Clinical Biomechanics 94 (2022) 105632

Contents lists available at ScienceDirect

Clinical Biomechanics

journal homepage: www.elsevier.com/locate/clinbiomech

Metabolic cost of transport and stance time asymmetry in individuals with unilateral transtibial amputation using a passive prostheses while walking

Ryan D. Wedge [a,b,c,1,*], Frank C. Sup IV [d], Brian R. Umberger [a,e]

[a] Department of Kinesiology, School of Public Health and Health Sciences, University of Massachusetts Amherst, 30 Eastman Lane, 110 Totman Building, Amherst, MA 01003-9258, United States
[b] Motion Analysis Laboratory, Quinnipiac University, 275 Mount Carmel Avenue, Hamden, CT 06518, United States
[c] Department of Physical Therapy, Health Sciences Building, East Carolina University, 600 Moye Blvd, Greenville, NC 27834, United States
[d] Department of Mechanical and Industrial Engineering, University of Massachusetts Amherst, 120 E Marston Hall, 160 Governor's Drive, Amherst, MA 01003-2210, United States
[e] School of Kinesiology, University of Michigan, SKB 1210, 830 North University, Ann Arbor, MI 48109-1048, United States

ARTICLE INFO

Keywords:
Gait
Locomotion
Energetics
Rehabilitation
Limb loss
Real-time feedback

ABSTRACT

Background: People with unilateral amputation typically walk with greater metabolic cost than able-bodied individuals, while preferring asymmetric walking characteristics. It is unclear if asymmetric walking is energetically optimal and how metabolic cost accounts for asymmetric patterns in people with amputation. The purpose of this study was to determine the effects of stance-time asymmetry on the metabolic cost of transport.
Methods: Fourteen participants (seven with amputation) completed two laboratory sessions where they walked on a treadmill while receiving real-time visual feedback about stance-time asymmetry. Expired gases were collected to determine the metabolic cost for a range of asymmetries (−15% to +15% in 5% increments, positive percentages represent more time on intact [dominant] limb).
Findings: Participants with amputation walked with greater ($P = 0.008$) stance-time asymmetry (4.34 ± 1.09%) compared with able-bodied participants (0.94 ± 2.44%). Stance-time asymmetry had a significant effect on metabolic cost ($P < 0.001$). The asymmetries coinciding with the predicted minimum metabolic cost for people with (3.23 ± 2.90%) and without (1.81 ± 2.18%) amputation were not different from preferred asymmetries ($P = 0.365$; $p = 0.513$), respectively. The cost of symmetric walking was 13.6% greater than near preferred walking for people with amputation (5% more time on intact limb).
Interpretation: Metabolic cost is not the only objective of walking, but like able-bodied individuals, it may influence how people with amputation walk. Rehabilitation typically tries to restore inter-limb symmetry after an injury, yet if the limbs are asymmetric, symmetric gait may not be optimal with current assistive devices.

1. Introduction

Metabolic energy expenditure is generally accepted as one of the key objectives in the multi-objective selection of locomotor patterns, along with other likely criteria such as stability, smoothness, and joint loading. It is unclear how energy expenditure is prioritized relative to other factors during walking in people with lower limb amputation. People with lower limb amputation who use a passive prosthesis generally have greater metabolic energy expenditure during walking compared with able-bodied individuals (Waters et al., 1976; Waters and Mulroy, 1999), with the exception of those who are highly fit, such as active-duty military personnel (Russell Esposito et al., 2014). Greater metabolic energy expenditure while walking can negatively impact function and quality of life (Pell et al., 1993). For most people with lower limb amputation, metabolic energy expenditure is important but is likely elevated because of prosthesis limitations compared to a biological limb. Therefore, even though people with lower limb amputation generally demonstrate greater metabolic energy expenditure than able-bodied individuals, they may still be selecting preferred gait patterns with the least metabolic energy expenditure.

* Corresponding author at: Department of Physical Therapy, Health Sciences Building, East Carolina University, 600 Moye Blvd, Greenville, NC 27834, United States

E-mail addresses: wedger19@ecu.edu (R.D. Wedge), sup@ecs.umass.edu (F.C. Sup), umberger@umich.edu (B.R. Umberger).

[1] Permanent Address

https://doi.org/10.1016/j.clinbiomech.2022.105632
Received 20 October 2021; Accepted 22 March 2022
Available online 25 March 2022
0268-0033/

While there are some exceptions in the literature (Gundersen et al., 1989), able-bodied people typically demonstrate nearly symmetrical inter-limb stride mechanics for preferred walking conditions (Eng and Winter, 1995; Forczek and Staszkiewicz, 2012; Hamill et al., 1983; Hannah et al., 1984; Seeley et al., 2008). When able-bodied individuals are constrained to walk with stride asymmetry (i.e., non-preferred pattern), metabolic rate increases directly with the amount of asymmetry (Ellis et al., 2013; Stenum and Choi, 2020). Hence, symmetric stride characteristics may be preferred because they lead to the lowest metabolic cost. In contrast, the connections between gait asymmetry and metabolic cost in people with unilateral lower limb amputation are unclear because of potential adaptations to compensate for limitations of the prosthesis.

