, that contributes to increased morbidity and mortality (Andersen, 2012; Pop-Busui et al., 2017). The varied levels of neurologic impairment manifest in the gait and posture of affected individuals, such as postural instability and lack of coordination and strength.

Biomechanical gait analysis helps researchers and clinicians to better understand these changes and, consequently, to provide the development of more effective interventions that can improve the health and quality of life of people with diabetes. Internal joint moments are a commonly assessed parameter in gait analysis (Hazari et al., 2016). However, there is still limited data available regarding the effect of diabetes and associated peripheral neuropathy in these variables (Alam et al., 2017).

Two original articles are presented in this dissertation: i) a systematic review with meta-analysis on the joint moments in the gait of diabetic people, with and without polyneuropathy and ii) a sagittal and frontal plane biomechanical analysis of the joint moments during walking, comparing diabetic individuals, with and without polyneuropathy, with healthy subjects.

By taking into account the existing gap in the literature, this dissertation aims at increasing the knowledge on the effects of diabetes and diabetic polyneuropathy on the lower-limb joint moments during gait.

2. Study I: Joint moments in the gait of diabetic individuals with and without peripheral neuropathy – a systematic review

2.1. Abstract

Background: Diabetes and diabetic polyneuropathy are associated with changes in the gait pattern, increasing the risk of foot ulcers and leading to higher morbidity and mortality. The evidence of the effects of the disease on joint moments, during gait, is inconsistent. This systematic review with meta-analysis investigated the effects of diabetes and diabetic polyneuropathy on the ankle, knee and hip joint moments, during gait.

Methods: A literature search was conducted, in line with the PRISMA guidelines, on PubMed, Scopus and Web of Science databases, for articles reporting joint moments in diabetic groups without polyneuropathy (DM) and/or with diabetic polyneuropathy (DPN), compared or not with healthy ones (CONTROL). Meta-analyses were carried out on joint moment parameters reported by two or more studies.

Results: Ten studies were included in the review, and meta-analysis were performed on eight joint moment parameters. A high level of heterogeneity was observed between studies. Meta analysis results suggested a higher ankle plantar flexion and knee flexion moments in CONTROL, when compared to DM and DPN groups, at a self-selected speed. No differences were observed in the hip joint moments. With an imposed speed of 1.2 m/s, evidence suggested higher ankle plantar flexion moments in the CONTROL group, when compared to the DM. No evidence of differences between DM and DPN was found in any of the reported joint moments.

Conclusion: The scarce literature and the elevated heterogeneity of the reported studies may have an impact on the clinical significance of data. These results provide evidence that subjects with diabetes, with or without associated peripheral neuropathy, present lower joint moment values than healthy subjects. However, no evidence of differences between subjects with diabetes and

subjects with diabetic polyneuropathy were observed. More studies are needed to establish the evidence regarding these findings.

Keywords: Biomechanics; Gait; Diabetes; Diabetic polyneuropathy; Joint moments; Systematic review; Meta-analysis.

2.2. Introduction

Diabetes is a group of metabolic disorders that are characterized by prolonged hyperglycemia in the absence of a specific treatment (World Health Organization, 2019). This disease has an increased worldwide expression with its prevalence estimated to reach 578 million people by 2030 and 700 million people by 2045 (Saeedi et al., 2019). Distal symmetrical polyneuropathy is one of the most common long-term complications of diabetes. It is characterized by progressive loss of nerve fibers affecting the somatic and autonomic nervous systems (Tesfaye et al., 2013), usually starting with sensory involvement and progressing to motor and autonomic dysfunction (Yavuzer et al., 2006). Musculoskeletal involvement includes progressive atrophy of the intrinsic foot muscles, which can lead to various types of foot deformities (Hazari et al., 2016).

The impairment of vibration sense, proprioception, tactile and thermal sensitivity, along with muscle weakness, lead to a set of manifestations in the gait and posture of individuals with diabetic polyneuropathy, such as postural instability and uncoordinated walking. These functional gait variations are associated with a diminished joint range of motion, reduced muscle power and changes in gait mechanics (Andersen, 2012) and can also modify the plantar pressure distribution, which contributes to the development of foot ulcers and are linked to higher morbidity and mortality (Andersen, 2012; Boulton et al., 2004; Pop-Busui et al., 2017).

Computerized biomechanical analysis is a standard technique used to quantify these changes in the gait and posture of individuals with diabetes. It can provide precise measurement of kinetic, kinematic, baropodometric and electric neuromuscular activity parameters related to the musculoskeletal mechanisms, strategies and movement compensations that occur as a response to, or a

consequence of the disease progression (Fernando et al., 2013; Hazari et al., 2016; Yavuzer et al., 2006). Several studies have been published regarding the kinematics and kinetics of the diabetic gait, with and without diabetic polyneuropathy, although with conflicting results (Hazari et al., 2016). Numerous outcome measures are usually reported, such as spatiotemporal gait parameters (gait velocity, stride length and stance period), kinematics (ankle, knee and hip ranges of motion), kinetics (ground reaction forces, plantar pressure and joint moments) and electromyography parameters.

The analysis of the joint moment waveforms during gait, can include several descriptive points, in both the sagittal and frontal planes, and during the whole gait cycle. In a systematic review with meta-analysis of the biomechanical characteristics of peripheral diabetic neuropathy by Fernando et al. (2013), from a series of 16 articles included, only two studies reported joint moments (ankle, knee, hip and support moments) in the sagittal plane. In another systematic review of the kinetic and kinematics of the diabetic foot, Hazari et al. (2016) also reported articles with joint moments only in the sagittal plane, but with inconsistent results.

To achieve a deeper understanding of the joint moments' characteristics in the gait of diabetic individuals, with and without polyneuropathy, a more complex assessment is needed. To address this gap, this systematic review aims to verify the effect of diabetes on the joint moment parameters during gait of individuals with diabetic neuropathy (DM), with diabetes and polyneuropathy (DPN), and healthy subjects (CONTROL).

2.3. Methods

2.3.1. Literature search protocol

The review process was performed according to the PRISMA guidelines (Page et al., 2021). The search was performed on March 2021, in PubMed, Scopus and Web of Science databases using the following key: Diabet* AND (joint AND moment) AND (walk* OR gait).

2.3.2. Study selection

The main database search was conducted by one reviewer, following an independently checked examination by a second reviewer. The inclusion criteria were:

- Articles published until December 2020;
- Articles published in the English language;
- Articles with adult subjects (≥ 18 years old);
- Articles with diabetic individuals without peripheral neuropathy and/or diabetic individuals with peripheral neuropathy compared or not to criteria matched healthy control subjects;
- Articles with biomechanical gait analysis, barefooted or shod;
- Articles reporting at least one type of lower limb joint moment value.

The exclusion criteria were:

- Systematic reviews, case reports, letters, or any document type other than experimental scientific papers;
- Articles not presenting a comparison between two or more different groups;
- Articles without an accurate and thorough methodology description, and presentation of quantitative results.
- Articles presenting joint moment results not normalized to the participants body mass (not expressed as N.m/kg or %BodyWeight x height).

2.3.3. Outcome measures

From the set of articles included in this review, the descriptive characteristics of the participants were extracted (age, height, weight, and BMI), along with reported joint moments in all anatomical planes.

2.3.4. Evaluation of the methodological quality of the studies

The methodological quality of the selected studies was independently evaluated by the two reviewers using the quality assessment tool by Downs and Black (1998), in the modified version reported by Fernando et al. (2013). Any

divergences in the classification were discussed to obtain unanimity. The modified version of the Downs and Black quality assessment tool contains five dimensions (reporting, external validity, internal validity, selection bias and power) with a total of 17 items and a maximum score of 18 points. Studies with a score ≤ 7 were classified as low quality, with a score between 8 and 11 as fair quality and score > 11 as good quality.

2.3.5. Statistical procedures

The statistical analysis of the outcomes was performed using the Cochrane Collaboration Review Manager (RevMan, version 5.4.1). A meta-analysis was conducted whenever two or more studies presented comparable outcomes. For articles with outcomes that could not be compared, only descriptive statistics are presented. The percentage of variation across studies was analyzed with the I^2 statistic and the χ^2 test. The random-effects model and the fixed-effect model were employed whenever $I^2 \geq 50\%$ and $I^2 < 50\%$, respectively. The effect size was computed using Hedge's g and interpreted as no effect (zero score), small effect (0.0 - 0.2), medium effect (0.2 - 0.8) and large effect (≥ 0.8), according to Cohen (1988). Results are reported as standardized mean difference (SMD) with 95% confidence intervals. A significance level of $\alpha = 0.05$ was established.

2.4. Results

2.4.1. Search results

A total of 80 research articles were retrieved from the database search on PubMed (27 results), Scopus (25 results) and Web of Science (28 results). From these, 46 were classified as duplicates and were removed. A total of 34 research articles was eligible for further analysis. In the title assessment phase, 14 articles were excluded due to bad indexing (1), analysis with non-diabetic subjects only (7), not performing biomechanical gait analysis and/or performing biomechanical analysis of tasks other than gait analysis (6). One additional article was added from other sources (references). During the abstract reading phase, a case report and an article not performing biomechanical gait analysis and/or performing

biomechanical analysis of tasks other than gait analysis were excluded. A total of 19 research articles were eligible for complete reading. At the end of this phase, nine articles were removed (not comparing two different groups, presenting non-normalized values and non-accurate presentation of results). A grand total of ten articles were qualified for review. The systematic review process is summarized in Figure 1.

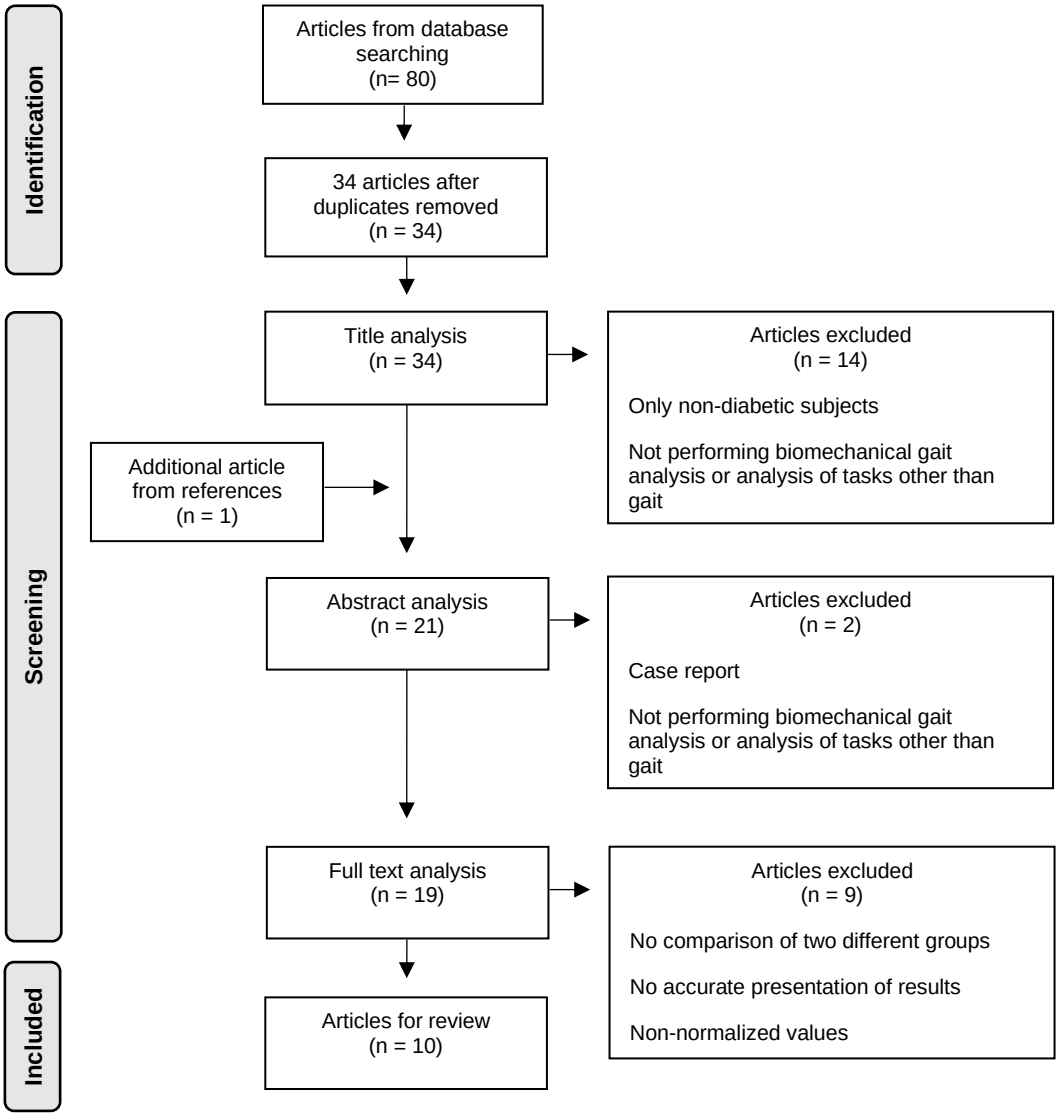


Figure 1. Summary of the systematic review process according to the PRISMA flow diagram.

2.4.2. Methodological quality

The results of the methodological quality assessment are depicted in Table 1. Five articles were classified as fair quality (≥ 8 and ≤ 11 points) and five

studies were classified as good quality (>11 points). No studies were graded as low quality.

Table 1. Assessment of the methodological quality of the studies using Downs and Black (1998).

Items[a]		**Articles**									
		Mueller et al. (1994)	Mueller et al. (1995)	Salsich & Mueller (2000)	Kwon et al. (2003)	Yavuzer et al. (2006)	Savelberg et al. (2009)	Melai et al. (2013)	Brown et al. (2014)	Sacco et al. (2015)	Petrovic et al. (2017)
Reporting	1	1	1	1	1	1	1	1	1	1	1
	2	1	1	1	1	1	1	1	1	1	1
	3	1	1	1	1	1	1	1	1	1	1
	5	1	1	1	1	2	2	1	1	1	1
	6	1	1	1	1	1	1	1	1	1	1
	7	1	1	1	1	1	1	1	1	1	1
	10	1	1	1	0	1	1	1	1	1	0
External Validity	11	-	-	-	-	-	-	-	-	-	-
	12	-	-	-	-	-	1	1	-	-	-
	13	-	-	-	1	1	1	0	-	-	-
Internal validity	16	1	1	1	1	1	1	1	1	1	1
	18	1	1	1	1	1	-	1	1	1	1
	20	1	1	1	1	1	1	1	1	1	1
Selection bias	21	0	1	0	0	1	1	-	-	-	-
	22	-	-	-	-	-	-	-	-	1	-
	25	-	-	-	-	-	0	-	1	1	1
Power[b]	27	0	0	1	0	0	0	1	1	1	0
	Total	10	11	11	10	13	13	12	12	13	10

[a]The modified version excludes the following items: 4, 8, 9, 14, 15, 17, 19, 23, 24 and 26; [b]Converted to a Yes/No answer to simplify the comparison; Answers that were unable to be determined are marked with an hyphen (-).

