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Research Article

Assessing Ground Reaction Forces and Degenerative Changes of Sound Limb in Unilateral Lower Extremity Amputees: A Systematic Review

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Abstract

Background: There is a rising number of individuals undergoing lower extremity amputation (LEA) and is associated with increased risk of comorbidities. Osteoarthritis (OA) and Degenerative Joint Disease (DJD) are conditions that cause reduction in an individual's function, independence, and quality of life.

Research Design: A search of multiple databases using terms associated with possible functional declines as evidenced by the International Classification of Functioning, Disability and Health (ICF), followed by assessment of evidence using the PEDro scoring method will be conducted. Multiple reviewers will screen, sort, rate and extract data from articles.

Methods: A computer-aided literature search of PubMed, CINAHL, and Google Scholar was performed to identify studies published beginning in 2009 that investigated factors that contribute to degenerative changes in the contralateral limb of a unilateral LEA.

Results: A total of 21 studies were selected from a total of 56 collected studies. Predictors of osteoarthritis (OA) following lower limb amputation include age, etiology, level of amputation, gender, Body Mass Index (BMI), comorbidity, pain, phantom pain, streng and OA. The impact of ground reaction forces on the sound limb varies between studies. In general, poor gait mechanics and resulting compensatory mechanisms are significant contributors to the occurrence of OA.

Conclusion: There is a dearth of information relating to the prevention of degenerative changes in those with LEA and protocols for pain management and training pre- and post-joint replacement. The incidence of OA in the contralateral limb is still not fully understood. Further investigation into the biomechanics of compensatory mechanisms is necessary to fully understand the functional impact on the population. It is imperative to develop thorough physical therapy protocols for individuals in early onset of OA and those undergoing joint replacement due to degeneration.

Keywords: Lower Extremity Amputation; Unilateral; Osteoarthritis; Degenerative Joint Disease; Ground Reaction Forces; Mobility; Prognosis; Total Arthroplasty; Prosthesis

Introduction

Lower extremity amputations (LEA) have become a rising concern for numerous populations around the world. The leading cause of amputations are dysvascular diseases such as Peripheral Vascular Disease (PVD) which includes Peripheral Arterial Disease (PAD) and Diabetes Mellitus (DM) [1].

The United States (U.S.) is estimated to have a population of 1.6 million persons with limb loss [2]. Approximately 1.3 million (86%) persons have undergone lower extremity amputation. In the U.S. 185,000 amputations occur annually, and the population of persons with limb loss is expected to increase to 3.6 million by 2050 [3].

Persons with LEA face significant physical limitations as a result of amputation surgery. Most traumatic amputees ambulate successfully and use their prostheses for many years. However, gait abnormalities from using their prosthetic legs promote abnormal functions such as increased energy expenditure, decreased walking speed, larger stride width, shorter stride length and increased sit to stand time and forces in the sound side limb. There is evidence that an increase in ground reaction forces contributes to sound side joint osteoarthritis (OA) in the LEA community [4]. These gait abnormalities, demonstrated by persons with LEA walking with a prosthesis, may result in abnormal joint loading that, with extended use, lead to joint pain and degeneration. Previous studies have shown that amputees are at a greater risk than nonamputees for developing OA in the knee and hip of the sound side limb. Also, risk of knee and hip OA increases with a higher amputation level [4].

Traumatic amputations account for 45% of all amputations with a majority of the population being members of the U.S. Armed Forces [5]. The use of the prosthetic or assistive devices may impact body image, vocation and cause other socialization issues for amputees [6]. The alteration of biomechanics can often develop into secondary conditions that impact the mobility and quality of life of those with LEA [6,7].

Most amputees lead active and successful lives post-amputation. However, there is a concern for long-term prosthesis users that includes knee and hip OA, degenerative joint disease (DJD), osteopenia, back pain and other musculoskeletal complications. The use of one or more prostheses over the course of the person's life can lead to degenerative changes that result in total hip arthroplasty (THA) and/or total knee arthroplasty (TKA). Proper fitting and alignment of the prosthesis can equalize force distribution over the residual and intact limbs and decrease the potential for OA [7].