People with lower limb amputation have an altered morphology (i.e., limb structure) and must rely on a prosthesis to replace the missing anatomy. The prosthesis may have energy assistance features using either passive components that can only manipulate energy flow (i.e., spring-like foot-ankles and damper knees) or active components that can contribute energy (i.e., motors). Even with a well-fitting prosthesis that replaces some of the lost biological power, people with lower limb amputation may have residual limb pain (Ehde et al., 2000), gait instability (Hak et al., 2014), and muscle weakness (Hewson et al., 2020). Due to these deficits, asymmetric anatomy, and prosthetic device constraints, a consistent finding is that people with unilateral amputations spend more time on the intact limb compared with the prosthetic limb during the stance phase (Isakov et al., 2000; Sadeghi et al., 2001; Sanderson and Martin, 1997). In a limited number of studies, people with unilateral limb amputation have been trained to walk with symmetric stride characteristics in a research setting (Dingwell et al., 1996; Davis et al., 2004; Mahon et al., 2019). In one small, heterogeneous sample (i.e., different causes of amputation and amputation levels), metabolic cost of walking was reduced when using real-time visual feedback to promote symmetrical push-off force (Davis et al., 2004). In contrast, in a two-participant case series, symmetric walking was not metabolically optimal, and each participant selected some form of asymmetry after adapting to split belts moving at different speeds (Mahon et al., 2019). While such studies have been insightful, it is problematic to draw firm conclusions based on the limited existing data. Therefore, more research is needed within the different subpopulations of people with lower limb amputation. Since energy expenditure is an important criterion for self-selected gait patterns, people with unilateral lower limb amputation may adopt asymmetric gait patterns to reduce the metabolic cost of walking. Conversely, if symmetry is energetically optimal, as in able-bodied walkers, promoting symmetric gait could reduce metabolic cost for people with lower limb amputation.

The purpose of this study was to determine the effects of stance time asymmetry on the metabolic cost of transport (CoT). Based on previous literature regarding stride symmetry in people with and without amputation, we hypothesized that for preferred gait patterns, participants with unilateral transtibial amputation would exhibit greater stance time on the intact side compared with the prosthetic side, while able-bodied participants would exhibit symmetrical stance times. Further, we hypothesized that the CoT versus inter-limb asymmetry would demonstrate a U-shaped curve for both groups, and the CoT would be least at preferred stride characteristics for both groups. A direct consequence of these hypotheses is that participants with unilateral transtibial amputation are predicted to have an elevated CoT when required to walk symmetrically, compared with the CoT for their preferred, asymmetrical gait pattern. Thus, we predict that people with unilateral lower limb amputation walk asymmetrically, at least in part, to reduce the metabolic cost of walking.

2. Methods

Seven participants with unilateral transtibial amputation and seven able-bodied participants took part in this study (Table 1). The participants with unilateral transtibial amputation were between 16 and 48 years old, rated a Medicare activity classification of K3 or K4 (Centers for Medicare and Medicaid Services, 2020), had the amputation more than one year ago due to non-vascular causes (e.g., trauma, cancer, congenital), and used a passive prosthesis (Table 2). People with a K3 or K4 rating are prescribed an energy storage with elastic return prosthetic foot and ankle because they are active and can walk with variable cadences. Participants were excluded from the study if they had any condition, other than amputation, that affected their ability to walk (e.g., chronic pain, neurological or cardiovascular disorders), or if they had lower limb surgery in the last year. We only recruited participants with unilateral transtibial amputation from non-vascular causes to avoid confounding effects of vascular disease such as neuropathy and decreased fitness that affect metabolic cost and walking. We recruited the same number of female and male able-bodied participants as in the group with lower limb amputation. Age, height, and mass were not directly controlled for; however, the primary dependent variables were scaled by body mass (metabolic cost) and expressed as a percentage (asymmetry), accounting for the effects of body size. This study was approved by the University of Massachusetts and Quinnipiac University Institutional Review Boards. All participants read and signed an informed consent document prior to participation.

Each participant attended two laboratory sessions, 12 of the 14 participants (5 with amputation and 7 able-bodied) at the Biomechanics Laboratory at the University of Massachusetts Amherst (Amherst, MA, USA), and 2 with amputation at the Motion Analysis Laboratory at Quinnipiac University (North Haven, CT, USA). During each session, participants walked on a treadmill (Treadmetrix, Park City, UT, USA at UMass, and Woodway, Waukesha, WI, USA at Quinnipiac) at their preferred overground walking speed while receiving real-time visual feedback about inter-limb stance time asymmetry. During the first session, preferred overground walking speed was determined, followed by training and familiarization with the real-time visual feedback conditions without metabolic measurement. Preferred walking speed was determined with an over ground 400-m walk that consisted of twenty consecutive 20-m lengths. A six-meter segment of each length was timed with photogates (Johnson et al., 2020). Overground speed was used

Table 1
Participant characteristics.

Group	Female/ male (#)	Age (yr)	Height (m)	Mass (kg)	Side: amputation or dominant	Years since amputation
amputation	2/5	37 ± 13	1.80 ± 0.08	83.9 ± 18.9	5 right/ 2 left	16.5 ± 11.7
able-bodied	2/5	29 ± 5	1.63 ± 0.37	85.4 ± 20.4	7 right/ 0 left	–

Characteristics of the participants with amputation and able-bodied participants. Values are mean ± 1 SD.

Table 2
Characteristics of participants with amputation.

Participant	Amputation cause	Years since amputation	Prosthesis ankle	Suspension type
S01	Congenital	28	Ossur Vari-Flex	End-bearing
S02	Congenital	24	OssurVari-Flex	End-bearing
S03	Trauma	4.4	Ossur Pro-Flex	Pin
S04	Trauma	3	Ottobock Sprinter	Suction
S05	Trauma	25	Ossur Cheetah Xplore	Suction
S06	Trauma	2	Freedom Innovations Kinterra	Pin
S07	Cancer	29	Ossur Vari-Flex	Suction

because it matches habitual speed more closely (Malatesta et al., 2017). During the second session, the real-time visual feedback conditions were repeated on the treadmill while metabolic data were collected. Each walking trial lasted five minutes.