2.4.3. Group characteristics

A diabetic group without neuropathy (DM) was part of the sample in 6 studies. A diabetic group with peripheral neuropathy (DPN) and a healthy control group (CONTROL) were assessed in all the publications (10). Six articles compared DM, DPN and Control groups, while four only compared DPN and Control. The group characteristics are summarized in Table 2.

Table 2. Group characteristics of the articles included in the systematic review.

Article	DM					DPN					CONTROL				
	(n)	Age (y)	Height (m)	Weight (kg)	BMI (kg/m^2)	(n=)	Age (y)	Height (m)	Weight (kg)	BMI (kg/m^2)	(n)	Age (y)	Height (m)	Weight (kg)	BMI (kg/m^2)
Mueller et al. (1994)	-	-	-	-	-	10	57.7±4.5	1.81±0.10	91.5±15.0	-	10	56.8±11.3	1.75±0.05	83.8±24.3	-
Mueller et al. (1995)	-	-	-	-	-	9	57.9±14.1	1.82±0.10	93.7±14.3	-	10	56.8±11.3	1.75±0.05	83.9±24.3	-
Salsich & Mueller (2000)	-	-	-	-	-	17	58.5±11.7	1.71±0.11	89.6±23.1	30.4±6.6	17	62.6±6.2	1.73±0.11	83.7±15.8	27.9±3.5
Kwon et al. (2003)	-	-	-	-	-	9	59.2±11.2	1.77±0.10	105.4±10.5	-	9	59.2±12.6	1.76±0.01	106.6±10.9	-
Yavuzer et al. (2006)	26	58.2±9.5	-	-	30.3±5.9	20	61.7±8.5	-	-	29.5±4.5	20	60.9±5.9	-	-	28.9±5.1
Savelberg et al. (2009)	10	60.5±6.9	1.67±0.10	81.3±13.3	29.2±3.7	8	68.9±6.3	1.73±0.06	84.1±10.9	28.0±3.2	10	72.4±6.0	1.70±0.07	71.5±10.0	24.7±2.9
Melai et al. (2013)	39	62.4±6.6	1.68±0.10	88.0±15.4	31.1±5.7	94	66.9±7.5	1.74±0.08	92.9±19.5	30.5±5.6	19	67.8±5.30	1.73±0.07	68.8±17.1	23.2±5.6
Brown et al. (2014)	33	58.0±12.0	1.67±0.10	78±13	27.0±4	20	59±9	1.74±0.10	94±22	31.0±6.0	27	51±19	1.71±0.09	75±13	25.0±4.0
Sacco et al. (2015)	12	58.0±6.6	1.69±0.10	77.5±14.3	-	14	59±4.4	1.63±0.1	73.9±12.8	-	12	53.3±8.4	1.68±0.1	66.9±9.2	-
Petrovic et al. (2017)	22	51.0±9.0	-	80.5±12	28.0±4.0	14	66±14	-	91.5±18	31.0±4.0	31	56±10	-	76±10	26.0±3.0

2.4.4. Walking speed, anatomical planes and joint moments

Most of the analyzed studies (8) used a self-selected walking speed for the data collection. Three articles reported an imposed gait speed. From these, one study presented a gait speed of 1.2 m/s, one a speed of 1.4 m/s, and one article with various walking speeds: 0.6 m/s, 0.8 m/s, 1.0 m/s, 1.2 m/s, 1.4 m/s and 1.6 m/s.

All the articles analyzed the joint moments in the sagittal plane (10). Only one study complemented with the frontal plane. No articles reported joint moments in the transverse plane.

Globally, the reported ankle moments were the maximum ankle dorsiflexor moment in the initial stance phase (Ankle DF1), the maximum ankle plantar flexor moment in late stance phase (Ankle PF1), and the ankle plantar flexor moment at 40% of the stance phase (Ankle FP40%).

The reported knee joint moments were the first maximum of the knee extensor moment in the initial stance phase (Knee EXT1), the second maximum of the knee extensor moment in late stance phase (Knee EXT2), the second maximum of the knee flexor moment in midstance to late stance phase (Knee FLEX2), and the first maximum of the knee valgus moment (Knee VAL1).

At the hip level, the reported moments were the first maximum of the hip extensor moment in the initial stance phase (Hip EXT1) and the maximum of the hip flexor moment in late stance phase (Hip FLEX1). All articles (10) reported joint moments at the ankle, six stated joint moments at the knee and seven described joint moments at the hip joint. Three studies presented values for ankle joint moments only. One article reported joint moments at the ankle (and hip, and six articles reported joint moments at the ankle, knee and hip joints (Table 3).

Table 3. Gait speed, anatomical planes and joint moments analyzed in the included articles.

Article	Speed		Anatomic plane		Joint moment		
	Self-selected	Imposed	Sagittal	Frontal	Ankle	Knee	Hip
Mueller et al. (1994)	X	-	X	-	PF1	-	FLEX1
Mueller et al. (1995)	X	-	X	-	PF1	-	-
Salsich & Mueller (2000)	X	-	X	-	PF1	-	-
Kwon et al. (2003)	X	-	X	-	DF1, PF1	EXT1	EXT1
Yavuzer et al. (2006)	X	-	X	X	PF1	EXT1, VAL1	FLEX1
Savelberg et al. (2009)	-	X[b]	X	-	PF1	EXT1, FLEX2	EXT1, FLEX1
Melai et al. (2013)	X	X[a]	X	-	PF1, PF40%	EXT1, FLEX2	EXT1, FLEX1
Brown et al. (2014)	X	-	X	-	DF1, PF1	EXT1, EXT2	EXT1, FLEX1
Sacco et al. (2015)	X	-	X	-	PF1	EXT1, FLEX2, EXT2	EXT1, FLEX1
Petrovic et al. (2017)	-	X[c]	X	-	PF1	-	-

[a]1.2 m/s; [b]1.4 m/s; [c]0.6 m/s, 0.8 m/s, 1.0 m/s, 1.2 m/s, 1.4 m/s and 1.6 m/s; Ankle DF1: maximum ankle dorsiflexor moment (initial stance phase); Ankle PF1: maximum ankle plantar flexor moment (late stance phase); Ankle FP40%: ankle plantar flexor moment at 40% of the stance phase; Knee EXT1: first maximum of the knee extensor moment (initial stance phase); Knee EXT2: second maximum of the knee extensor moment (late stance phase); Knee FLEX2: second maximum of the knee flexor moment (midstance to late stance phase); Knee VAL1: first maximum of the knee valgus moment; Hip EXT1: first maximum of the hip extensor moment (initial stance phase); Hip FLEX1: maximum of the hip flexor moment (late stance phase).

2.4.5. Ankle joint moments at self-selected gait speed

Regarding the ankle DF1 variable, Kwon et al. (2003) reported data comparing DPN and CONTROL, while Brown et al. (2014) presented data comparing DM, DPN and CONTROL. In terms of ankle PF1 data, four studies (Kwon et al., 2003; Mueller et al., 1994; Mueller et al., 1995; Salsich & Mueller, 2000) compared DPN and CONTROL and four articles (Brown et al., 2014; Melai et al., 2013; Sacco et al., 2015; Yavuzer et al., 2006) compared DM, DPN and CONTROL groups. Melai et al. (2013) also presented PF40% values and Sacco et al. (2015) reported the values as %body weight * height. No ankle joint moments in the frontal plane were reported. These results are summarized in Table 4.

Table 4. Ankle joint moments in the sagittal plane at a self-selected speed.

Article	Ankle joint moment (N.m/kg)					
	DF1			PF1		
	DM	DPN	CONTROL	DM	DPN	CONTROL
Mueller et al. (1994)	-	-	-	-	1.03 ± 0.34	1.36 ± 0.30
Mueller et al. (1995)	-	-	-	-	1.01 ± 0.35	1.36 ± 0.30
Salsich & Mueller (2000)	-	-	-	-	1.31±0.29	1.57±0.16
Kwon et al. (2003)	-	0.04±0.05	0.10±0.03	-	1.18±0.19	1.54±0.16
Yavuzer et al. (2006)				1.1±0.3	1.2±0.2	1.3±0.2
Melai et al. (2013)	-	-	-	1.55±0.04 0.65±0.02[b]	1.54±0.02 0.76±0.02[b]	1.59±0.04 0.74±0.05[b]
Brown et al. (2014)	0.28±0.08	0.25±0.10	0.22±0.15	1.32±0.18	1.28±0.23	1.48±0.17
Sacco et al. (2015)	-	-	-	8.2±0.4[a]	7.5±2.1[a]	8.4±0.5[a]

[a](%bw*h); [b]PF40% stance;

The meta-analysis results regarding the ankle DF1 parameter, comparing DPN with CONTROL are summarized in Figure 2. No statistically significant differences were found between DPN and CONTROL (SMD = -0.52, 95% CI = 2.09 – 1.06, p = 0.52).

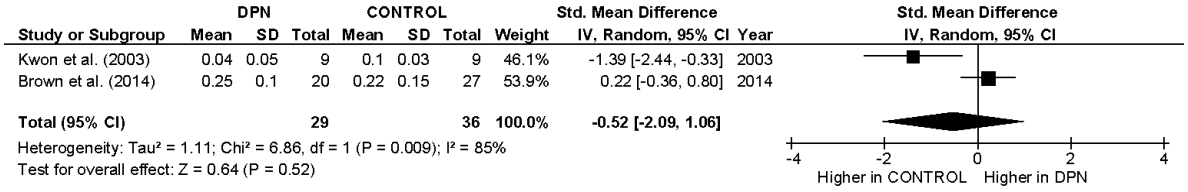


Figure 2. Forest plot of ankle DF1 at a self-selected gait speed in DPN and CONTROL groups.

The results of the meta-analysis concerning the ankle PF1 parameter are presented in Figure 3, Figure 4 and Figure 5, comparing DM with DPN, DM with CONTROL and DPN with CONTROL, respectively. When comparing DM with DPN in terms of ankle PF1 (Figure 3) no statistically significant differences were observed (SMD = 0.19, 95% CI = -0.07 – 0.45, p = 0.15). The CONTROL group presented significantly higher values, when compared to the DM group (SMD = -0.82, 95% CI = -1.12 – -0.51, p < 0.001) and to the DPN group (SMD = -1.12, 95% CI = -1.56 - -0.69, p <0.001), both with large effects. A meta-analysis for the PF40% variable was not possible.

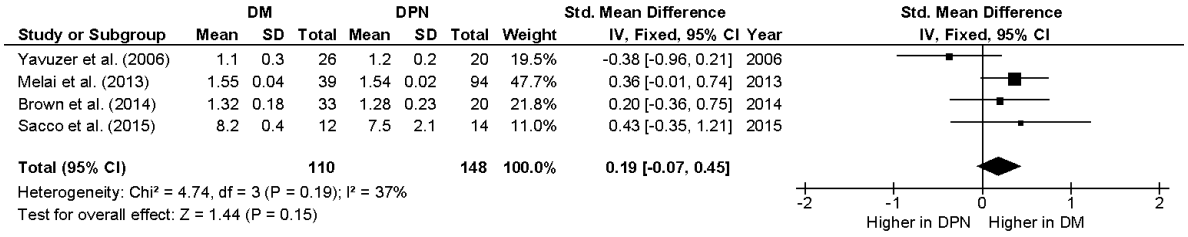


Figure 3. Forest plot of ankle PF1 at a self-selected speed in DM and DPN groups.

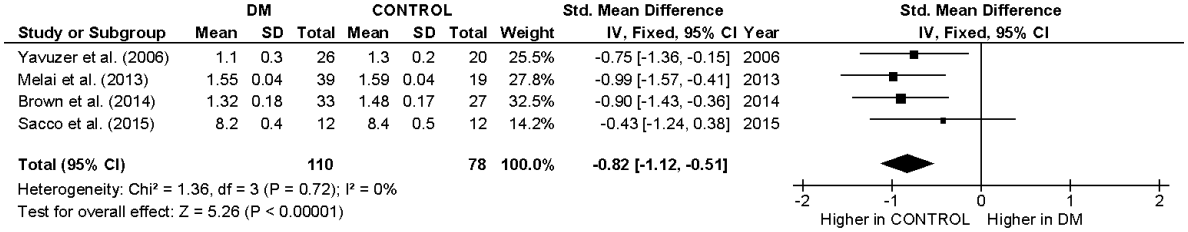


Figure 4. Forest plot of ankle PF1 at a self-selected speed in DM and CONTROL groups.

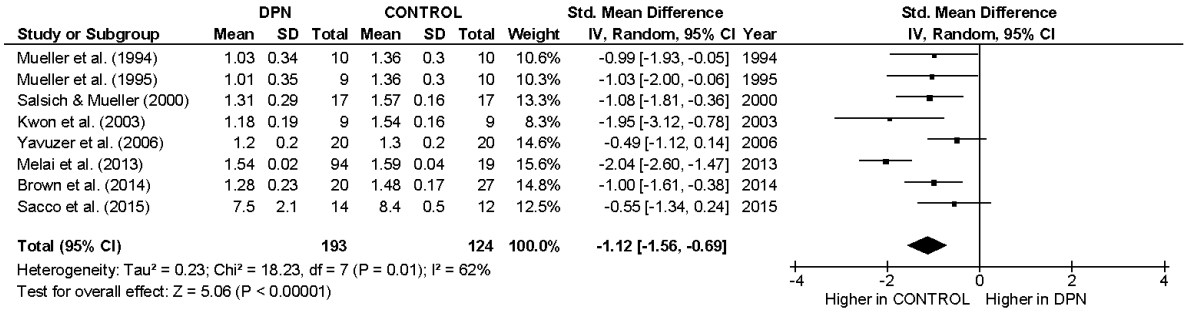


Figure 5. Forest plot of ankle PF1 at a self-selected speed in DPN and CONTROL groups.

2.4.6. Knee joint moments at self-selected gait speed

Regarding the knee EXT1 in the sagittal plane, only one study (Kwon et al., 2003) reported data comparing DPN and CONTROL, while five articles compared the DM, DPN and CONTROL groups (Brown et al., 2014; Melai et al., 2013; Sacco et al., 2015; Savelberg et al., 2009; Yavuzer et al., 2006). The knee FLEX2 variable was reported in three studies (Melai et al., 2013; Sacco et al., 2015; Savelberg et al., 2009) comparing DM, DPN and CONTROL. Concerning the knee EXT2 parameter, one article reported values comparing DPN and CONTROL groups (Mueller et al., 1994) and two studies presented values comparing DM, DPN and CONTROL (Brown et al., 2014; Sacco et al., 2015). All

values by Sacco et al. (2015) are presented as %body weight * height. These results are depicted in Table 5.