In comparison to the prevalence of OA in the general population, Struyf., *et al.* found a significantly higher prevalence of OA of the intact hip and knee among traumatic lower extremity amputees. Their data demonstrated a 27% prevalence of knee OA, 14% of hip OA, and 10.3% of those with both hip and knee OA of the sound limb [8].

Various factors such as level of amputation, time since amputation, prosthesis type, age, and mobility are hypothesized to, over time, lead to joint pain and degeneration. Grabowski and D'Andrea revealed a greater prevalence of knee OA in the sound limb of individuals with LEA using a passive-elastic prosthesis. These individuals adapted compensatory patterns such as increased dependency of the sound limb, thus resulting in increased vertical forces [9].

Snyder., *et al.* assessed the effects of five prosthetic feet on the vertical force sustained by the sound limb during gait. They identified the type of foot prosthesis used by transtibial amputees may cause an increase in vertical ground reaction force on the sound limb, decreased gait velocity, and compensatory patterns. Snyder., *et al.* hypothesized that transtibial dysvascular amputees employ a decreased ambulatory speed to protect their sound limbs from increased vertical ground reaction forces. The authors suggest that compensatory patterns to decrease the force through the sound limb result in increased loading responses. This is likely due to increase in body weight on the sound limb to 111% that of a nondisabled individual, whereas the residual limb demonstrated near normal vertical forces [10].

Approximately 63% of transfemoral amputees (TFA) exhibited degenerative changes of the knee and hip in the sound limb, compared with 41% of transtibial amputees (TTA) and 21% of matched controls [8,11].

Purpose

This purpose of this study is to determine the current extent of literature regarding degenerative changes in the contralateral limb of a unilateral LEA. Additionally, it aims to identify rehabilitation protocols for the treatment of individuals with unilateral LEA who are pre- or post- arthroplasty on the contralateral limb secondary to degenerative changes. The findings of this study may lead future research in the identification of rehabilitation protocols for those currently experiencing degenerative changes of the sound limb and in preventative measures for those who have recently undergone LEA. In particular, this evidence may result in the future education of the effects of increased load bearing through the sound limb, during gait, on degenerative joint changes.

Methods

A computer-aided systematic literature search was performed using PubMed (from 2008), CINAHL (from 2009), and Google Scholar (from 2009) using the following keywords in the title or abstract.

Search: amput*, ambulat*, unilateral, mobil*, walk*, prognos*, predict*, osteoarthritis, degenerative joint disease, total knee replacement, total knee arthroplasty, total hip replacement, total hip arthroplasty, prosthe*. The search was limited to literature published within the past 10 years. References from identified studies were also examined to extend the search.

Inclusion criteria

- Lower extremity amputation
- Lower limb amputation
- Above knee/transfemoral amputation
- Below knee/transtibial amputation
- Unilateral amputation
- Incidence of DJD, OA, degenerative changes.

The sampling method included meta-analysis, systematic reviews, randomized controlled trials, and case studies. We included all causes of amputation, such as those of vascular disease, congenital, traumatic and cancer.

Exclusion criteria

- Animals
- Upper extremity amputation
- Bilateral amputation
- DJD/OA residual limb
- Pediatric/non-adult cases
- Amputation due to autoimmune or neurological causes
- K0 and K1 level ambulators

Article screening

Articles identified from the initial search of the three databases were compiled and citation tracked to identify further potential articles meeting inclusion criteria. Initial screening consisted of title and abstract review. Duplicate references were eliminated, and articles not meeting relevance standards or inclusion criteria were excluded. The remaining articles were independently assessed for content, quality and critical appraisal.

Data were extracted and categorized according to study population (TFA, TTA, LEA nondifferentiated), compensatory mechanisms (gait mechanics, musculoskeletal patterns, exercise habits) and type of degenerative joint disease (OA, hip OA, knee OA, spinal degeneration).