Stance times were determined from insole foot switches (B&L Engineering, Santa Ana, CA, USA; collected at 500 Hz) and a custom MATLAB (Math Works, Natick, MA, USA) program. The amount of asymmetry between limb stance times was calculated using an asymmetry index (Dingwell et al., 1996):

$$Asymmetry_a = \frac{Intact\ stance\ time - Prosthetic\ stance\ time}{Intact\ stance\ time + Prosthetic\ stance\ time} \times 100\% \quad (1)$$

$$Asymmetry_c = \frac{Dominant\ stance\ time - Nondominate\ stance\ time}{Dominate\ stance\ time + Nondominant\ stance\ time} \times 100\% \quad (2)$$

$Asymmetry_a$ is the asymmetry index for the participants with an amputation, and $Asymmetry_c$ is the asymmetry index for the able-bodied participants. Real-time visual feedback on stance time asymmetry consisted of a two-stride moving average line graph of the stance time symmetry index with a dashed black target line and ±2.5% bounds with solid red lines (Fig. 1). The participants were oriented to the feedback during the first session before completing the experimental trials by instructing them to walk with more time on one limb over multiple strides, observe the changes to the displayed data, and then walk with more time on the other limb. This guided-exploration time helped participants understand what they needed to do to complete each condition. During pilot testing, we found that a two-stride moving average permitted participants to make consistent adaptations to meet the asymmetry goal without having differences from stride-to-stride displayed that were too large (i.e., no averaging) or too small (i.e., three to four stride average).

The asymmetry feedback conditions were -15% to +15% in 5% increments, with 0% representing symmetric stance times between limbs, and performed in randomized order. Positive values indicated greater stance time on the intact limb for participants with lower limb amputation, and the dominant limb for able-bodied participants. The dominant limb was defined as the limb the participants self-reported to be the limb they preferred to use to kick a ball (van Melick et al., 2017). Negative values indicated greater stance time on the prosthetic limb and non-dominant limb, respectively. Participants with an amputation did not perform the -15% condition because this extreme condition was not consistently attainable during pilot testing. To avoid the effects of fatigue, participants were given five minutes of seated rest after each walking trial. Participants reported their perceived exertion on a scale from 1 to 10 (i.e., 1 was resting and 10 was extremely difficult) during each condition (Borg, 1982). Rating of perceived exertion (RPE) was collected to determine how participants subjectively assessed each condition. A condition may be perceived as difficult due to other factors beyond metabolic cost, such as abnormal joint loading or feeling less stable.

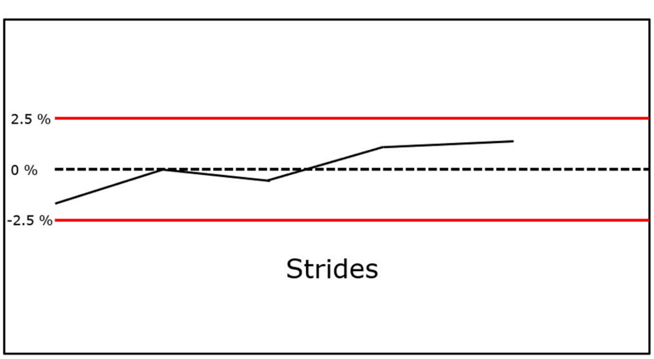

Fig. 1. Representation of Real-time Visual Feedback: Participants had real-time visual feedback of stance time asymmetry with a two-stride moving average line graph, with a dashed target line (0% in this figure) and solid red lines that were +/− 2.5% of the target. The x-axis would shift to keep most recent feedback right of center. The graph was displayed on a monitor at eye-level at the front of the treadmill.

Expired gases were collected via open-circuit spirometry (Parvo Medics, Sandy, UT, USA). Prior to the gait trials, pulmonary gases were collected for five minutes during quiet standing to determine the metabolic cost of standing. The metabolic cost from the last minute of each five-minute walking trial was averaged, representing a time by which all participants had attained metabolic steady state. The gross rate of metabolic energy expenditure was estimated from the approach developed by Brockway (Brockway, 1987) and is based on the amount of oxygen consumed and carbon dioxide produced. Net metabolic energy expenditure during walking was derived by subtracting the energy expenditure during quiet standing from the gross energy expenditure during the walking trials. A normalized net CoT was calculated by dividing the rate of metabolic energy expenditure by both walking speed ($m \cdot s^{-1}$) and body mass (kg) (Ralston, 1958).

The results were evaluated statistically using a combination of binomial hypothesis tests, effect sizes, and 95% confidence intervals (CI) (Cohen, 1988). Preferred stance time asymmetry was compared between groups with an unpaired *t*-test ($\alpha \leq 0.05$), effect size, and CI. The effects of group and stance time asymmetry on CoT were analyzed with a two-way (group x asymmetry) analysis of variance. In the event of a significant *F* value, orthogonal polynomial contrasts were used to determine the mathematical trends describing net CoT versus the amount of asymmetry within each group (Keppel, 1991). The highest-order statistically significant trend (e.g., linear, quadratic, cubic) was then used to estimate the degree of asymmetry corresponding to minimum metabolic cost. A goodness of fit between the experimental values and trend line was determined with an r-squared value. The preferred asymmetry and predicted minimum cost asymmetry within each group were compared with a paired *t*-test, effect size, and 95% CI. The effect sizes were characterized using expanded ranges as defined by Sawilowsky (Sawilowsky, 2009). The effects of group and stance time asymmetry on RPE were analyzed with a two-way (group x asymmetry) analysis of variance, followed by polynomial contrasts. Statistical analyses were performed using R-Studio version 3.2.2 (R-Studio Inc., Boston, MA, USA).