Table 5. Knee joint moments in the sagittal plane at a self-selected speed.

Article	Knee joint moment (N.m/kg)								
	EXT1			FLEX2			EXT2		
	DM	DPN	CONTROL	DM	DPN	CONTROL	DM	DPN	CONTROL
Mueller et al. (1994)	-	-	-	-	-	-	-	0.35 ± 0.39	0.59 ± 0.53
Kwon et al. (2003)	-	0.10±0.17	0.30±0.15	-	-	-	-	-	-
Yavuzer et al. (2006)	0.52±0.56	0.81±0.56	0.48±0.63	-	-	-	-	-	-
Savelberg et al. (2009)	0.42±0.22	0.23±0.30	0.45±0.36	-0.16±0.11	-0.29±0.21	-0.28±0.27	-	-	-
Melai et al. (2013)	0.13±0.02	0.19±0.03	0.24±0.04	0.48±0.04	0.43±0.02	0.52±0.06	-	-	-
Brown et al. (2014)	0.90±0.20	0.95±0.38	1.15±0.26	-	-	-	0.90±0.20	0.95±0.38	1.15±0.26
Sacco et al. (2015)	2.3±1.3[a]	1.8±1.2[a]	1.4±1.2[a]	-2.3±1.1[a]	-2.7±1.3[a]	-3.2±1.0[a]	0.8±0.5[a]	0.8±0.4[a]	0.7±0.4[a]

[a](%bw*h);

Only one study presented data for the frontal plane (Yavuzer et al., 2006). This study compared the DM, DPN and CONTROL groups in terms of the knee VAL1 variable, as reported in Table 6.

Table 6. Knee joint moments in the frontal plane at a self-selected speed.

Article	Knee joint moment (N.m/kg)		
	VAL1		
	DM	DPN	CONTROL
Yavuzer et al. (2006)	0.43±0.12	0.81±0.18	0.47±0.19

The results of the meta-analysis concerning the knee EXT1 parameter are presented in Figure 6, (DM with DPN), Figure 7 (DM with CONTROL) and Figure 8 (DPN with CONTROL). No significant differences were found when comparing DM with DPN (SMD = -0.39, 95% CI = -1.45 – 0.68, p = 0.48), DM with CONTROL (SMD = -0.84, 95% CI = -2.16 - -0.48, p = 0.21) and DPN with CONTROL (SMD = -0.52, 95% CI = -1.25 – 0.22, p = 0.17).

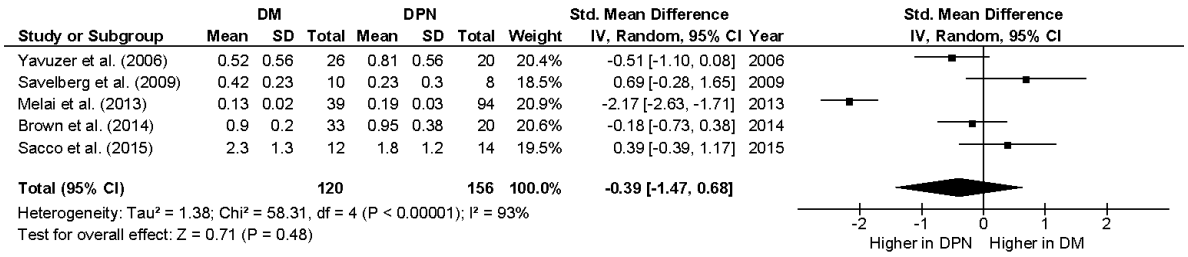


Figure 6. Forest plot of knee EXT1 at a self-selected speed in DM and DPN groups.

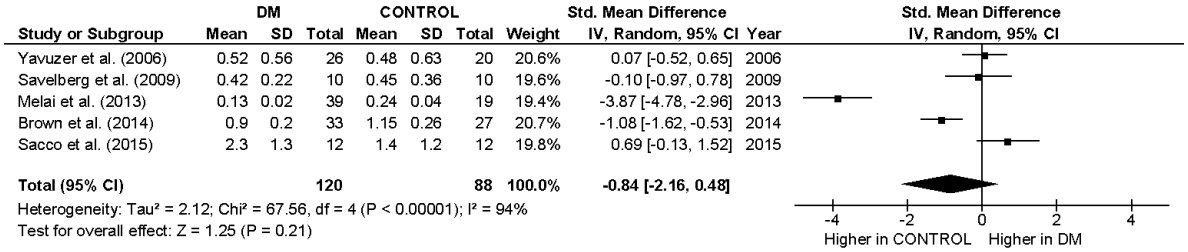


Figure 7. Forest plot of knee EXT1 at a self-selected speed in DM and CONTROL groups.

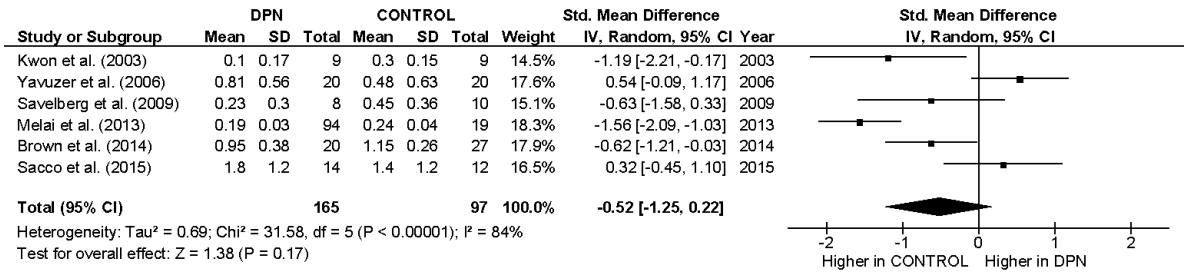


Figure 8. Forest plot of knee EXT1 at a self-selected speed in DPN and CONTROL groups.

In terms of the knee FLEX2 variable, the results of the meta-analysis are summarized in Figure 9 (DM with DPN), Figure 10 (DM with CONTROL) and Figure 11 (DPN with CONTROL). A significant difference was observed in the comparison of DM with the CONTROL groups (SMD = -0.77, 95% CI = -1.19 - -0.35, $p < 0.001$), with higher values reported in the CONTROL group, with a medium effect. When comparing DM with DPN (SMD = 0.28, 95% CI = -1.48 – 2.04, $p = 0.76$) and DPN with CONTROL (SMD = -1.13, 95% CI = -3.08 – 0.82, $p = 0.26$), no significant differences were observed.

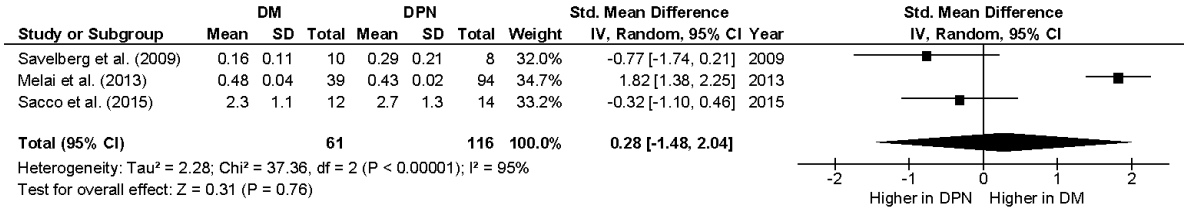


Figure 9. Forest plot of knee FLEX2 at a self-selected speed in DM and DPN groups.

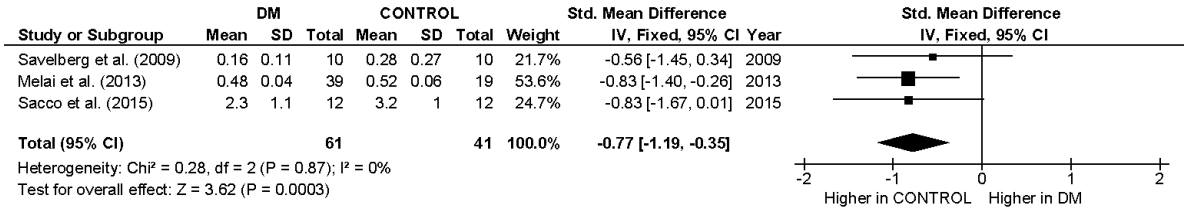


Figure 10. Forest plot of knee FLEX2 at a self-selected speed in DM and CONTROL groups.

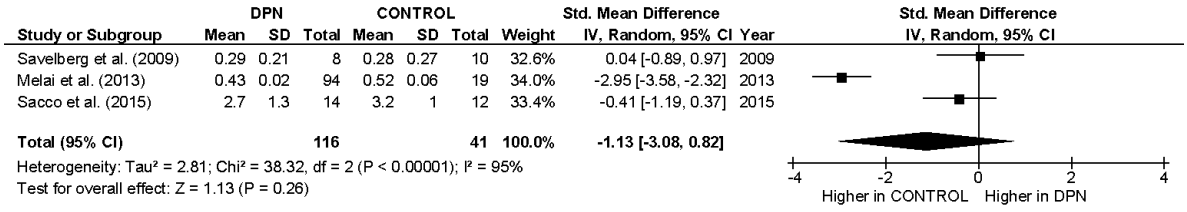


Figure 11. Forest plot of knee FLEX2 at a self-selected speed in DPN and CONTROL groups.

The results from the meta-analysis regarding the knee EXT2 joint moment are presented in Figure 12 (DM with DPN), Figure 13 (DM with CONTROL) and Figure 14 (DPN with CONTROL). No significant differences were found concerning the comparison of DM with DPN (SMD = -0.12, 95%-CI = -0.57 – 0.34, p = 0.62), DM with CONTROL (SMD = -0.47, 95%-CI = -1.73 – 0.80, p = 0.47) and DPN with CONTROL (SMD = -0.23, 95% CI = -1.07 – 0.62, p = 0.60).

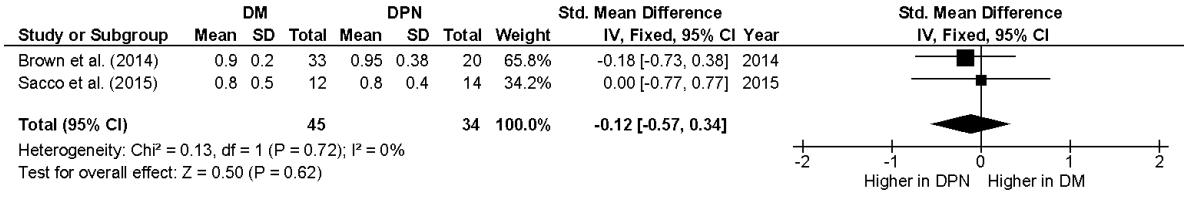


Figure 12. Forest plot of knee EXT2 at a self-selected speed in DM and DPN groups.

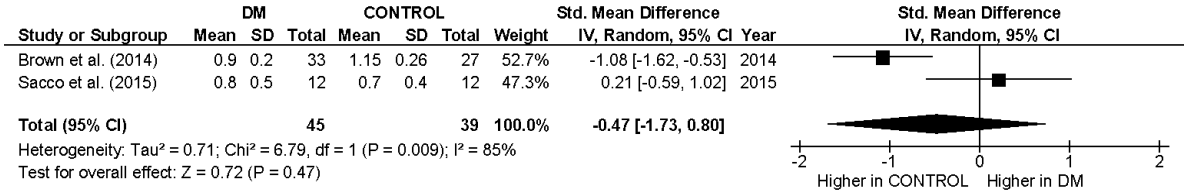


Figure 13. Forest plot of knee EXT2 at a self-selected speed in DM and CONTROL groups.

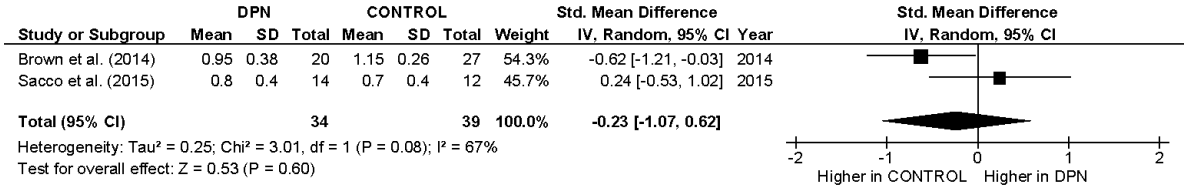


Figure 14. Forest plot of knee EXT2 at a self-selected speed in DPN and CONTROL groups.

2.4.7. Hip joint moments at self-selected gait speed

Regarding the hip EXT1, one article compared DPN and CONTROL (Kwon et al., 2003) and four studies presented data comparing DM, DPN and CONTROL groups (Brown et al., 2014; Melai et al., 2013; Sacco et al., 2015; Savelberg et al., 2009). Sacco et al. (2015) also reported the hip EXT1 data in the push-off phase. The hip FLEX1 was presented in one study comparing DPN and CONTROL (Mueller et al., 1994) and in five studies comparing DM, DPN and CONTROL groups (Brown et al., 2014; Melai et al., 2013; Sacco et al., 2015; Savelberg et al., 2009; Yavuzer et al., 2006). All the values presented by Sacco et al. (2015) are in the %body weight * height format. No articles analyzed the hip joint moments in the frontal plane. These results are depicted in Table 7.

Table 7. Hip joint moments in the sagittal plane at a self-selected speed.

Article	**Hip joint moment (N.m/kg)**					
	EXT1			FLEX1		
	DM	DPN	CONTROL	DM	DPN	CONTROL
Mueller et al. (1994)	-	-	-	-	0.83 ± 0.26	1.10 ± 0.03
Kwon et al. (2003)	-	0.67±0.40	0.60±0.29	-	-	-
Yavuzer et al. (2006)	-	-	-	0.5±0.39	0.49±0.32	0.51±0.2
Savelberg et al. (2009)	1.09±0.25	1.08±0.39	0.85±0.40	-0.55±0.26	-0.75±0.36	-0.70±0.12
Melai et al. (2013)	0.62±0.05	0.66±0.03	0.79±0.07	0.42±0.05	0.51±0.03	0.57±0.07
Brown et al. (2014)	0.69±0.21	0.74±0.32	0.90±0.24	1.11±0.24	1.02±0.25	0.94±0.69
Sacco et al. (2015)	4.5±1.1[a] 4.8±1.6[a,b]	4.1±1.1[a] 4.2±1.4[a,b]	5.3±1.3[a] 5.6±1.[2a,b]	-4.4±1.5[a]	-4.6±2.0[a]	-3.2±1.2[a]

[a](%bw*h);[b]EXT push-off phase;

In what concerns the hip EXT1 joint moment, the results of the meta-analysis are summarized in Figure 15 (DM with DPN), Figure 16 (DM with CONTROL) and Figure 17 (DPN with CONTROL). No significant differences were observed when comparing DM with DPN (SMD = -0.28, 95% CI = -0.98 – 0.42, p = 0.43), DM with CONTROL (SMD = -0.97, 95% CI = -2.28 – 0.35, p = 0.15) and DPN with CONTROL (SMD = -0.84, 95% CI = -2.21 – 0.54, p = 0.23).