Critical Appraisal: Analysis of each article was conducted using the Physiotherapy Evidence Database (PEDro) scale. This approach evaluates internal validity of selected papers in order determine their use in guiding clinical decision-making. Articles were scored on a scale of 0-10 where points were only awarded when a criterion was clearly satisfied. The criteria evaluated were the following

- Eligibility criteria were specified
- Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)
- Allocation was concealed
- The groups were similar at baseline regarding the most important prognostic indicator
- There was blinding of all subject
- There was blinding of all therapists who administered the therapy
- There was blinding of all assessors who measured at least one key outcome
- Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups

- All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by "intention to treat"
- The results of between-group statistical comparisons are reported for at least one key outcome
- The study provides both point measures and measures of variability for at least one key outcome

Articles scoring 3 or less are considered poor quality, scores of 4 to 6 are deemed medium quality, and those scoring 7 or above are regarded as high quality.

Similar to Sansam., *et al.* [12] a standardized checklist was used to extract each report's methods, population, outcome measures, and predictive factors. Additionally, the UK National Service Framework for Long-term Conditions to assess the quality of each study as it allows assessment of quality in non-randomized cohort studies. Each article was scored by two researchers without knowledge of the others scores to prevent internal bias from occurring. The principal investigator analyzed these scores and calculated the mean. Triangulation of data was conducted by using multiple investigators to provide numerous findings, analyses, and conclusions.

Limitations

We expected there to be a dearth of information relating to the prevention of degenerative changes in those with LEA and protocols for pain management and training pre- and post-joint replacement. As a result, interpretation of the results should be done with caution as generalizations can be difficult to make with few sources.

Delimitations

This study did not include articles published prior to 2008. The reason for this is our research is meant to evaluate the current body of knowledge that includes new prosthetic componentry and technology.

Results

Number of identified studies

A total of 141 studies were identified through electronic search. Of these, 85 were eliminated due to duplication leaving a total of 56. Of these 56 articles, 12 were eliminated when titles and abstracts were screened, leaving a total of 26. Lastly, 4 were excluded when the full article was reviewed. This left 21 articles for full evaluation.

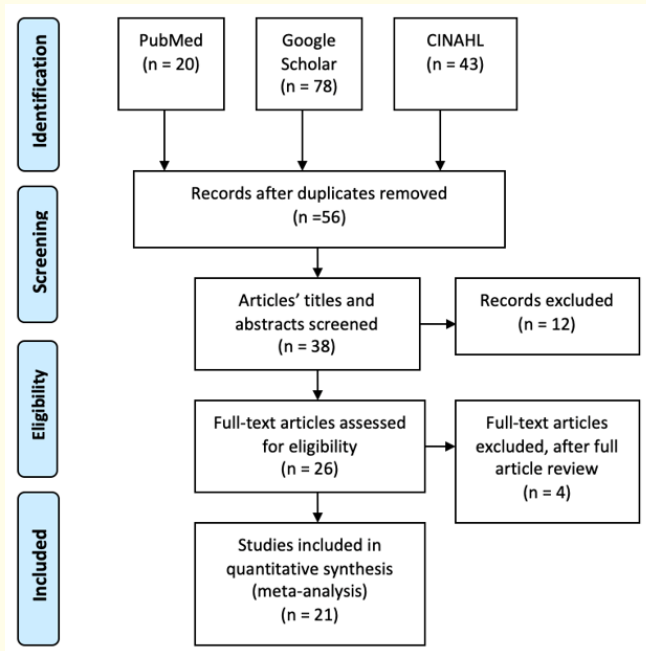

Figure 1: Prisma Flow Diagram.

Description of sample

Conclusions from this study are drawn from 21 systematically reviewed studies of high and medium quality with a total of 20,318 subjects. There were some raw data that were inconsistent or incomplete. For example, mean height and/or weight were not reported for nine of the studies. However, four of these studies were narrative/systematic reviews (NR/SR) or simulation studies which did not rely on such information for validity.