3. Results

Participants with amputation walked with significantly greater stance time asymmetry (4.34 ± 1.09%, 95% CI: 3.54% - 5.15%) compared with able-bodied participants (0.94 ± 2.44%, 95% CI: −0.86% - 2.75%) during the preferred walking condition, with a very large effect size ($P = 0.008$, $d = 1.93$) (Fig. 2, Table 3). This expected finding indicates that among our participants, people with unilateral transtibial amputation spent more time on the intact limb than the prosthetic limb, and the inter-limb asymmetry is greater in our participants with amputation.

CoT was significantly greater in participants with amputation than able-bodied participants ($F = 6.224$, $P = 0.015$), and there was a significant effect of asymmetry on COT ($F = 4.643$, $P < 0.001$). There was not a significant group by asymmetry condition interaction ($F = 0.357$, $P = 0.876$). A quadratic trend best described the relationship between CoT and stance time asymmetry ($F = 25.560$, $P < 0.001$; $R^2_{amputee} = 0.84$, $R^2_{control} = 0.96$) (Fig. 2). The asymmetry that coincided with the predicted minimum metabolic cost (3.23 ± 2.90%, 95% CI: 1.24% - 5.22%) and the preferred asymmetry (4.34 ± 1.09%) for participants with amputation were not significantly different and had a medium effect size ($P = 0.365$, $d = 0.557$). The asymmetry that coincided with the predicted minimum cost (1.81 ± 2.18%, 95% CI: 0.32% - 3.31%) and the preferred asymmetry (0.94 ± 2.44%) for able-bodied participants was also not significantly different and had a small effect size ($p = 0.513$,

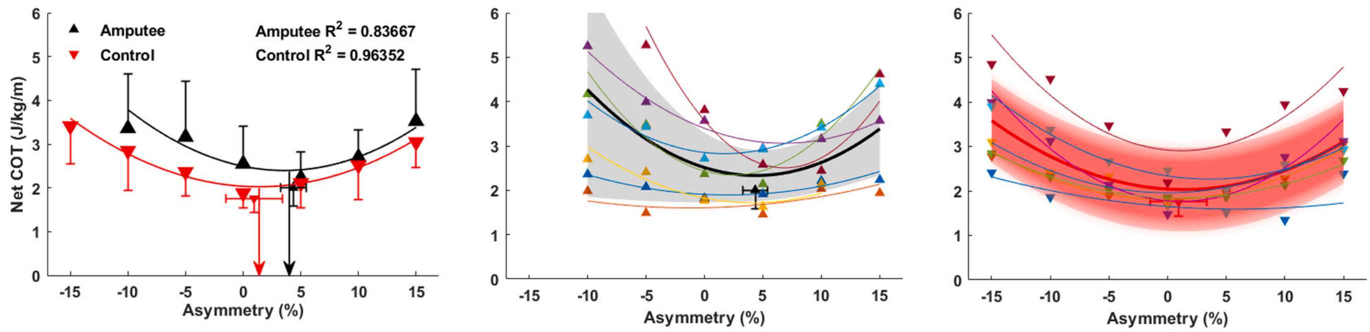

Fig. 2. Group and Individual Net Cost of Transport (CoT): Net CoT for people with (black upward triangles, left and middle figures) and without (red downward triangles, right and middle figures) unilateral lower limb amputation across asymmetry conditions (vertical error bars and shading representing 1 SD), and when walking with preferred patterns (including horizontal error bars representing 1 SD percent asymmetry). Quadratic trend lines of the group averages for people with (black) and without (red) amputation across (a)symmetry conditions. Individual participant trend lines are presented for people with (center pane) and without (right pane) amputation. Asymmetries corresponding to the predicted minimum net CoT are denoted with the downward facing arrows. Preferred and predicted stance time asymmetry was greater (significantly greater for preferred) for people with amputation. Our participants preferred more time on the intact limb, and a similar asymmetry was predicted from the asymmetry that coincided with the minimum CoT.

Table 3
Preferred speed, preferred and predicted asymmetries based on minimum-cost of transport.

Group	Preferred Speed ($m{\cdot}s^{-1}$)	Preferred Asymmetry (%)	Predicted Asymmetry (%)
amputation	1.13 ± 0.22	4.34 ± 1.09	3.23 ± 2.90
able-bodied	1.42 ± 0.12	0.94 ± 2.44	1.81 ± 2.18
p-value	0.021	0.008	0.323
d	1.71	1.93	0.556
95% CI AMP	0.97–1.29	3.54% - 5.15%	1.24% - 5.22%
95% CI ABLE	1.33–1.51	−0.86% - 2.75%	0.32% - 3.31%

Preferred walking speed, preferred asymmetry and predicted asymmetry of the people with amputation and able-bodied participants. Values are mean ± 1 SD.

d = 0.378). The asymmetries corresponding to predicted minimum cost for participants with amputation (3.23 ± 2.90%) and without amputation (1.81 ± 2.18%) were not significantly different and had a medium effect size ($P = 0.323$, d = 0.556) (Fig. 2). When connecting the asymmetries predicted by metabolic cost minima to preferred walking asymmetries, predicted and preferred were not significantly different and the range of asymmetries from the 95% confidence intervals overlap within each group (Table 1). The preferred asymmetries were significantly different, and the 95% CI ranges do not overlap between groups; yet, the predicted asymmetries between groups were not significantly different and the 95% CI did overlap (Table 1).

The effect of stance time asymmetry on RPE was not significantly different between groups ($F = 2.679$, $P = 0.106$), but was significantly different across asymmetry conditions ($F = 2.240$, $P = 0.048$) (Fig. 3). As with COT, a quadratic trend best described the relationship between RPE and stance time asymmetry ($F = 7.914$, $P = 0.006$, $R^2_{amputee} = 0.97$, $R^2_{control} = 0.89$) (Fig. 3).