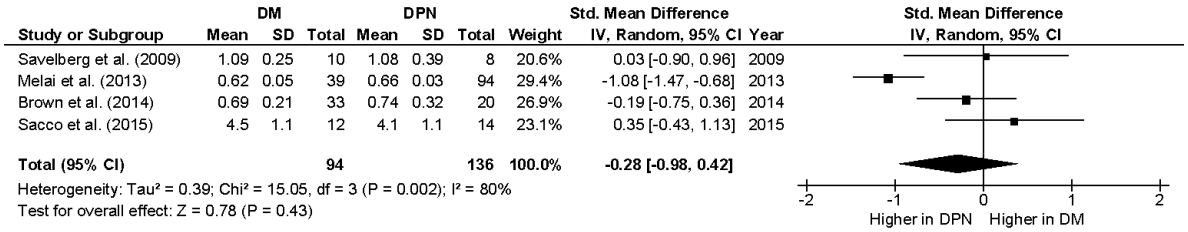


Figure 15. Forest plot of hip EXT1 at a self-selected speed in DM and DPN groups.

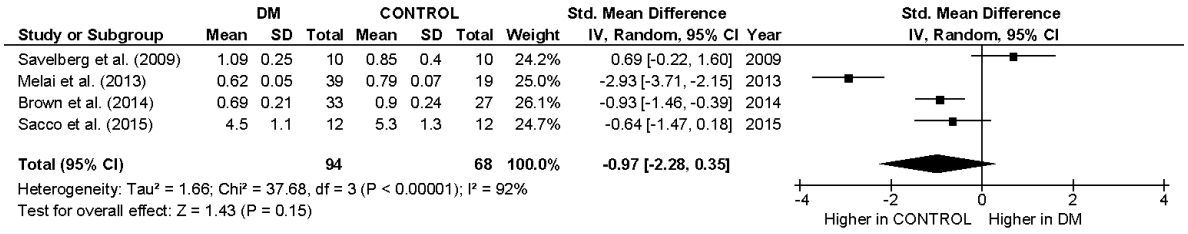


Figure 16. Forest plot of hip EXT1 at a self-selected speed in DM and CONTROL groups.

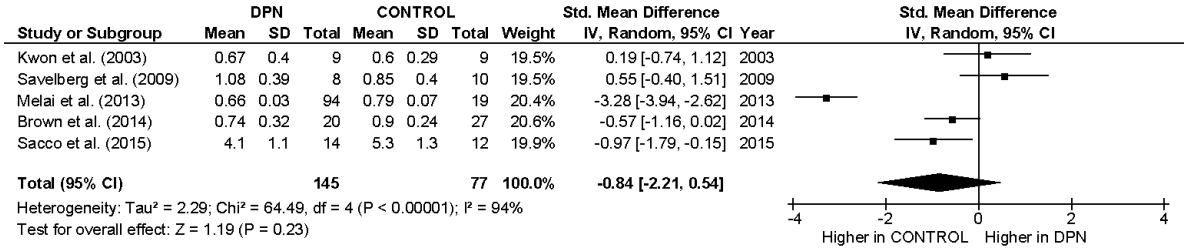


Figure 17. Forest plot of hip EXT1 at a self-selected speed in DPN and CONTROL groups.

The results of the meta-analysis concerning the hip FLEX1 joint moment are presented in Figure 18 (DM with DPN), Figure 19 (DM with CONTROL) and Figure 20 (DPN with CONTROL). No significant differences were found, when

comparing DM with DPN (SMD = -0.56, 95% CI = -1.76 – 0.64, p = 0.36), DM with CONTROL (SMD = -0.42, 95% CI = -1.53 – 0.69, p = 0.46) and DPN with CONTROL (SMD = -0.31, 95% CI = -1.07 – 0.46, p = 0.43).

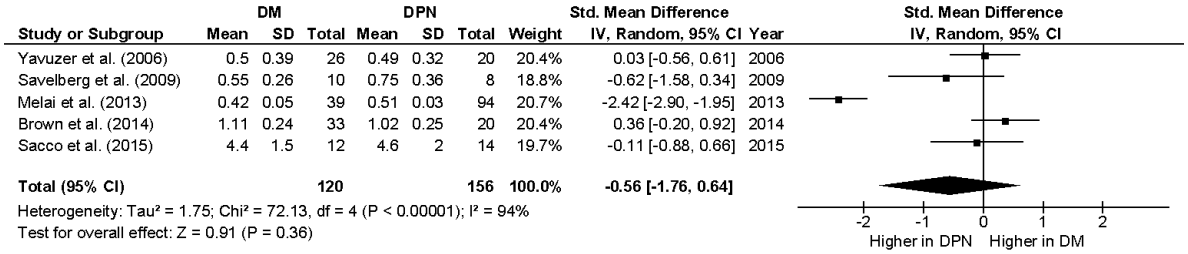


Figure 18. Forest plot of hip FLEX1 at a self-selected speed in DM and DPN groups.

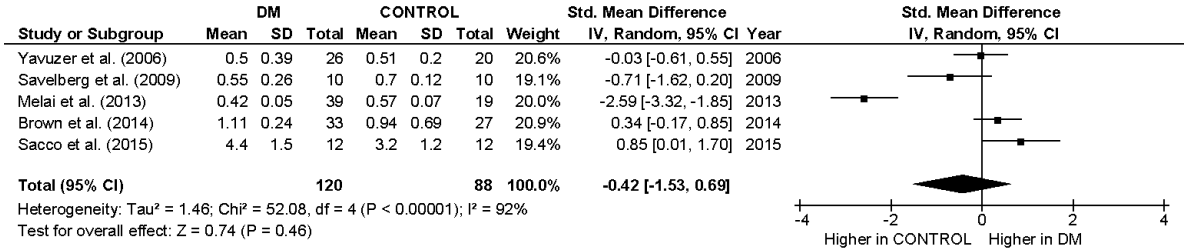


Figure 19. Forest plot of hip FLEX1 at a self-selected speed in DM and CONTROL groups.

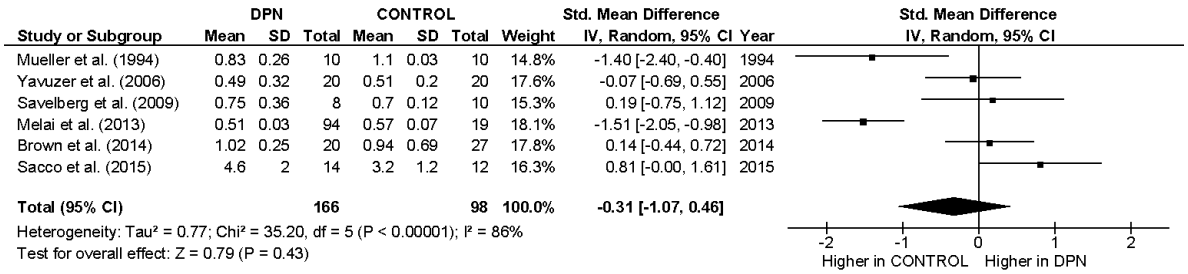


Figure 20. Forest plot of hip FLEX1 at a self-selected speed in DPN and CONTROL groups.

2.4.8. Ankle Joint moments at imposed gait speeds

All presented articles compared DM, DPN and CONTROL at different imposed speeds, reporting ankle PF1 values only. Two articles presented results for a single imposed speed of 1.2 m/s (Melai et al., 2013) or 1.4 m/s (Savelberg et al., 2009). Petrovic et al. (2017) reported data at six different walking speeds, ranging from 0.6 m/s up to 1.6 m/s, with 0.2 m/s increments. Melai et al. (2013) and Savelberg et al. (2009) also presented the ankle PF1 at 40% of the stance phase. No ankle joint moments in the frontal plane were reported. These results are summarized in Table 8.

Table 8. Ankle joint moments in the sagittal plane at an imposed speed.

Article		Ankle joint moment (N.m/kg)		
		PF1		
	Speed (m/s)	DM	DPN	CONTROL
Savelberg et al. (2009)	1.4	1.51±0.21 0.82±0.17[a]	1.64±0.26 0.97±0.21[a]	1.59±0.17 0.70±0.12[a]
Melai et al. (2013)	1.2	1.55±0.04 0.67±0.02[a]	1.57±0.02 0.75±0.03[a]	1.58±0.04 0.71±0.05[a]
Petrovic et al. (2017)	0.6	1.47±0.47	1.28±0.45	1.53±0.53
	0.8	1.57±0.50	1.32±0.41	1.69±0.59
	1.0	1.45±0.57	1.40±0.52	1.52±0.53
	1.2	1.50±0.58	1.56±0.55	1.74±0.60
	1.4	1.68±0.66	1.46±0.55	1.99±0.74
	1.6	1.8±0.67	1.62±0.60	2.09±0.81

[a]PF40% stance;

The results of the meta-analysis of the ankle PF1 at an imposed speed of 1.2 m/s are summarized in Figure 21 (DM with DPN), Figure 22 (DM with CONTROL) and Figure 23 (DPN with CONTROL). The CONTROL group presented significant lower values, when compared to DM group (SMD = -0.57, 95% CI = -0.96 - -0.17, p = 0.005), with a medium effect. No significant differences were observed when comparing DM with DPN (SMD = -0.48, 95% CI = -1.08 – 0.12, p = 0.12) and DPN with CONTROL (SMD = -0.37, 95% CI = -0.76 – 0.02, p = 0.07).

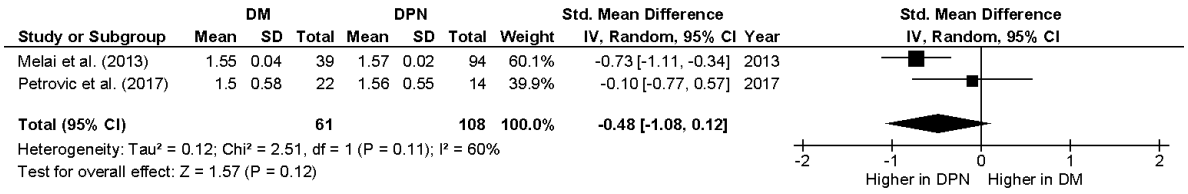


Figure 21. Forest plot of ankle PF1 at an imposed speed of 1.2 m/s in DM and DPN groups.

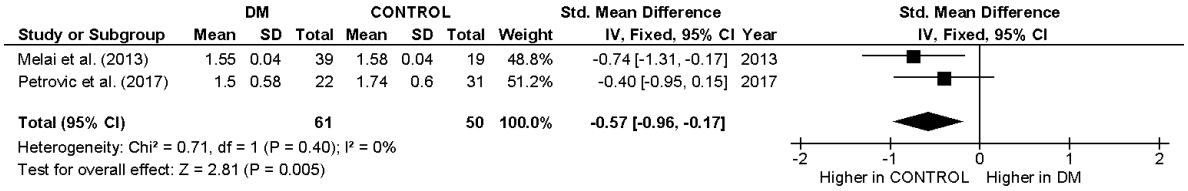


Figure 22. Forest plot of ankle PF1 at an imposed speed of 1.2 m/s in DM and CONTROL groups.

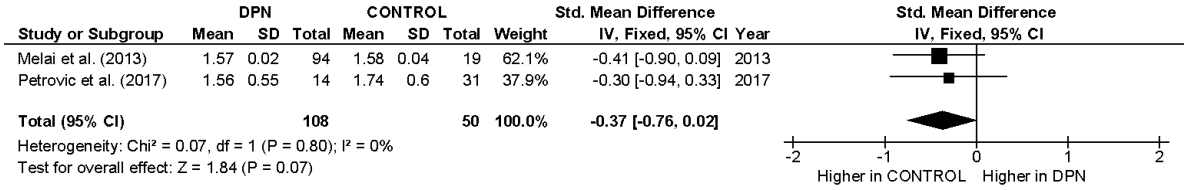


Figure 23. Forest plot of ankle PF1 at an imposed speed of 1.2 m/s in DPN and CONTROL groups.

The results of the meta-analysis of the ankle PF1 at an imposed speed of 1.4 m/s are presented in Figure 24 (DM with DPN), Figure 25 (DM with CONTROL) and Figure 26 (DPN with CONTROL). No significant differences were observed, when comparing DM with DPN (SMD = -0.03, 95% CI = -0.88 – 0.82, p = 0.95), DM with CONTROL (SMD = -0.42, 95% CI = -0.89 – 0.05, p = 0.08) and DPN with CONTROL (SMD = -0.33, 95% CI = -1.28 – 0.63, p = 0.50).

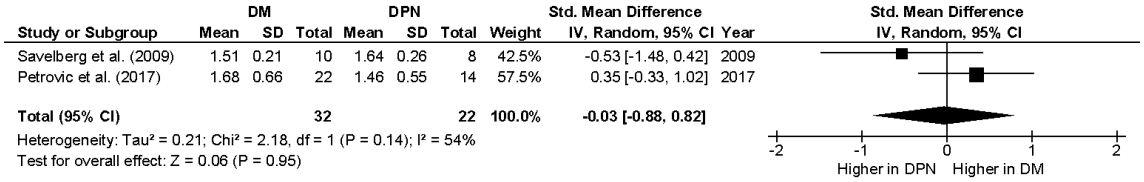


Figure 24. Forest plot of ankle PF1 at an imposed speed of 1.4 m/s in DM and DPN groups.

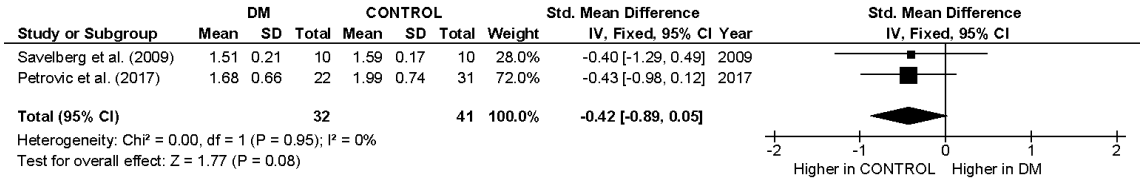


Figure 25. Forest plot of ankle PF1 at an imposed speed of 1.4 m/s in DM and CONTROL groups.