In this systematic review there were two sub-groups: an experimental group of LEAs (TTA, TFA) and a control group of non-amputees. For age and etiology of amputation data, of those students sufficiently reporting this information, LEA had the following distribution: 97.6% trauma, 1.3% vascular, 0.8% cancer and 0.3% infection. Within this current review's experimental group of persons with LEAs, the subjects described had a mean age of 42.1y with a range of 27y to 63.5y.

Author	Etiology	Total n	Outcome Measures	Conclusions	Quality
Amanatullah., *et al.* (2015)	NR	35	Time from LEA to THA	The mean time from lower extremity amputation to total hip arthroplasty was 12.2 ± 12.8 years after a contralateral amputation and 5.4 ± 6.0 years after an ipsilateral amputation. The mean time to total hip arthroplasty was 15.6 ± 15.4 years after an above knee amputation and 6.4 ± 6.1 years after a below knee amputation. Patients with an ipsilateral amputation or a below knee amputation progress to total hip arthroplasty faster than those with a contralateral amputation or an above knee amputation, respectively.	High
Caldwell., *et al.* (2019)	NR	25	Exercise habits and their relation to ACSM exercise guidelines and any contralateral (intact)-limb knee injuries	Sixty-eight percent met the recommended ACSM guidelines for cardiorespiratory (CR) exercise before amputation and 48% of individuals met CR guidelines after amputation, and, of those, 41.7% reported sustaining intact-limb knee injuries. Respondents who met CR guidelines were at significantly higher risk of knee injury. Also, those engaged in greater than moderate intensity CR exercise had significantly higher rates of intact knee injury compared with those exercising at low or moderate intensities.	Medium
Chang., *et al.* (2011)	Trauma	33	Hip and knee adduction moments in the coronal plane of TFAs	Intact knee adduction moment of amputees increased by 32% compared to the prosthetic side and more than twice compared to the control group at terminal stance. But the bilateral hip adduction moment was decreased compared to the control group. Therefore, it is expected that the higher knee adduction moment on the intact side may cause secondary complication to unilateral transfemoral amputees, but it is difficult to make connection with hip osteoarthritis.	Medium
Cutti., *et al.* (2018)	Trauma	70	Reference values for gait temporal and loading symmetry	Percentagewise, transfemoral amputees tend to overload the sound side with increased impulse, while TT with increased peak GRF. This might be suggestive of two separate mechanisms for the onset of knee osteoarthritis.	Medium
Donias., *et al.* (2018)	Trauma	214	OA prevalence and risk factors	14 (7%) had documented new contralateral knee pain. Of those 14, only 3 (21%) underwent surgical intervention, and 6 (43%) had radiographic evidence of knee OA on radiographs. All 3 of the service members who underwent surgical intervention had radiographic evidence of knee OA. Two of the ser- vice members who underwent surgical intervention sustained above-the- knee amputations, while the other sustained a below-the-knee amputation	High
Farrokhi., *et al.* (2016)	Trauma	NR	Compile and present evidence regarding prevalence of nonsystemic and potentially modifiable knee OA risk factors	Evidence does suggest an elevated prevalence of the nonsystemic knee OA risk factors in young military Service Members with unilateral lower limb amputation. Available scientific evidence to date supports that young military Service Members with traumatic, unilateral lower limb amputations may be at increased risk for developing knee OA compared to nonamputees.	N/A