4. Discussion

The purpose of this study was to determine the effects of stance time asymmetry on the metabolic CoT in people with and without unilateral lower limb amputation. We hypothesized that for preferred gait patterns, participants with unilateral transtibial amputation would exhibit greater stance time on the intact side compared with the prosthetic side, while able-bodied participants would exhibit symmetric stance times. We also hypothesized that the metabolic cost versus inter-limb asymmetry would demonstrate a U-shaped curve for both groups, and the CoT would be least at the preferred stride characteristics for both groups. Our hypotheses were generally supported in that: 1) participants with amputation had greater stance time asymmetry (i.e., more time on intact compared with prosthetic limb) compared with able-bodied participants, 2) a quadratic, U-shaped trend best explained the relationship between CoT and stance time asymmetry for both groups, and 3) the asymmetry that coincided with the predicted minimum metabolic CoT was similar to the preferred asymmetry (Fig. 2, Table 3). However, this latter result should be viewed cautiously, as this study may not have been adequately powered to detect such differences due to the small sample size.

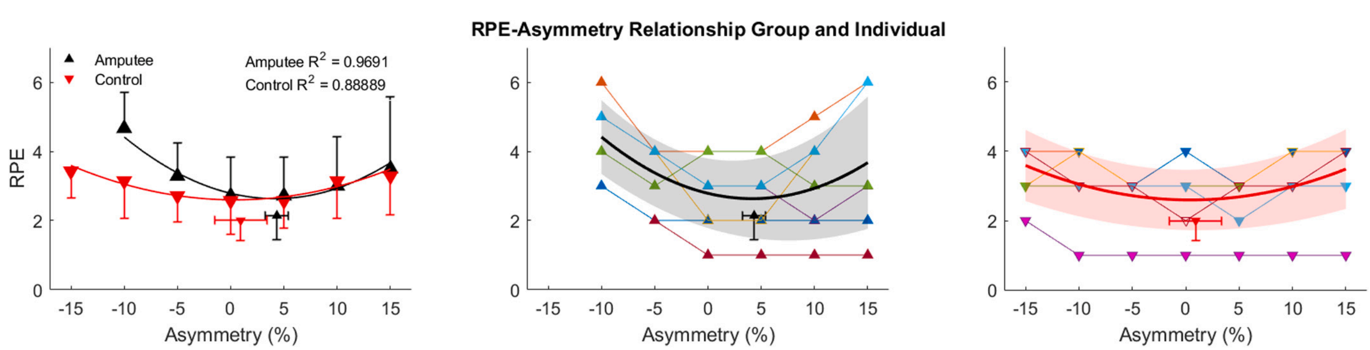

Fig. 3. Rating of Perceived Exertion. people with (upward triangles; left and middle figures) and without (downward triangles; right and middle figures) unilateral lower limb amputation across asymmetry conditions (vertical error bars and shading representing 1 SD), and when walking with preferred patterns (including horizontal error bars representing 1 SD percent asymmetry). Quadratic trend lines for people with (black) and without (red) amputation across (a)symmetry conditions. Our participants reported greater difficulty when walking with more asymmetry in either direction (i.e., more time on the intact or prosthetic limb), and more time on the prosthetic limb was consistently rated as more difficult.

As has been previously shown, our participants with unilateral amputation preferred to walk with more time on the intact limb compared with the prosthetic limb (Isakov et al., 2000; Sadeghi et al., 2000; Sanderson and Martin, 1997), and able-bodied participants preferred more time on the dominant limb versus the non-dominant limb (Vanden-Abeele, 1980). However, the degree of asymmetry was less than 1% for the able-bodied participants and may not be related to limb laterality (Sadeghi et al., 2000). The asymmetries that coincided with the predicted minimum metabolic CoT were greater for participants with amputation than without amputation. This difference had a moderate effect size but was not statistically significant, likely due to the modest sample size, and thus should be interpreted cautiously. Stance time asymmetry may be a compensation for structural asymmetry (i.e., residual limb and prosthesis) and influenced by metabolic cost as evident by the asymmetry predicted from minimum metabolic CoT being similar to the preferred asymmetry (Fig. 2).

Minimum CoT has been shown to be associated with symmetric stride timing in able-bodied individuals, with CoT increasing directly with greater stride asymmetry (Ellis et al., 2013). CoT was lowest for our able-bodied participants near symmetric stance timing, similar to previous findings (Ellis et al., 2013), and was lowest for our participants with amputation when walking with asymmetric stance timing (Fig. 2). The predicted CoT minima were not statistically different between groups (Fig. 2), but the predicted minima trended toward each group's preferred asymmetry and was greater for people with amputation than able-bodied. Two studies (Davis et al., 2004; Mahon et al., 2019) have had people with amputation walk symmetrically while measuring metabolic cost but no studies have had people walk with a large range of inter-limb asymmetry like our study, therefore direct comparisons to the literature cannot be made. Our asymmetry results are similar to the relationship between CoT and walking speed in that people with amputation and able-bodied individuals have greater net CoT when walking slower and faster than preferred speed (Genin et al., 2008; Ralston, 1958), and people with amputation have a greater net CoT than able-bodied (Genin et al., 2008).