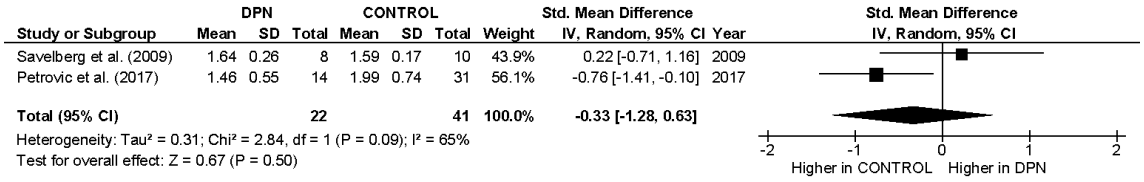


Figure 26. Forest plot of ankle PF1 at an imposed speed of 1.4 m/s in DPN and CONTROL groups.

2.4.9. Knee joint moments at imposed gait speed

Two articles (Melai et al., 2013; Savelberg et al., 2009) presented knee EXT1 and knee FLEX2 data, based on the comparison of DM, DPN and CONTROL groups, with a respective imposed speed of 1.2 m/s and 1.4 m/s. No studies analyzed knee joint moments in the frontal plane, with an imposed speed. A meta-analysis was not possible to perform. These results are presented in Table 9.

Table 9. Knee joint moments in the sagittal plane at an imposed speed.

Article	Knee joint moment (N.m/kg)						
		EXT1			FLEX2		
	Speed (m/s)	DM	DPN	CONTROL	DM	DPN	CONTROL
Savelberg et al. (2009)	1.4	0.42±0.22	0.23±0.30	0.45±0.36	-0.16±0.11	-0.29±0.21	-0.28±0.27
Melai et al. (2013)	1.2	0.12±0.02	0.20±0.03	0.23±0.04	0.57±0.03	0.53±0.03	0.54±0.04

2.4.10. Hip joint moments at imposed gait speed

In terms of hip joint moments with an imposed speed, two articles (Melai et al., 2013; Savelberg et al., 2009) compared DM, DPN and CONTROL groups in terms of hip EXT1 and hip FLEX1 parameters, with imposed walking speeds of 1.2 m/s and 1.4 m/s, respectively. No articles reported hip joint moments in the frontal plane. A meta-analysis was not possible to conduct. These results are summarized in Table 10.

Table 10. Hip joint moments in the sagittal plane at an imposed speed.

Article	Hip joint moment (N.m/kg)						
		EXT1			FLEX1		
	Speed (m/s)	DM	DPN	CONTROL	DM	DPN	CONTROL
Savelberg et al. (2009)	1.4	1.09±0.25	1.08±0.39	0.85±0.40	-0.55±0.26	-0.75±0.36	-0.70±0.12
Melai et al. (2013)	1.2	0.65±0.05	0.74±0.03	0.74±0.06	0.53±0.05	0.63±0.03	0.56±0.06

2.5. Discussion

The main objective of this systematic review was to assess the effect of diabetes with or without associated polyneuropathy on the lower limbs' joint moments during gait. One of the main outcomes of this study is the heterogeneity and variability among the included articles in the reporting of joint moment findings. An analysis of the forest plots confirms that 18 meta-analyses were considered heterogeneous (I^2 > 50 %), while six comparisons were considered consistent (I^2 < 50 %). This is especially relevant when considering hip joint moment data, with all the meta-analysis presenting inconsistent results. Regarding the ankle joint moment comparisons, the DF1 and PF1 parameters were considered heterogeneous, when comparing DPN with CONTROL. Comparing DM with DPN and DM with CONTROL, the PF1 meta-analysis results were considered consistent in terms of homogeneity. In terms of knee joint moment, the EXT1, FLEX2 and EXT2 parameters were also presented with marked heterogeneity among all compared groups, except for DM with CONTROL meta-analysis for the FLEX2 and DM with DPN for the EXT2. Concerning the imposed speed condition, at 1.2 m/s and for the ankle PF1 parameter, all analysis were considered homogeneous except for the DM with DPN comparison. At the imposed speed of 1.4 m/s and for the ankle PF1 joint moment, heterogeneity was observed in the DM with DPN, and DPN with CONTROL comparisons. The DM with CONTROL meta-analysis was considered homogeneous, regarding the ankle PF1 parameter.

When comparing the differences among DM, DPN and CONTROL at the ankle joint, in terms of the joint moment meta-analysis results, statistically significant differences were only observed in the ankle PF1 (DM with CONTROL; DPN with CONTROL), with higher values reported in the CONTROL groups. This finding was also verified when comparing the DM and CONTROL groups at an imposed speed of 1.2 m/s, but no differences were observed with the imposed speed of 1.4 m/s. No differences were observed when comparing DM with DPN, in both imposed speeds. The diabetic polyneuropathy condition, presenting impaired protective sensation and vibration and decreased lower-extremity force production, muscle morphology and function, can have a significant negative

impact on the human gait pattern (Alam et al., 2017; Reeves et al., 2021). Nevertheless, patients with diabetes without an overt peripheral neuropathy can also present altered and less efficient gait patterns compared to non-diabetic subjects, even in early stages of the disease (Ko et al., 2011). These findings support that the lower plantar flexor joint moments can be an early manifestation of the diabetes condition, preceding the development of the neuropathic process.

In terms of knee joint moments, significant differences were only observed in the comparison of DM with CONTROL, for the knee FLEX2 parameter, with higher joint moments reported in the CONTROL groups. There were no differences regarding the remaining knee joint moment parameters. It was expected that, with the disease progression and the establishment of the neurologic compromise, compensatory strategies started to manifest concerning the role of each joint in the propulsion phase (Mueller et al., 1994). Subjects with diabetes may experience difficulties in the push-off phase, by generating lower ankle joint moments, and producing higher flexor moments at the knee joint as a compensatory mechanism (Sacco et al., 2015). As DPN subjects rely on a greater hip role in moving the body forward, it was expected that this group also presented lower knee FLEX 2 joint moments, when compared to the CONTROL and the DM groups, but this was not observed. This might be attributed to differences in methodological factors and statistical power of the analyzed articles, such as sample size.

No significant differences were observed between all groups at the hip joint level. It was expected that DM and DPN groups presented evidence of lower hip joint moment values, especially at push-off phase (Sacco et al., 2015). These results confirm that there is a lack of good evidence to support differences in joint moment values at the hip, considering the comparison between DM, DPM and CONTROL groups (Hazari et al., 2016).

It was not possible to carry out a meta-analysis concerning the ankle PF40% and the knee VAL1 parameters and hip extensor moment at push-off phase, with a self-selected speed. This is due to the lack of a minimum number of studies available reporting these joint moment values. Melai et al. (2013)

reported higher ankle PF40% joint moments in the DPN group, when compared to the DM group. It was expected that the reduced muscle strength in this group could contribute to a higher plantar flexion moment in early stance phase (Savelberg et al., 2009), even though more studies are needed in order to build evidence that supports these claims. Only one article analyzed the joint moments in the frontal plane, more specifically the knee VAL1 parameter. Technical aspects may contribute to the small prevalence of articles analyzing the joint moments in the frontal plane, since values extracted from the reconstruction with markers placed directly on the skin were not considered reliable (Della Croce et al., 2005; Ferrari et al., 2008; Kerkhoff et al., 2020; Sawacha et al., 2009).

With an imposed speed, one article presented results at several walking velocities, namely in the ankle PF1 parameter (Petrovic et al., 2017), while other reported PF1 values with an imposed speed of 1.4 m/s (Savelberg et al., 2009). This study, along with Melai et al. (2013) also reported knee EXT1 and FLEX2 and hip EXT1 and FLEX1 joint moments, but with different imposed velocities. However, it was not possible to conduct the meta-analysis with these results. Although literature shows that subjects with diabetes exhibit slower self-selected speeds than healthy subjects, these differences tend to disappear, when they are asked to walk at the same gait velocity (Melai et al., 2013; Sawacha et al., 2009).

2.6. Conclusion

The biomechanical literature on the effects of diabetes and diabetic polyneuropathy in joint moment parameters during gait is scarce. This fact, combined with the high heterogeneity of the reported studies, may have an impact on the clinical significance of this systematic review with meta-analysis. These results provide evidence that subjects with diabetes, with or without associated peripheral neuropathy, present lower-limb joint moment values lower than healthy subjects. However, there is insufficient data to confirm the differences between the DM and DPN groups in terms of joint moments. Most of the studies in this review focused on the joint moments in the sagittal plane and presented small sample sizes. Future biomechanical studies should address these limitations, by broaden the assessment of lower limb joint moments to the

frontal and transverse planes and with larger groups, to establish evidence regarding these findings.

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3. Study II: Joint moment analysis during gait: a comparison between diabetic patients with and without peripheral neuropathy and healthy subjects

3.1. Abstract

Background: Biomechanical gait analysis can provide important insights in the gait variations of people with diabetes. However, there is still limited data on the joint moments, with some authors reporting conflicting results. The aim of this study is to compare the lower-limb joint moments at the ankle, knee and hip, in the sagittal and frontal planes, between subjects with diabetes (DM), subjects with diabetes and peripheral neuropathy (DPN) and healthy individuals (CONTROL).

Methods: Eight DM participants (age: 38.75 ± 18.09 years old; height: 1.68 ± 0.12 m; mass: 70.39 ± 16.46 kg; BMI: 24.70 ± 2.89 kg/m^2) and eight DPN subjects (age:64.63 ± 11.46 years old; height: 1.70 ± 0.13 m; mass: 87.14 ± 12.71 kg; BMI: 30.04 ± 2.65 kg/m^2) participated in this study and were compared to the data of ten CONTROL individuals (age: 48.50 ± 7.75 years old; height: 1.73 ± 0.07 m; mass: 69.06 ± 13.52 kg; BMI: 22.86 ± 3.24 kg/m^2) from a public multimodal database. The ankle, knee and hip joint moments, in the sagittal and frontal planes, were analyzed, at a self-selected gait speed.

Results: When compared to the DM group, the DPN group presented reduced ankle plantar flexion, ankle evertor, knee extension, knee flexion and hip flexion moments. The DM revealed increased knee flexion, knee extension and hip extensor moments, and reduced ankle evertor, knee valgus and hip abductor moments, when compared to CONTROL. The DPN presented higher knee flexion and knee varus moments, and reduced ankle evertor, ankle invertor and knee valgus moments, when compared to CONTROL.

Conclusion: The diabetic condition may contribute to altered lower limb joint moments which go beyond the sagittal plane of motion, even without the establishment of neurological deficits. These findings may assist researchers and

health professionals to develop more effective interventions in the healthcare of people with diabetes.

Keywords: Biomechanics; Gait; Diabetes; Diabetic polyneuropathy; Joint moments.

3.2. Introduction

Diabetes and diabetic polyneuropathy have been associated with changes in the gait pattern, with intensive biomechanical research over the past decades (Sacco et al., 2015). As a consequence of the disease, anatomic, musculoskeletal, and neurologic involvement are linked to diminished joint range of motion, reduced muscle power and changes in the lower-limb joint moments (Andersen, 2012).

The analysis of joint moments in the gait of people with diabetes has focused mainly on the sagittal plane of motion during the stance phase. While the ankle plantar flexion moment is one of the most prevalent reported parameters, as it is associated with the gait changes and adaptations induced by diabetes and diabetic polyneuropathy, some authors report conflicting results (Brown et al., 2014; Kwon et al., 2003; Melai et al., 2013; Yavuzer et al., 2006). Additionally, there is still limited data available on the knee and hip joints moments (Alam et al., 2017). Consequently, this gap prompts the need for conducting more studies comparing healthy individuals to those with diabetes with and without peripheral neuropathy (Fernando et al., 2013; Hazari et al., 2016; Sacco et al., 2015).

A comprehensive joint kinetic gait analysis of people with diabetes, in the sagittal and frontal planes, can provide important insights to understand the lower-limb gait variations in this population (Lee & Hidler, 2008). Therefore, the aim of this study is to compare the lower-limb joint moments at the ankle, knee, and hip, both in the sagittal and frontal planes of motion, between participants with diabetes without peripheral neuropathy (DM), diabetic individuals with polyneuropathy (DPN) and healthy individuals (CONTROL).

3.3. Methods

3.3.1. Participants

Sixteen diabetic participants were recruited from the diabetes outpatient clinic of the Hospital de São João (HSJ). All patients were classified according to the International Working Group on the Diabetic Foot (IWGDF) risk classification system and distributed in two groups: eight participants (3 female, 5 male) with diabetes without peripheral neuropathy (DM) and eight participants (1 female, 7 male) with diabetes with associated polyneuropathy (DPN). For the constitution of the healthy group (CONTROL), data from ten (6 female, 4 male) healthy participants were used from a multimodal data set of human gait (Schreiber & Moissenet, 2019). A diagnosis of type 1 or type 2 diabetes was mandatory for the inclusion in the DM group and/or the DPN group. The diagnosis of peripheral neuropathy, based on previous medical assessment, was required for the subject's inclusion in the DPN group. The study was conducted with the HSJ Ethics Committee approval with the number CEs 213-16. All subjects in the DM and DPN groups read and freely signed an informed consent.

3.3.2. Experimental setup

Diabetic gait kinematic data was captured using a 12-camera motion capture system (Qualisys, AB, Sweden) operating at 200 Hz sampling frequency. A performance volume of approximately 6.0 x 1.5 x 2.0 m (18.0 m^3) was calibrated in the center of a 10-meter walkway, were four Bertec force platforms (Bertec Inc, USA), recording at a 2000 Hz sampling rate, were embedded on the floor, to capture three consecutive steps. The participants were equipped with a full-body marker setup based on the IOR model (Cappozzo et al., 1995), comprising sixty-six retroreflective markers. A set of four clusters of markers were also placed on the right and left thigh and shank for segment tracking.

3.3.3. Protocol

Prior to the data collection, a familiarization period was observed with the participants walking barefooted at a comfortable pace along the 10-meter walkway, until reporting enough adaptation. A single static trial was then

performed with each participant standing in anatomical position for 30 seconds, within the calibrated volume. Participants were then asked to walk in a straight line, at a self-selected comfortable speed. A total of five valid trials were recorded for each participant.