Fey and Neptune (2012)	11 trauma, 3 vascular	24	Loading rate (impulse) between intact amputee knee and control knee at various walking speeds	No difference in joint impulse forces between the intact knees and the control knees. Knee impulse force in the intact limb was greater than in the residual limb at higher walking speeds.	Medium
Gailey., *et al.* (2008)	NR	NR	Secondary physical conditions associated with LLA and long-term prosthesis use	An alteration of biomechanics occurs with the use of one or more prostheses. Individuals with amputation tend to favor their intact limb and stress it more during mobility and daily activities. This tendency can cause degenerative changes of the intact limb, such as osteoarthritis of the knee and/ or hip joints.	N/A
Karimi., *et al.* (2017)	2 trauma, 4 tumor, 1 bone abscess	17	Joint contact forces (JCF) calculated by a musculoskeletal model in the intact side	GRF in the sound side of subjects with BK did not differ substantially from those in the RG group which may be due to the type of prosthetic feet (ESAR) used in the study. However, slightly increased hip and knee joint moments were found within the BK group.	Medium
Kesikburun., *et al.* (2015)	Trauma	83	Femoral articular cartilage thickness	Amputees had significantly more cartilage thinning in intact knee (specifically LFCCT about .18mm thinner, but did not fully match OA criteria to be considered higher risk)	High
Koelewijn and van den Bogert (2016)	N/A	N/A	A Pareto front constructed to study and analyze the effect of increasing joint moment symmetry	When the optimization placed more weight on moment symmetry, walking effort increased and kinematics became less normal, confirming the hypothesis. TTA gait improved with a moderate increase in joint moment symmetry. At a small cost of effort and abnormal kinematics, the peak hip extension moment in the intact leg was decreased significantly, and so was the joint contact force in the knee and hip. Additional symmetry required a significant increase in walking effort and the joint contact forces in both hips became significantly higher than in able-bodied gait.	Medium
Lloyd., *et al.* (2010)	4 Trauma, 2 vascular, 1 cancer, 1 infection	16	Three gait variables related to OA risk: knee external adduction moment, knee adduction moment load rate, and vertical ground reaction force load rate	Four of the six variables were more asymmetrical in the amputee group than the control group. Knee extension strength asymmetry was significantly related to knee adduction moment load rate asymmetry, and knee flexion strength asymmetry was moderately related to the vertical ground reaction force on the intact limb. Results suggest that strength asymmetry in unilateral trans-tibial amputees has a moderate relationship with osteoarthritis risk.	Medium
Miller., *et al.* (2017)	Trauma	20	Joint moments and medial knee JCF	Peak JCF and maximum JCF loading rate were significantly greater in limb loss (184% BW, 2,469% BW/s) vs. controls (157% BW, 1,985% BW/s). Results support a ‘‘mechanical overloading’’ hypothesis for the risk of developing knee OA in the intact limb of limb loss subjects.	Medium

Norvell., *et al.* (2005)	Trauma	854	OA prevalence and risk factors	Overall prevalence of symptomatic knee OA of 16.1% and 11.7% for amputees and nonamputees, respectively. Prevalence ratio of OA for knee of intact limb was 1.4 for transtibial amputees and 1.3 for transfemoral amputees.	Medium
Pruziner., *et al.* (2014)	Trauma	109	Difference in peak GRF between groups based on time with prosthesis (6 mo. or less vs 2 yrs. or more), TT or TF amputee, amputee vs control group	Larger intact limb loading in individuals with traumatic transtibial loss were only noted early in the rehabilitation process, but these variables were present early and late in the rehabilitation process for those with transfemoral limb loss. Such evidence suggests an increased risk for early onset and progression of arthritis in the intact limb, especially in those with transfemoral limb loss.	Medium
Russell Esposito., *et al.* (2015)	Trauma	28	OA prevalence and risk factors	No significant differences in peak GRF between TFA group and control group at three varied walking speeds. Peak loading rates (N/s) were significantly higher in TFA group vs control group. Loading rate and influence on OA prevalence/risk factors needs further study.	High
Russell Esposito and Wilken (2014)	Trauma	20	OA biomechanical risk factors, comparing powered vs. non powered prostheses	The powered prosthesis did not decrease the sound limb's peak adduction moment or its impulse, but did decrease the external flexor moment, peak vertical force and loading rate as speed increased. The powered prosthesis decreased the loading rate from controls. The sound limb did not display a significantly greater risk for knee osteoarthritis than the intact limb or than controls in either device.	Medium
Sansam., *et al.* (2009)	Varied	9,095	Predictors of good walking ability	Predictors of good walking ability following lower limb amputation include cognition, fitness, ability to stand on one leg, independence in activities of daily living and pre-operative mobility. In general, unilateral and distal amputation levels, and younger age were predictive of better walking ability.	N/A
Silverman and Neptune (2014)	11 Traumatic 3 Vascular	24	Compare knee joint contact forces and the muscles contributing to these forces between amputees and non-amputees during walking using forward dynamics simulations	Peak GRF higher in TT amputees of 6 mo. or less compared to control. Both experienced and inexperienced TF amputee groups had higher peak GRF than controls. Impulse or loading rate was higher for TF amputee groups compared to controls.	Medium
Struyf., *et al.* (2009)	Trauma	237	OA prevalence and risk factors	OA prevalence 27% of amputee group and less than 2% of general population.	Medium
Welke., *et al.* (2019)	NR	9,414	Prevalence of six selected diagnoses regarding musculoskeletal disorders	A significantly decreased prevalence of OA and specific disorders of the spine in transfemoral amputees compared to a control group was found. The amputees with OA are significantly younger than patients with OA in the control group.	High