We predicted the asymmetries corresponding to minimum CoT using polynomial fits across conditions separated by 5% intervals, which is subject to some uncertainty but demonstrated good fits as indicated by the R^2 values (≥ 0.84) (Fig. 2). More closely spaced intervals (e.g., 2.5%) would permit more precision in predicting minima, but would require more trials which could cause fatigue, and would be unlikely to lead to a fundamentally different result. Focusing on the measured data, the experimental feedback condition with the lowest CoT for participants with amputation was at the +5% condition, which is closest to their preferred asymmetry and the asymmetry predicted to yield the minimum CoT. Similarly, the experimental feedback condition with the lowest CoT for able-bodied participants was at the symmetrical (i.e., 0%) condition, which is closest to their preferred asymmetry and the asymmetry predicted to yield the minimum CoT. Based on the experimental data points (Fig. 2), able-bodied participants had the lowest cost at 0% and a deviation to +5% asymmetry would result in a trivial 0.87% increase in cost. In contrast, participants with amputation had the lowest cost at +5% asymmetry and a deviation to symmetrical walking (0%) would result in a 13.6% increase in cost (Tables S2 and S4). A 13.6% cost associated with restoring symmetric gait may be clinically meaningful, and this finding warrants replication in a broader range of participants. Potential causes for greater CoT associated with symmetric gait for people with amputation could include greater muscle activation (Bae et al., 2007; Isakov et al., 2000) or altered muscle fiber dynamics (Franz and Thelen, 2016). The individual-participant curve fits generally show minima corresponding to asymmetries with more time on the intact limb for individuals with amputation and around 0% for able-bodied individuals (Fig. 2 center panel = amputee, right panel = able-bodied). While our individual-participant predictions of minimum-cost asymmetries are subject to some uncertainty, overall, the results indicate that people with unilateral lower limb amputation may adopt asymmetrical stance times to achieve a reduction in metabolic CoT.

Consistent with the greater CoT, the participants with amputation subjectively reported that the negative (i.e., more time on prosthetic limb) conditions were more difficult than preferred walking, as reflected in the RPE (Fig. 3). The RPE increased more when walking with more time on the prosthetic limb compared to more time on the intact limb (Fig. 3). RPE is a subjective measure that accounts for metabolic cost but also encompasses other factors (e.g., stability, discomfort) that influence perception of difficulty. People with amputation have adapted to spend more time on the intact limb, thus walking with more time on the prosthetic limb may be perceived as harder because it requires more metabolic energy expenditure, as well as other factors such as decreased stability. Spending more time on the prosthesis may not feel as stable and is therefore perceived as more difficult, resulting in more time on the intact limb. Similar to other individuals who present with structural and neurologic asymmetry, such as people with cerebral palsy, people with amputation are most likely balancing multiple criteria simultaneously, such as metabolic cost, stability, and walking symmetry (Jeng et al., 1996). Adequate stability in walking may be why CoT is elevated but does not result in RPE being minimized at a different amount of asymmetry.

Perception of greater difficulty and lack of gait stability with more time on the prosthetic limb may explain why more time is spent on the intact limb, and metabolic energy expenditure may not be the primary reason. A previous study (Russell Esposito et al., 2014) found that people with a unilateral transtibial amputation who were still in the military did not have a statistically different metabolic cost compared with able-bodied participants when walking with preferred characteristics. Our participants were not in the military but were a group of active people who had an amputation from non-vascular causes and had a similar CoT at their preferred asymmetry (Fig. 2 left panel). Even in active and relatively fit people with amputation, like the military and our participants, they walk asymmetrically, potentially for reasons aside from metabolic cost. People with amputation are constrained by the limitations of the prostheses and the connection between the residual limb and socket. The residual limb-socket interface can be uncomfortable and people with amputation may spend more time on the intact limb to reduce loading on the residual limb. Results of a previous simulation study (Handford and Srinivasan, 2016) suggest that more time on the prosthetic may be best for lowering metabolic energy expenditure, but due to current prosthesis limitations, this is not preferred by people with amputation. Therefore, other factors (e.g., gait stability and joint loading) that also influence preferred patterns warrant further investigation.

The number of participants in this study was a limitation that we tried to address by collecting data at two different sites. Our sample size was influenced by time and the sparsity of the target population (Lakens, 2021). In our region, it was difficult to find willing participants who met the inclusion criteria. This is not surprising considering most amputations are due to vascular pathology (Ziegler-Graham et al., 2008), and our age range was limited to people between 16 and 50 years old. However, due to the novelty of having people with amputation walk with a wide range of non-preferred gait patterns, the results of this study provide important, initial insights into how people with amputation prioritize metabolic energy expenditure. Moreover, while the *P*-values reported here should be interpreted cautiously, the effect sizes and confidence intervals provide critical information for planning future studies on gait asymmetry and CoT in people with amputation.

There was an age disparity between groups (Table 1), but the age disparity should not have influenced our conclusions because significant changes with gait usually do not occur until later in life (Judge et al., 1996). While the sample size was limited, the group was homogenous, representing relatively active participants rated at a K3 or K4 activity level, making it possible to directly compare the effect of amputation on the CoT-asymmetry relationship without confounding factors such as advanced age, comorbidities, or substantial differences in mobility.

Even with the small sample size (Cumming, 2014), minimum metabolic cost asymmetry predictions and preferred asymmetries within groups were not different for participants with and without amputation, respectively. Participants walked at their preferred speeds, which were significantly slower for participants with amputation. Preferred walking speed is the most relevant condition for the comparisons presented here; however, it is currently unknown how asymmetry may interact with walking speed and how that might influence the results. Further research is needed in people with transfemoral amputation and amputation from vascular disease to better understand how CoT relates to gait asymmetry in people with amputation.