3.3.4. Data processing and analysis

Kinematic and kinetic data were pre-processed using the Qualisys Track Manager (Qualisys, AB, Sweden) through its Clinical Gait Project Automation Framework (PAF) Module. The trajectories of the markers were filtered with a 6-Hz low-pass Butterworth filter. The final processing was performed in Visual3D (C-Motion Inc., USA), according to the PAF module specifications. Gait events were automatically identified using the software's built-in functions and any corrections were made through visual inspection. A lower-body model with six degrees of freedom was used to calculate and obtain joint moment signals at the ankle, knee, and hip, both in the sagittal and frontal planes. Joint moments and time were normalized by the subject's body mass and duration of the gait cycle (support and aerial phases), respectively. The joint moment characterization was performed according to the literature (Lee & Hidler, 2008). Discrete points were extracted from the average signal of each subject right limb, in all analyzed joints (**Error! Reference source not found.**) as follows: maximum ankle dorsiflexor (ADF1); maximum ankle plantar flexor (APF1); first knee maximum flexor (KFLEX1); first knee maximum extensor (KEXT1); second knee maximum flexor (KFLEX2); second knee maximum extensor (KEXT2); third knee maximum flexor (KFLEX3); first hip maximum extensor (HEXT1); first hip maximum flexor (HFLEX1); second hip maximum extensor (HEXT2); first ankle maximum evertor (AEV1); first ankle maximum invertor (AINV1); second ankle maximum evertor (AEV2); first knee maximum valgus (KVAL1); second knee maximum valgus (KVAL2); third knee maximum valgus (KVAL3); first knee maximum varus (KVAR1); first hip maximum abductor (HAB1); second hip maximum abductor (HAB2); third hip maximum abductor (HAB3); and first hip maximum adductor (HAD1).

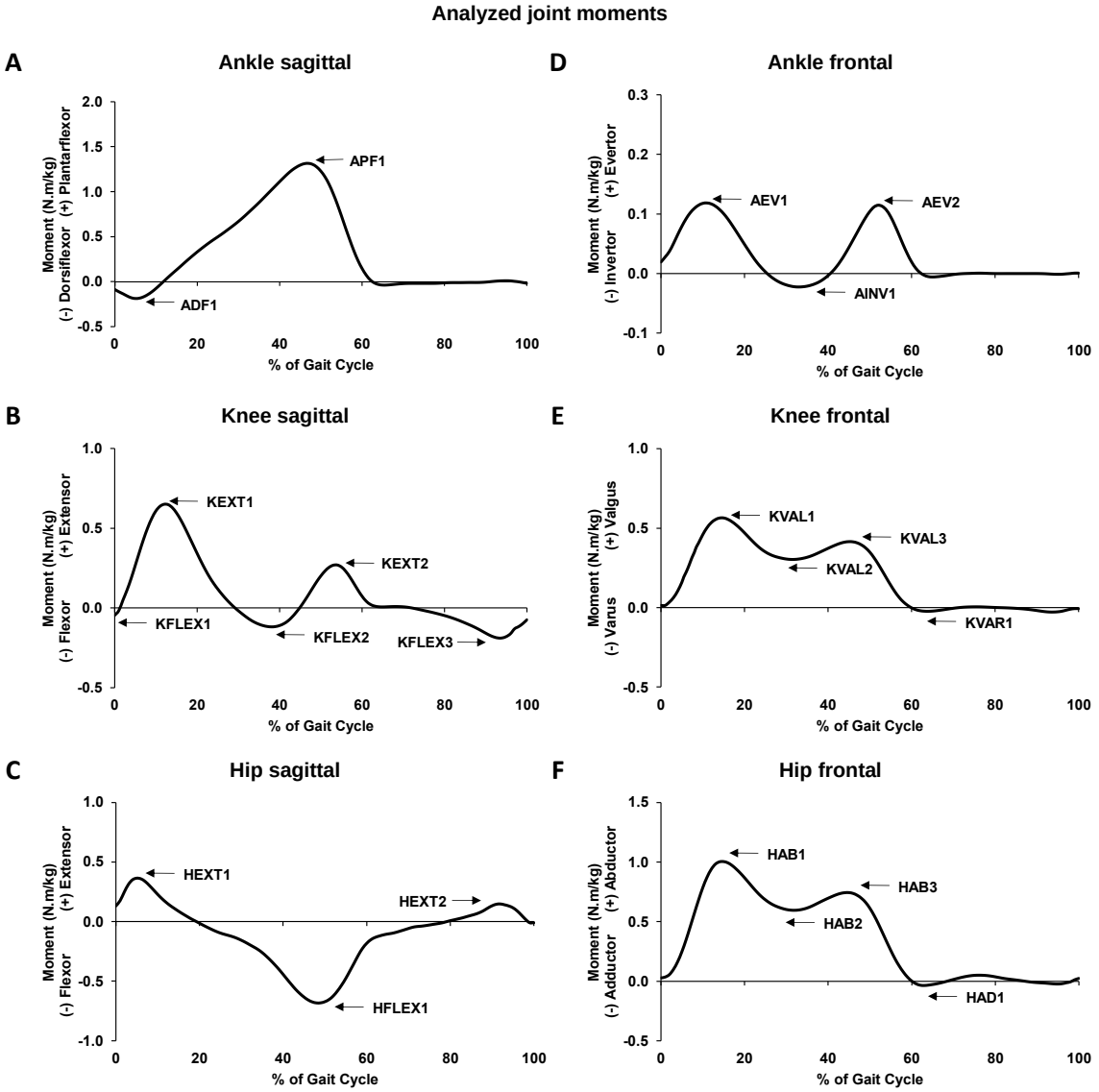


Figure 1. Ankle, knee, and hip joint moment profiles in sagittal (A, B, C) and frontal (D, E, F) planes. ADF1: maximum ankle dorsiflexor; APF1: maximum ankle plantar flexor; KFLEX1: first knee maximum flexor; KEXT1: first knee maximum extensor; KFLEX2: second knee maximum flexor; KEXT2: second knee maximum extensor; KFLEX3: third knee maximum flexor; HEXT1: first hip maximum extensor; HFLEX1: first hip maximum flexor; HEXT2: second hip maximum extensor; AEV1: first ankle maximum evertor; AINV1: first ankle maximum invertor; AEV2: second ankle maximum evertor; KVAL1: first knee maximum valgus; KVAL2: second knee maximum valgus; KVAL3: third knee maximum valgus; KVAR1: first knee maximum varus; HAB1: first hip maximum abductor; HAB2: second hip maximum abductor; HAB3: third hip maximum abductor; HAD1: first hip maximum adductor. Adapted from "Biomechanics of overground vs. treadmill walking in healthy individuals", by S. J. Lee and S. Hidler, 2008, Journal of Applied Physiology, 104(3), p. 749. Copyright 2008 by the American Physiological Society.

3.3.5. Statistical procedures

Data normality was assessed with the Shapiro-Wilk test, by visual inspection of the histograms and the skewness/kurtosis values. Descriptive statistics are presented as mean ± standard deviation. Univariate analysis of

variance (ANOVA), followed by *post hoc* tests, was conducted to assess differences between groups in terms of participant's characteristics.

Due to pattern variability, some joint moment parameters were not possible to identify in all subjects. Since multivariate statistics could not be performed, multiple Independent Student's *t*-tests were employed with a Bonferroni correction. Cohen's *d* is presented as a measure of effect size (Cohen, 1988). All tests were performed using SPSS Statistics version 27 (IBM, USA). A significance level of $\alpha = 0.05$ was established for all statistical tests.

3.4. Results

3.4.1. Characteristics of the participants

The results of the participant's characteristics comparisons are presented in Table . When comparing the DM with the DPN groups, the DM presented lower values of age and body mass index (BMI). Higher values of age, mass and BMI were found in the DPN, when compared to the CONTROL group. No significant differences were observed, in terms of mass and BMI, between DM and DPN groups. With regards to height, there were no significant differences between groups. There were no observed differences between DM and CONTROL on all variables.

Table 1. ANOVA and *post hoc* results for the comparison of the participant's characteristics. Significant differences are highlighted in bold.

	DM	**DPN**	**CONTROL**	***p***
Age (years)	38.75 ± 18.09	64.63 ± 11.46	48.50 ± 7.75	**0.002**[a, b]
Height (m)	1.68 ± 0.12	1.70 ± 0.13	1.73 ± 0.07	0.551
Mass (kg)	70.39 ± 16.46	87.14 ± 12.71	69.06 ± 13.52	**0.028**[b]
BMI (kg/cm^2)	24.70 ± 2.89	30.04 ± 2.65	22.86 ± 3.24	**< 0.001**[a, b]

[a] Differences between DM and DPN; [b] Differences between DPN and CONTROL.

3.4.2. Joint moments

The average waveforms of the ankle, knee and hip joint moments, in the sagittal plane, for the DM, DPN and CONTROL groups, by sex and with all subjects, are depicted in Figure 2, Figure 3 and Figure 4.

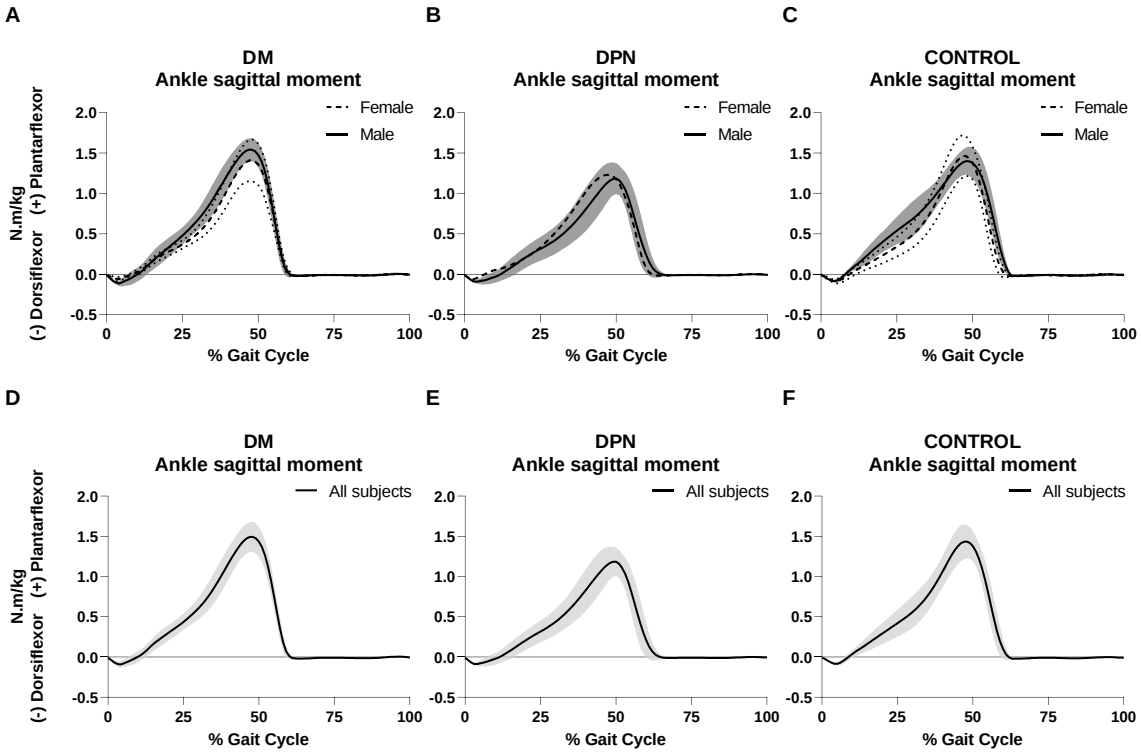


Figure 2. Ankle joint moment average waveforms in the sagittal plane for the DM, DPN and CONTROL groups, by sex (A, B C) and with all subjects (D, E, F). Standard deviation is represented with dark grey shade (Male), dotted lines (Female) and light grey shade (all subjects).

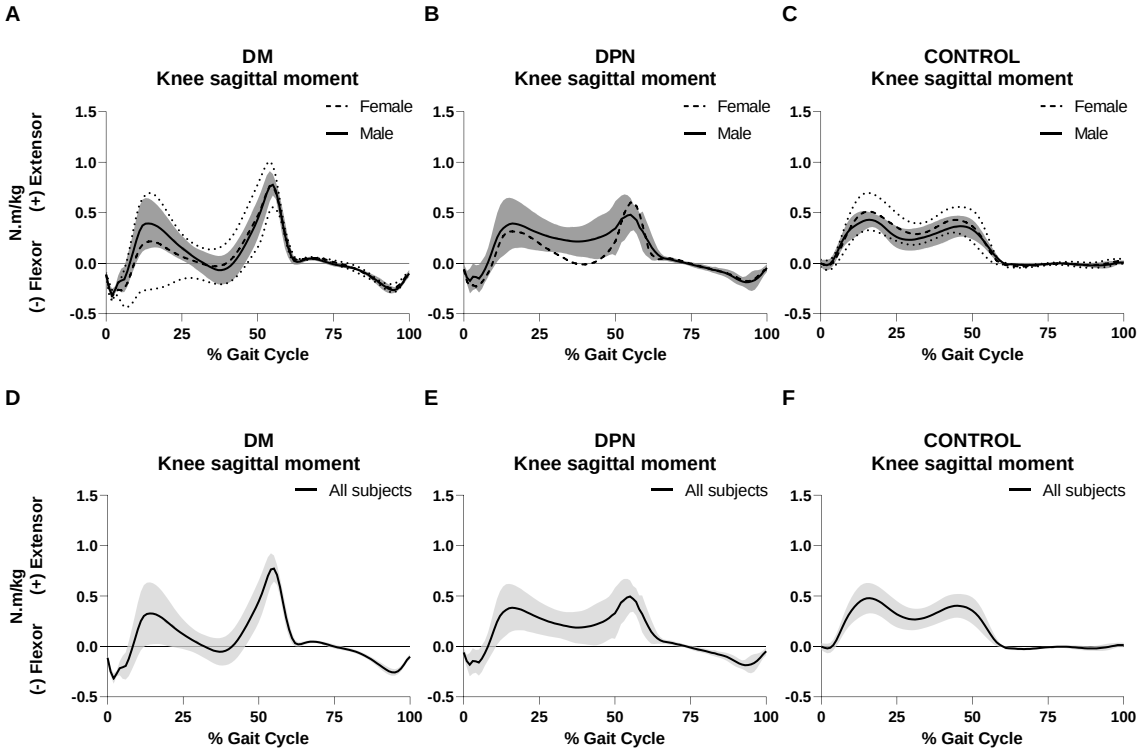


Figure 3. Knee joint moment average waveforms in the sagittal plane for the DM, DPN and CONTROL groups, by sex (A, B C) and with all subjects (D, E, F). Standard deviation is represented with dark grey shade (Male), dotted lines (Female) and light grey shade (all subjects).