Table 1: Summary of Studies included in Literature Research.

Setting, Study Designs and Independent Variables

Due to the variation in study design, comparison of the results was difficult. The time at which information was collected differed between studies, with some recorded pre-amputation or immediately post-amputation and others retrieved retrospectively. Seven (33%) were retrospective cohort studies, gathering data from hospital records or patient recall. The remainder were cross-sectional experimental studies (29%), cohort studies (19%), NR/SRs (14%) or simulation studies (5%). No studies used a prospective cohort design. The majority of studies compared amputees to non-amputees/healthy individuals and examined more than one factor and its potential to contribute to DJD. Simple tests of association such as $\chi 2$ or paired t-tests were commonly employed.

Subject selection varied; some studies only examined certain amputation levels or etiology, whereas others included all subjects who had gone any type of lower limb amputation. Subjects were studied in varied organizations including prosthetic rehabilitation programs, Veteran's Administration hospitals and university hospitals. In addition to these, data was also collected from hospital settings, army hospitals, and university laboratories. The predominant independent variable was type of LEA (TTA, TFA).

Many studies used a three-dimensional motion analysis system to approximate contact forces, moments, and impulses in real time. Some studies specified prosthetic componentry and discussed their potential influence on the results of the study. There was great diversity in the measures used to approximate incidence of OA, ranging from validated measures to patient reported severity of pain and symptomatic factors.

Discussion

The purpose of this study was to determine the current body of knowledge pertaining to degenerative changes in the contralateral limb of a person with unilateral LEA. This systematic review aims to interpret the results of this body of knowledge, dating back ten years, as a means of educating on the effects of increased load bearing through the sound limb during gait. We hypothesized that there would be dearth of information on degenerative changes of the sound limb, its contributory factors and preventative measures. This hypothesis was confirmed. Many of the studies examined were contradictory in nature which implies the etiology of OA remains elusive. It is imperative that future prospective studies are performed to validate the findings of these studies and determine adequate changes to rehabilitation protocols to ensure persons with LEA's quality of life remains uncompromised.