A common objective of rehabilitation is to restore inter-limb symmetry after an injury (e.g., joint arthroplasty, amputation); yet, after anatomical structures have been altered, symmetric function may not result in optimal performance. Participants with amputation in our study preferred more time on the intact limb compared with the prosthetic limb, while able-bodied participants preferred walking almost symmetrically. In both cases, preferred asymmetry coincided closely with the lowest CoT, therefore we expect that having our participants with amputation walk symmetrically would increase metabolic cost. However, minimizing metabolic cost is likely not the only factor driving the selection of gait patterns (Jeng et al., 1996). Further investigation is needed regarding how asymmetry affects factors such as joint and residual limb loading, smoothness, and stability to better understand how preferred gait patterns emerge after an injury, and if these factors evolve with more time after amputation, aging, and physical fitness. If asymmetrical patterns naturally emerge in people after the initial learning and adaptation phase of prosthesis use, perhaps some degree of gait asymmetry should be expected, and symmetric walking should not be a goal for rehabilitation and prosthesis in people with lower limb amputation. Given the modest sample size and focus on only one performance criterion, metabolic cost, our results should be interpreted cautiously. Nevertheless, our results raise the possibility that asymmetrical gait patterns may represent a beneficial adaptation when using specific types of prostheses and does not represent a problem that should be corrected.

Declaration of Competing Interest

We did not have any conflicts of interest with this study or submission.

Acknowledgements

The study was funded by a University of Massachusetts Amherst Graduate Student Dissertation Award. The funders played no role in the design, conduct, or reporting of this study. We thank Russell Johnson, Jan Stenum, and Jacob Banks for comments and discussion about this manuscript. We thank all our participants for their time and effort.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clinbiomech.2022.105632.

References

Bae, T.S., Choi, K., Hong, D., Mun, M., 2007. Dynamic analysis of above-knee amputee gait. Clin. Biomech. 22 (5), 557–566. https://doi.org/10.1016/j.clinbiomech.2006.12.009.

Borg, G., 1982. Psychophysical bases of perceived exertion. Med. Sci. Sports Exerc. 14 (5), 377–381.

Brockway, J., 1987. Derivation of formulae used to calculate energy expenditure in man. Hum. Nutr. Clin. Nutr. 41 (6), 463–471.

Centers for Medicare and Medicaid Services, 2020. Local Coverage Determination (LCD): Lower Limb Prostheses (L33787). CMS. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=33787&ver=22.

Cohen, J., 1988. tatistical Power Analysis for the Behavioral Sciences, 2nd ed. L. Erlbaum Associates.

Cumming, G., 2014. The new statistics: why and how. Psychol. Sci. 25 (1), 7–29. https://doi.org/10.1177/0956797613504966.

Davis, B.L., Cater, Ortolano M., Richards, K., Redhed, J., Kuznicki, J., Sahgal, V., 2004. Realtime visual feedback diminishes energy consumption of amputee subjects during treadmill locomotion. JPO J Prosthet Orthot 16 (2), 49–54. https://doi.org/10.1097/00008526-200,404,000-00004.

Dingwell, B., Davis, B.L., Frazier, D.M., 1996. Use of an Instrumented Treadmill for Real-Time Gait Symmetry Evaluation and Feedback in Normal and Trans-Tibia1amputee Subjects. Prosthet Orthot Int., pp. 101–110

Ehde, D.M., Czerniecki, J.M., Smith, D.G., et al., 2000. Chronic phantom sensations, phantom pain, residual limb pain, and other regional pain after lower limb amputation. Arch. Phys. Med. Rehabil. 81 (8), 1039–1044. https://doi.org/10.1053/apmr.2000.7583.

Ellis, R.G., Howard, K.C., Kram, R., 2013. The metabolic and mechanical costs of step time asymmetry in walking. Proc. R. Soc. B Biol. Sci. 280 (1756), 20122784. https://doi.org/10.1098/rspb.2012.2784.

Eng, J.J., Winter, D.A., 1995. Kinetic analysis of the lower limbs during walking: What information can be gained from a three-dimensional model? J. Biomech. 28 (6), 753–758. https://doi.org/10.1016/0021-9290(94)00124-M.

Forczek, W., Staszkiewicz, R., 2012. An evaluation of symmetry in the lower limb joints during the able-bodied gait of women and men. J Hum Kinet. 35 (1), 47–57. https://doi.org/10.2478/v10078-012-0078-5.

Franz, J.R., Thelen, D.G., 2016. Imaging and simulation of Achilles tendon dynamics: Implications for walking performance in the elderly. J. Biomech. 49 (9), 1403–1410. https://doi.org/10.1016/j.jbiomech.2016.04.032.

Genin, J.J., Bastien, G.J., Franck, B., Detrembleur, C., Willems, P.A., 2008. Effect of speed on the energy cost of walking in unilateral traumatic lower limb amputees. Eur. J. Appl. Physiol. 103 (6), 655–663. https://doi.org/10.1007/s00421-008-0764-0.

Gundersen, L.A., Valle, D.R., Barr, A.E., Danoff, J.V., Stanhope, S.J., Snyder-Mackler, L., 1989. Bilateral analysis of the knee and ankle during gait: an examination of the relationship between lateral dominance and symmetry. Phys. Ther. 69 (8), 640–650. https://doi.org/10.1093/ptj/69.8.640.

Hak, L., van Dieën, J.H., van der Wurff, P., Houdijk, H., 2014. Stepping asymmetry among Individuals with unilateral transtibial limb loss might be functional in terms of gait stability. Phys. Ther. 94 (10), 1480–1488. https://doi.org/10.2522/ptj.20130431.

Hamill, J., Bates, B., Knutzen, K., 1983. Ground reaction forces symmetry during walking and running. Med. Sci. Sports Exerc. 15 (2), 170.

Handford, M.L., Srinivasan, M., 2016. Robotic lower limb prosthesis design through simultaneous computer optimizations of human and prosthesis costs. Sci. Rep. 7. https://doi.org/10.1038/srep19983. Published online.