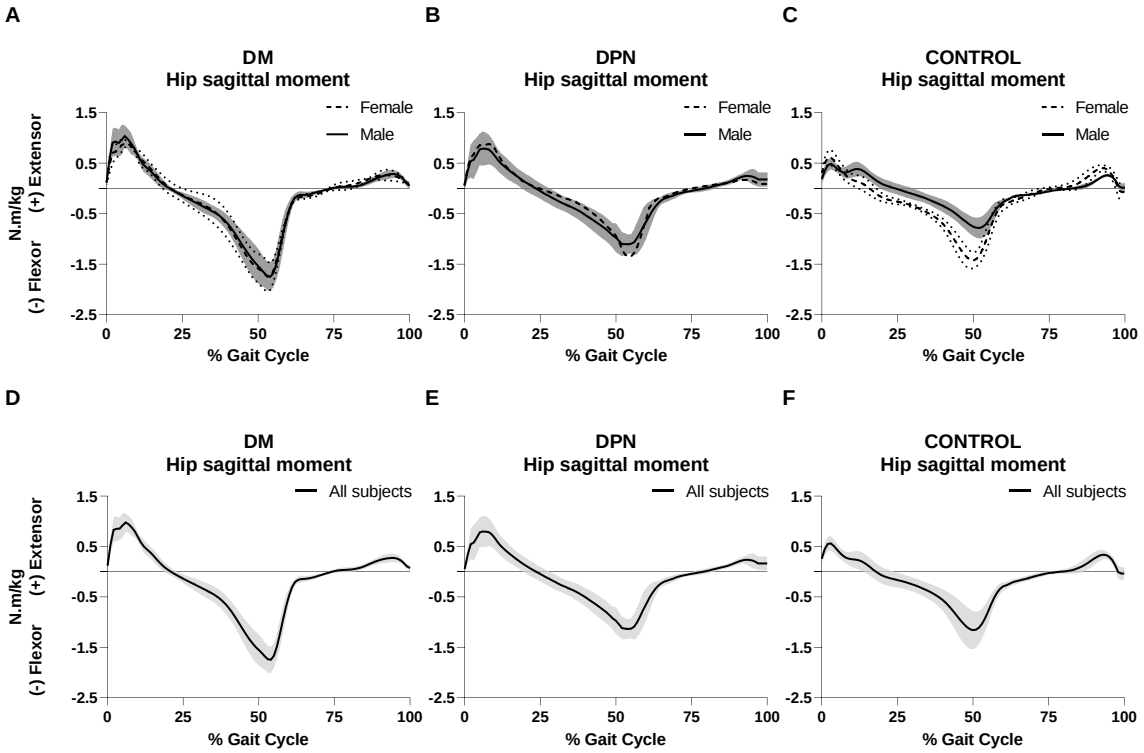


Figure 4. Hip joint moment average waveforms in the sagittal plane for the DM, DPN and CONTROL groups, by sex (A, B C) and with all subjects (D, E, F). Standard deviation is represented with dark grey shade (Male), dotted lines (Female) and light grey shade (all subjects).

Due to the reduced number of participants, a statistical analysis could not be performed in terms of sex differences. The standard deviation of the female subjects, in the DPN group, could not be calculated since this group has only one female participant. The presented results suggest similar variability, in terms of sex comparisons, except for a seeming higher variability in the frontal plane ankle and knee joint moments, for the DM female group. The female participants of the CONTROL group presented a perceptible lower knee flexor moment, and a higher hip flexor moment, in the sagittal plane. In terms of the parameter's characterization, the KFLEX2 was only observed in the DM group. Therefore, differences in this parameter, in the DPN and CONTROL groups, were not possible to assess. Since the DPN and CONTROL groups presented a minimum extensor moment value between the KEXT1 and KEXT2 parameters, this variable was added to the analysis (KDIP).

The average waveforms of the ankle, knee and hip joint moments, in the frontal plane, for the DM, DPN and CONTROL groups, by sex and with all subjects, are depicted in Figure 5, Figure 6 and Figure 7.

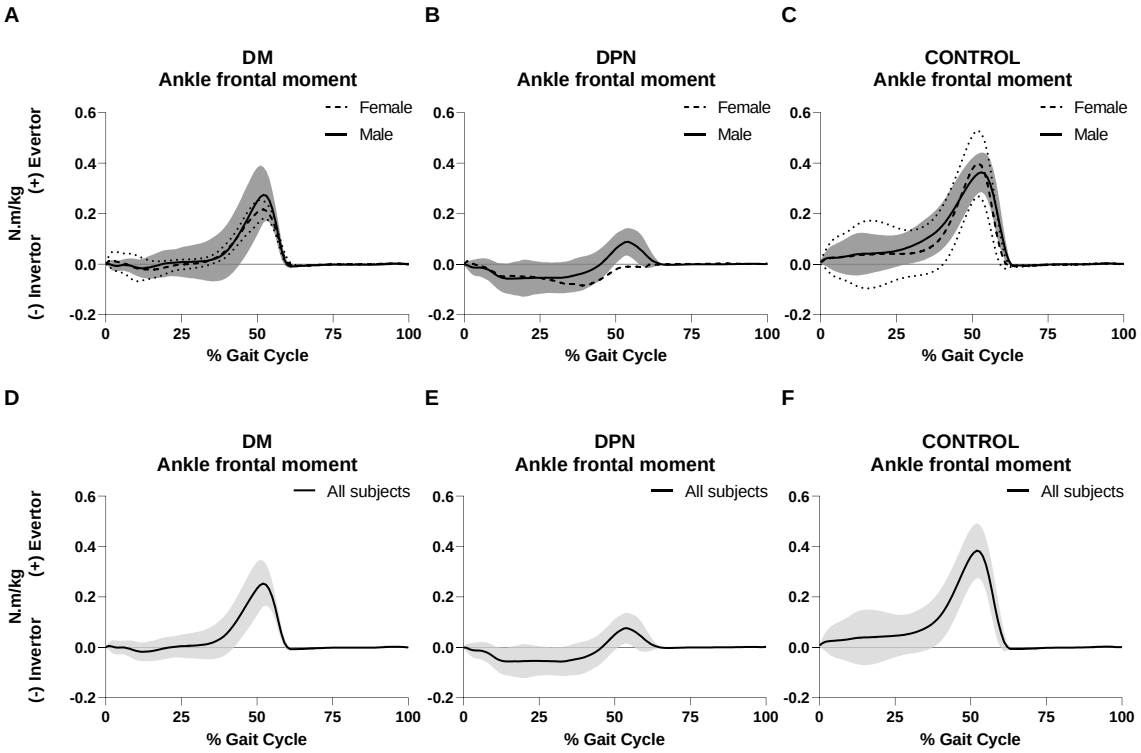


Figure 5. Ankle joint moment average waveforms in the frontal plane for the DM, DPN and CONTROL groups, by sex (A, B C) and with all subjects (D, E, F). Standard deviation is represented with dark grey shade (Male), dotted lines (Female) and light grey shade (all subjects).

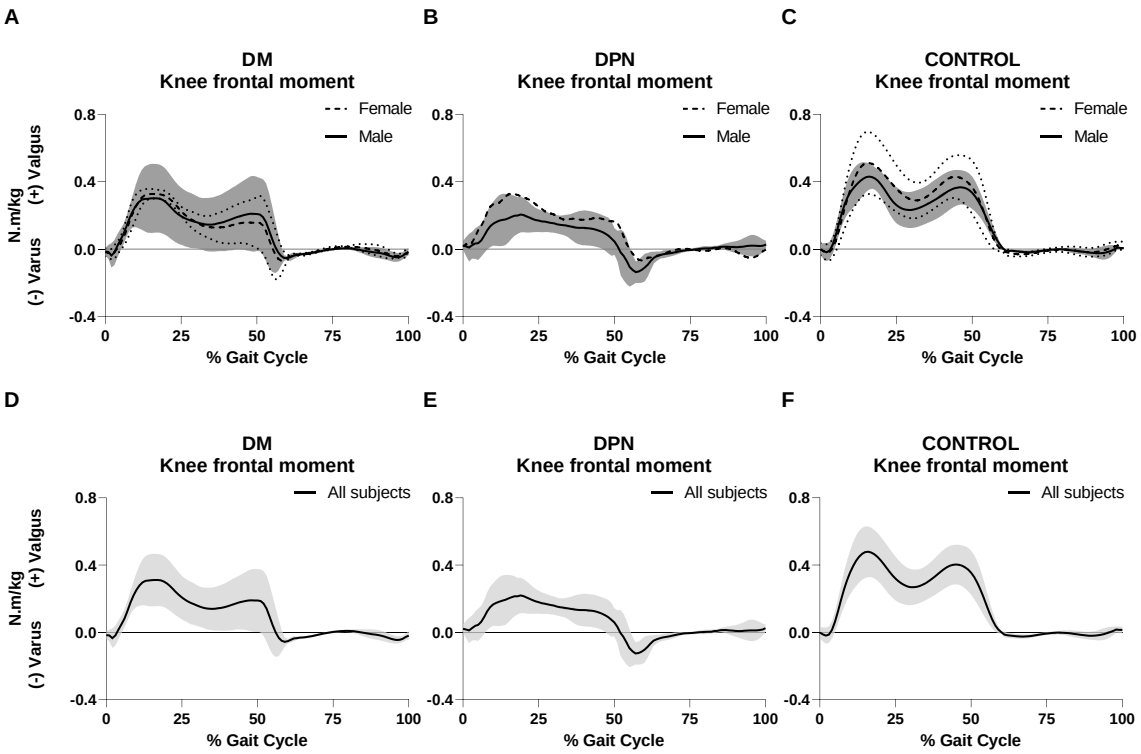


Figure 6. Knee joint moment average waveforms in the frontal plane for the DM, DPN and CONTROL groups, by sex (A, B C) and with all subjects (D, E, F). Standard deviation is represented with dark grey shade (Male), dotted lines (Female) and light grey shade (all subjects).

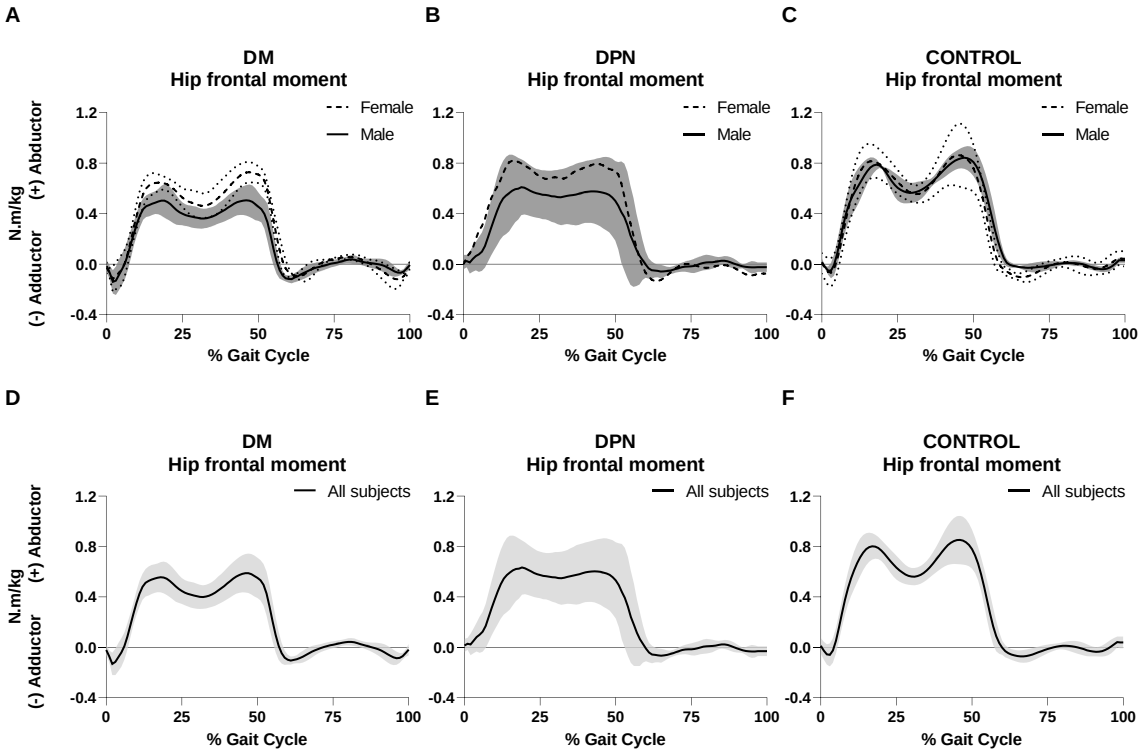


Figure 7. Hip joint moment average waveforms in the frontal plane for the DM, DPN and CONTROL groups, by sex (A, B C) and with all subjects (D, E, F). Standard deviation is represented with dark grey shade (Male), dotted lines (Female) and light grey shade (all subjects).

In the frontal plane, the average waveforms suggest differences between male and female subjects, especially in the DM group at the ankle, knee and hip joint moments. A high variability is observed in the DM group, in the frontal knee joint moments, and in the DPN group at the hip frontal moment level. The average waveforms of the frontal ankle moments also revealed high variability in this parameter, namely in the AEV1 and AEV2, with and without controlling for sex differences. Simultaneously, the AEV1 parameter was not observed in the DPN group average waveform.

The results of the DM, DPN and CONTROL joint moment comparisons are presented in Table 2 and Table 3, for the sagittal and frontal planes, respectively. As the DM and DPN groups did not present a waveform with the KFLEX2 parameter, these results are not reported. The KDIP parameter, on the other hand, is only presented in these groups.

Table 2. Joint moments in the sagittal plane for the DM, DPN and CONTROL groups. Statistically significant differences are highlighted in bold.

Joint	Moment	Group	Mean ± *SD* (N.m/kg)
Ankle	ADF1	DM	-0.10 ± 0.04
		DPN	-0.10 ± 0.03
		CONTROL	-0.09 ± 0.02
	APF1	DM	**1.50 ± 0.19[a]**
		DPN	1.22 ± 0.20
		CONTROL	1.46 ± 0.20
Knee	KFLEX1	DM	**-0.35 ± 0.06[a, b]**
		DPN	**-0.21 ± 0.10[c]**
		CONTROL	-0.05 ± 0.04
	KEXT1	DM	0.50 ± 0.09
		DPN	0.46 ± 0.19
		CONTROL	0.49 ± 0.15
	KFLEX2	DM	-0.14 ± 0.12
		DPN	-
		CONTROL	-
	KDIP	DM	-
		DPN	0.15 ± 0.07
		CONTROL	0.26 ± 0.11
	KEXT2	DM	**0.80 ± 0.15[a, b]**
		DPN	0.55 ± 0.18
		CONTROL	0.41 ± 0.12
	KFLEX3	DM	**-0.26 ± 0.03[b]**
		DPN	**-0.21 ± 0.03[c]**
		CONTROL	-0.04 ± 0.02
Hip	HEXT1	DM	**1.02 ± 0.20[b]**
		DPN	0.83 ± 0.31
		CONTROL	0.57 ± 0.14
	HFLEX1	DM	**-1.77 ± 0.26[a, b]**
		DPN	-1.27 ± 0.16
		CONTROL	-1.19 ± 0.38
	HEXT2	DM	0.29 ± 0.08
		DPN	0.27 ± 0.07
		CONTROL	0.36 ± 0.09

[a] DM with DPN; [b] DM with CONTROL; [c] DPN with CONTROL

In the sagittal plane, when comparing the DM with DPN groups, the DPN presented statistically significant reduced joint moments at APF1 ($t(14) = 2.914$, $p = 0.03$, $d = 1.46$), KFLEX1 ($t(14) = -3.334$, $p = 0.01$, $d = 1.67$), KEXT2 ($t(14) = 2.919$, $p = 0.03$, $d = 1.46$), and HFLEX1 ($t(14) = -4.691$, $p < 0.01$, $d = 2.35$).