Hannah, R., Morrison, J., Chapman, A.E., 1984. Kinematic symmetry of the lower limbs. Arch. Phys. Med. Rehabil. 65 (4), 155–158.

Hewson, A., Dent, S., Sawers, A., 2020. Strength deficits in lower limb prosthesis users: A scoping review. Prosthetics Orthot. Int. 44 (5), 323–340.

Isakov, E., Keren, O., Benjuya, N., 2000. Transtibial amputee gait: Time distance parameters and EMG activity. Prosthetics Orthot. Int. 24 (3), 216–220. https://doi.org/10.1080/03093640008726550.

Jeng, S.F., Holt, K.G., Fetters, L., Certo, C., 1996. Self-optimization of walking in nondisabled children and children with spastic hemiplegic cerebral palsy. J. Mot. Behav. 28 (1), 15–27. https://doi.org/10.1080/00222895.1996.9941729.

Johnson, R.T., Hafer, J.F., Wedge, R.D., Boyer, K.A., 2020. Comparison of measurement protocols to estimate preferred walking speed between sites. Gait Posture 77, 171–174. https://doi.org/10.1016/j.gaitpost.2020.01.007.

Judge, J.O., Ounpuu, S., Davis 3rd., R.B., 1996. Effects of age on the biomechanics and physiology of gait. Clin. Geriatr. Med. 12 (4), 659–678.

Keppel, G., 1991. Design and Analysis: A Researcher's Handbook, , 3rd ed.xiii. Prentice-Hall, Inc, p. 594.

Lakens, D., 2021. Sample size justification. PsyArXiv. https://doi.org/10.31234/osf.io/9d3yf.

Mahon, C.E., Darter, B.J., Dearth, C.L., Hendershot, B.D., 2019. The relationship between gait symmetry and metabolic demand in individuals with unilateral transfemoral amputation: a preliminary study. Mil. Med. 184 (7–8), e281–e287. https://doi.org/10.1093/milmed/usy424.

Malatesta, D., Canepa, M., Menendez, Fernandez A., 2017. The effect of treadmill and overground walking on preferred walking speed and gait kinematics in healthy, physically active older adults. Eur. J. Appl. Physiol. 117 (9), 1833–1843. https://doi.org/10.1007/s00421-017-3672-3.

Pell, J.P., Donnan, P.T., Fowkes, F.G.R., Ruckley, C.V., 1993. Quality of life following lower limb amputation for peripheral arterial disease. Eur. J. Vasc. Surg. 7 (4), 448–451. https://doi.org/10.1016/S0950-821X(05)80265-8.

Ralston, J., 1958. Energy-speed relation and optimal speed during level walking. *Int Z Angew Physiol Einschl Arbeitsphysiologie*. 17 (4), 277–283.

Russell Esposito, E., Rodriguez, K.M., Ràbago, C.A., Wilken, J.M., 2014. Does unilateral transtibial amputation lead to greater metabolic demand during walking? J. Rehabil. Res. Dev. 51 (8), 1287–1296. https://doi.org/10.1682/JRRD.2014.06.0141.

Sadeghi, H., Allard, P., Prince, F., Labelle, H., 2000. Symmetry and limb dominance in able-bodied gait: a review. Gait Posture 12 (1), 34–45. https://doi.org/10.1016/S0966-6362(00)00070-9.

Sadeghi, H., Allard, P., Duhaime, M., 2001. Muscle power compensatory mechanisms in below-knee amputee gait. Am J Phys Med Rehabil. 80 (1), 25–32. https://doi.org/10.1097/00002060-200,101,000-00007.

Sanderson, D.J., Martin, P.E., 1997. Lower extremity kinematic and kinetic adaptations in unilateral below-knee amputees during walking. Gait Posture 6, 126–136.

Sawilowsky, S.S., 2009. New effect size rules of thumb. J. Mod. Appl. Stat. Methods 8 (2), 597–599. https://doi.org/10.22237/jmasm/1257035100.

Seeley, M.K., Umberger, B.R., Shapiro, R., 2008. A test of the functional asymmetry hypothesis in walking. Gait Posture 28 (1), 24–28. https://doi.org/10.1016/j.gaitpost.2007.09.006.

Stenum, J., Choi, J.T., 2020. Step time asymmetry but not step length asymmetry is adapted to optimize energy cost of split-belt treadmill walking. J. Physiol. 598 (18), 4063–4078. https://doi.org/10.1113/JP279195.

van Melick, N., Meddeler, B.M., Hoogeboom, T.J., 2017. Nijhuis-van der Sanden MWG, van Cingel REH. How to determine leg dominance: The agreement between self-reported and observed performance in healthy adults. Macaluso A, ed PLoS One 12 (12). https://doi.org/10.1371/journal.pone.0189876. e0189876.

Vanden-Abeele, J., 1980. Comments on the functional asymmetries of the lower extremities. *Cortex J Devoted Study Nerv Syst Behav*. 16, 325–329. https://doi.org/10.1016/S0010-9452(80)80069-4.

Waters, R.L., Mulroy, S., 1999. The energy expenditure of normal and pathologic gait. Gait Posture 9 (3), 207–231. https://doi.org/10.1016/S0966-6362(99)00009-0.

Waters, R.L., Perry, J., Antonelli, D., Hislop, H., 1976. Energy cost of walking of amputees: the influence of level of amputation. J Bone Jt Surg. 58 (1), 42–46.

Ziegler-Graham, K., MacKenzie, E.J., Ephraim, P.L., Travison, T.G., Brookmeyer, R., 2008. Estimating the prevalence of limb loss in the United States: 2005 to 2050. Arch. Phys. Med. Rehabil. 89 (3), 422–429. https://doi.org/10.1016/j.apmr.2007.11.005.