Comparing the DM with CONTROL groups in the sagittal plane, significantly increased joint moment values were observed in the DM for the

KFLEX1 ($t(13) = -11.068$, $p < 0.01$, $d = 5.73$), KEXT2 ($t(16) = 5.966$, $p < 0.01$, $d = 2.83$), KFLEX3 ($t(12) = -13.900$, $p < 0.01$, $d = 7.51$), HEXT1 ($t(16) = 5.745$, $p < 0.01$, $d = 2.73$) and HFLEX1 ($t(16) = -3.759$, $p = 0.01$, $d = 1.78$).

The sagittal plane analysis of the DPN and CONTROL revealed significant higher joint moment values in the DPN group for the KFLEX1 ($t(13) = -3.991$, $p < 0.01$, $d = 2.07$) and KFLEX3 ($t(12) = -10.871$, $p < 0.01$, $d = 5.87$).

Table 3. Joint moments in the frontal plane for the DM, DPN and CONTROL groups. Statistically significant differences are highlighted in bold.

Joint	Moment	Group	Mean ± *SD* (N.m/kg)
Ankle	AEV1	DM	**0.04 ± 0.03[b]**
		DPN	-
		CONTROL	0.18 ± 0.04
	AINV1	DM	-0.05 ± 0.01
		DPN	-0.09 ± 0.03
		CONTROL	-0.07 ± 0.02
	AEV2	DM	**0.26 ± 0.10[a]**
		DPN	**0.08 ± 0.06[c]**
		CONTROL	0.39 ± 0.11
Knee	KVAL1	DM	0.38 ± 0.09
		DPN	**0.26 ± 0.11[c]**
		CONTROL	0.49 ± 0.15
	KVAL2	DM	0.18 ± 0.11
		DPN	**0.13 ± 0.06[c]**
		CONTROL	0.26 ± 0.11
	KVAL3	DM	0.30 ± 0.14
		DPN	**0.16 ± 0.08[c]**
		CONTROL	0.41 ± 0.12
	KVAR1	DM	**-0.10 ± 0.06[b]**
		DPN	**-0.16 ± 0.09[c]**
		CONTROL	-0.03 ± 0.02
Hip	HAB1	DM	**0.57 ± 0.12[b]**
		DPN	0.68 ± 0.22
		CONTROL	0.81 ± 0.10
	HAB2	DM	**0.39 ± 0.09[b]**
		DPN	0.56 ± 0.21
		CONTROL	0.55 ± 0.07
	HAB3	DM	**0.60 ± 0.15[b]**
		DPN	0.68 ± 0.22
		CONTROL	0.87 ± 0.18
	HAD1	DM	-0.12 ± 0.03
		DPN	-0.14 ± 0.07
		CONTROL	-0.08 ± 0.05

[a] DM with DPN; [b] DM with CONTROL; [c] DPN with CONTROL

In the frontal plane, comparing DM with DPN, lower values were observed in the DPN group at the AEV2 ($t(14) = 4.369$, $p < 0.01$, $d = 2.18$).

When comparing the DM with CONTROL groups, the DM presented lower values at the AEV1 ($t(5) = -5.362$, $p = 0.01$, $d = 4.10$), HAB1 ($t(16) = -4.524$, $p < 0.01$, $d = 2.15$), HAB2 ($t(16) = -4.041$, $p < 0.01$, $d = 1.92$) and HAB3 ($t(16) = -3.389$, $p = 0.01$, $d = 1.61$). Higher values were observed, in the CONTROL group, for the KVAR1 parameter ($t(16) = -3.402$, $p = 0.01$, $d = 1.61$).

In the DPN with CONTROL comparison, in the frontal plane, the DPN presented lower values in the AEV2 ($t(16) = -7.113$, $p < 0.01$, $d = 3.37$), KVAL1 ($t(16) = 3.673$, $p = 0.01$, $d = 1.74$), KVAL2 ($t(14.001) = -3.122$, $p = 0.02$, $d = 1.38$) and KVAL3 ($t(14) = -4.497$, $p < 0.01$, $d = 2.32$). The CONTROL group presented higher values at the KVAR1 ($t(7.377) = -4.195$, $p = 0.01$, $d = 2.23$).

3.5. Discussion

The main objective of this study was to compare the ankle, knee, and hip joint moments, in the sagittal and frontal planes, between DM, DPN and CONTROL groups. Findings suggest differences between the groups in terms of the pre-described metrics of interest; results for some of these metrics are absent in the literature. In the sagittal plane, while some parameters are widely reported, such as the ankle or knee moments, there are few publications on the joint moments in the frontal plane. Additionally, the available literature is not exhaustive in characterizing the joint moment waveforms, and even the limited information found does not include all possible descriptor events. Therefore, this study proposes new events that allow a more detailed description of the joint moment waveform patterns.

In terms of sagittal ankle joint moments, the DPN group presented a reduced APF1 joint moment when compared to the DM group, but no significant differences were found when comparing DM and DPN with the CONTROL group. The literature is inconsistent regarding these findings. Diabetic patients with associated peripheral neuropathy are found to exhibit reduced plantar flexion moments (DiLiberto et al., 2015; Rao et al., 2010; Yavuzer et al., 2006).

Conversely, Petrovic et al. (2017) found no differences in plantar flexion moments between DM and DPN groups but found significantly lower values when comparing DM and DPN with CONTROL group. Evidence of lower peak plantar flexion moments in DPN, when compared to CONTROL group, are also reported by Mueller et al. (1994) and Salsich and Mueller (2000). Brown et al. (2014) also described lower plantar flexion moments in DM and DPN groups when compared to CONTROL. The deficits induced by musculoskeletal limitations, as a result of a peripheral neuropathy, are associated with reduced ankle motion and ankle moments (Mueller et al., 1994). Nevertheless, since patients with diabetes without polyneuropathy can also present altered and less efficient gait patterns when compared to non-diabetic subjects (Ko et al., 2011), a difference between DM and CONTROL was expected. As the current study relies on a small sample size, the achieved power could not have been sufficient to detect this expected effect.

No significant differences were found in the ADF1 joint moments between groups. Brown et al. (2014) also found no significant differences between DM, DPN and CONTROL groups. On the other hand, Kwon et al. (2003) reported lower peak dorsiflexion moments in the DPN group, when compared to the CONTROL group. The authors indicate that these results could be explained by a compensatory adaptive strategy to maintain balance, inducing a more stable gait to compensate diminished sensory information at the ankle, even though the findings in the present study do not corroborate these results.

In the frontal plane, also at the ankle joint level, the average waveforms (Figure 5, D, E, F) were not consistent with those reported in the literature (Figure 1, D). In the present study, the AEV1 and AINV1 were not observed in all subjects, representing a high individual variability. When comparing the DM with CONTROL group, the AEV1 parameter was significantly lower in DM, but no comparisons were possible with the DPN group. This could reflect the proprioceptive changes in the DM group, with a more neutral position of the foot at the initial contact providing higher balance. However, and due to the variability of the data and the impossibility of comparing with the DPN group, these differences should be interpreted with caution.

Considering the AEV2 joint moment parameter, the DPN group presented significantly lower values, when compared to the DM and CONTROL. Still, no significant differences were observed between the DM and CONTROL groups. There is limited literature available on joint moment analysis in the frontal plane, regarding diabetics with or without polyneuropathy. Katoulis et al. (1997) reported higher frontal plane peak ankle moment in a DPN group, when compared to a CONTROL group. According to the authors, the results could be explained by the increased lateral positioning of the foot, induced by the proprioceptive deficit. The findings in the current study suggest, on the other hand, a progressive decreased ankle joint moment in the frontal plane, with marked reduction in the DPN group. This could represent motor and sensory deficits at the ankle, manifesting as a less stable ankle joint and lower ankle evertor moments.

In the sagittal knee joint moments, the CONTROL group presented lower values in the KFLEX1 parameter, followed by the DPN and DM groups. In the KEXT2 parameter, the DM presented higher values when compared to DPN and CONTROL. Nevertheless, no differences were observed when comparing DPN and CONTROL. In the KFLEX3 parameter, lower values were observed in the CONTROL group, when comparing with DM and DPN. No differences were observed in the KEXT1 and KDIP. Additionally, no comparisons could be made in terms of the KFLEX2 parameter. Sacco et al. (2015) reported lower knee flexion moments at late mid-stance in DM and DPN groups, when compared to CONTROL. The lower knee joint flexion moments could represent difficulties in the act of push-off imposed by the changes in the gait pattern of both diabetic groups. Since this was not the case in the present study, these results could represent differences apart from the group conditions, such as age or weight. More studies are needed to clarify these findings.

In the KEXT2 joint moment, the DM exhibited higher values when compared to the DPN and CONTROL groups. No differences were found when comparing the CONTROL with DPN moment values, but the time values for the occurrence of the peaks apparently are different. DM and DPN groups usually present higher knee extension moments in early midstance when compared to CONTROL groups (Sacco et al., 2015). In the current study, the higher values of

the DM group in the KEXT2 parameter may be a consequence of the differences at the knee flexion level. While the DPN and CONTROL groups do not exhibit a flexion moment in the midstance, the DM group had to compensate with an exaggerated knee extension moment in late midstance, to attain an adequate propulsion. Concerning the KEXT1 parameter, no significant differences were found between groups, in line with the findings of Yavuzer et al. (2006) in terms of knee extension moments.

Analyzing the knee joint moments in the frontal plane, the DPN group presented significantly reduced KVAL1 values, when compared to the CONTROL group. There were no significant differences in this parameter between the DM and DPN and when comparing the DM with CONTROL. Katoulis et al. (1997) found no differences in the knee joint moments, in the frontal plane, in a study comparing DM, DPN and CONTROL groups. Similar results were also reported by Yavuzer et al. (2006), when comparing DM and CONTROL groups. The findings of the present study in the KVAL1 parameter, suggest a progressive reduction from the CONTROL to DM to DPN groups.

The KVAL2 and KVAL3 joint moments were also reduced in the DPN, when compared to the CONTROL group. No differences were found between DM and DPN in these parameters. In terms of the KVAR1 joint moment, increased values were observed in the DM and DPN groups, when compared to the CONTROL. The neurologic compromise in the DPN group is associated with distal to proximal weakness. The quadriceps muscle is capable of applying an abductor moment at the knee joint, in the stance phase (Schipplein & Andriacchi, 1991). As the disease progresses and the neurologic deficit becomes established, the resulting loss of force production from the quadriceps should reflect as lower KVAL1, KVAL2 and KVAL3, and elevated KVAR1 joint moment values.

At the hip joint level, in the sagittal plane, the DM presented higher HEXT1 and HFLEX1 values when compared to the CONTROL group. DM and DPN differences were only observed at the HFLEX1 parameter. Previous studies have reported no differences when comparing hip joint moments between DM and/or

DPN and CONTROL groups (Kwon et al., 2003; Mueller et al., 1994; Savelberg et al., 2009; Yavuzer et al., 2006). However, Sacco et al. (2015) observed significantly lower hip extension moments at the initial contact, greater hip flexor moments at the push-off phase and lower hip extension moments at the end of the stance phase in DM and DPN groups when compared to CONTROL. These results partially corroborate the findings in the present study. It was expected that the DM and DPN groups presented lower HEXT1 values, since it usually correlates with less extensor moment activity to overcome the gravity force at the weight acceptance phase. Still, the increased HEXT1 joint moments found in the DM, in the present study, may be related with changes in distal to proximal sensory and proprioceptive impairment in both diabetic groups. These changes may induce a hip compensation strategy starting at the initial contact, to maintain balance during the loading response.

The DM group presented lower hip joint moments, in the frontal plane, in the HAB1 HAB2 and HAB3 parameters, when compared to the CONTROL. No significant differences were found when comparing the DM and DPN groups. To our knowledge, no similar results were previously reported in the literature. These findings might be explained by factors other than diabetes and its neurologic consequences, such as differences in age and body mass, which highlights the relevance of conducting analysis controlling these variables.

Despite the novelty of the current findings, the interpretation and generalization of results should consider some limitations. The reduced number of participants could have hampered the statistical power and, consequently, increased the type II error. The data from the CONTROL group, even though it was processed from raw acquisition signals, was selected from a public multimodal dataset of human gait. Therefore, a selection bias may be present in terms of external validity. Simultaneously, differences between groups in age, body mass and BMI should also be considered as potential biasing factors.

3.6. Conclusion

The analysis of joint moments allowed for an in-depth understanding on the biomechanical differences between individuals with diabetes, with and

without peripheral neuropathy, and healthy ones. To our knowledge, this is the first study performing this type of comparison both in the sagittal and frontal planes, during a gait cycle. A major conclusion that can be drawn from the results is that the diabetic polyneuropathy may contribute to altered lower limb joint moments which go beyond the sagittal plane of motion. Concurrently, evidence indicate that these alterations can become apparent with the diabetic condition alone, even without the establishment of neurological deficits. The identification of these changes may assist researchers and health professionals to develop more effective interventions aiming at minoring the negative effects of diabetes and diabetic polyneuropathy.

3.7. Funding

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4. General Conclusion

The studies presented in this dissertation revealed important findings regarding the joint moment analysis of diabetic subjects, during gait, some of which are undocumented in the literature. First and foremost, it was demonstrated that most of the previous research emphasizes the sagittal plane of motion, with few publications assessing the joint moments in the frontal plane. Secondly, diabetes and diabetic polyneuropathy can contribute to an altered gait pattern that can be assessed through joint moment parameters. Moreover, these changes manifest not only in the sagittal plane, but also on the frontal plane of motion and they can be present in the diabetic condition alone, without an overt polyneuropathy. These findings may contribute to the development of more effective interventions in the diabetic population, reducing morbidity and mortality and increasing their quality of life, highlighting the relevance of the biomechanical gait analysis in this context.

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