	Cause of Amputation (Etiology)	Amputation Level	Age	Gender (Sex)	BMI-Height, Weight	Comorbidities	Pain	Phantom Pain	Strength	Ability to Stand on 1 Leg (SLS)	Osteoarthritis (OA)
Amanatullah., *et al.* (2015)	1	1	1	1	1						1
Caldwell., *et al.* (2019)	1	1	1	1	1		1		1		1
Chang., *et al.* (2011)	1	1	1		1		1		1	1	1
Cutti., *et al.* (2018)	1	1	1		1	1				1	1
Donias., *et al.* (2018)	1	1	1	1			1				1
Farrokhi., *et al.* (2016)	1	1	1		1	1	1		1	1	1
Fey & Neptune (2012)	1	1	1	1	1				1		1
Gailey., *et al.* (2008)	1	1	1	1	1	1	1		1	1	1
Karimi., *et al.* (2017)	1	1	1	1	1		1				1
Kesikburun., *et al.* (2015)	1	1	1	1	1		1			1	1
Koelewijn & van den Bogert (2016)		1									
Lloyd., *et al.* (2010)	1	1	1	1	1				1		1
Miller., *et al.* (2017)	1	1	1		1						
Norvell., *et al.* (2005)	1	1	1		1		1	1			1
Pruziner., *et al.* (2014)	1	1	1	1	1	1	1				1
Russell Esposito., *et al.* (2015)	1	1	1		1						
Russell Esposito & Wilken (2014)	1	1	1	1	1				1		
Sansam., *et al.* (2009)	1	1	1	1	1	1	1	1		1	
Silverman & Neptune (2014)	1	1	1		1				1		
Struyf., *et al.* (2009)	1	1	1	1	1		1	1			1
Welke., *et al.* (2019)		1	1	1		1	1				1
Total	19	21	20	13	18	6	12	3	8	6	15

Table 2: Predictive Factors Investigated.

Osteoarthritis

Osteoarthritis is primarily a noninflammatory disorder of movable joints that is characterized by an imbalance between the synthesis and degradation of the articular cartilage, leading to the classic pathological changes of wearing away and destruction of cartilage [6,7]. The bone in an osteoarthritic joint is less able to absorb the forces, causing them to be transmitted back to the cartilage [6]. In an able-bodied population, the majority will begin to see some evidence of cartilage deterioration by age 40. Local biomechanical factors are obesity, joint deformity, malalignment, trauma (intra-articular fractures), meniscus pathology, ligament injury, muscular weakness, ligament laxity, proprioceptive problems, overloading by risk sports, and occupations [13].

Although the etiology of OA remains largely unknown, it has been attributed to increased and/or atypical joint loading [14] and tends to develop within 10 years of a major joint related injury [15]. After injury, there is a tendency to favor the uninjured (sound) side which increases the magnitude and duration of mechanical loads borne during ambulation. This is confounded particularly after LEA. Ambulation with a lower limb prosthesis alters gait mechanics and some of these alterations are consistent with the biomechanical variables that have been associated with arthritis, including larger and more prolonged forces transmitted through the intact limb [16]. If people with amputation do not learn to properly use their prosthesis or bear weight equally between the prosthetic and intact limbs, they may further compromise the integrity of their intact limb [6]. Multiple studies have shown OA to be predominant in the contralateral limb when compared to the residual limb of persons with LEA [4,6-8,14,16-18,22]. Norvel., *et al.* identified that among transtibial amputees, the knee of the amputated limb was at a significantly reduced risk of knee pain and symptomatic knee OA, whereas the knee of the intact limb was at greater risk of knee pain, especially among transfemoral amputees, compared with the corresponding knee of a nonamputee [4].

Past research has shown that persons with traumatic LEAs in general are at a relatively high risk for developing OA, with the prevalence greater in people with TFA than TTA [6]. In a study of persons with traumatic LEAs, Struyf., *et al.* [8] found a prevalence of 14% hip and 27% knee OA, whereas an age adjusted general population showed prevalence of 1.1% and 1.5% respectively. In a Dutch study, the prevalence of knee OA was 27% among traumatic leg amputees, which was much higher than in the general population (1.6%) [17]. Intact-limb knee pain seems to occur with a higher prevalence in individuals with traumatic LEAs when compared with the general population (40.3% vs 20.2%) [18].

Symptoms of OA often precede the appearance of radiographic abnormalities, implying the existence of a potentially detectable "prodromal phase" in the transition from pre-radiographic to radiographic stages of OA [7]. Even so, one study found that 50% of the subject in the general population with radiographic knee OA did not have pain [4]. Conventional radiographs are known to be insensitive to detecting early stages of OA which is particularly problematic for persons with LEA since long-term prosthesis use has been associated with a greater prevalence of OA [7,18].

In the study conducted by Norvell., *et al.* [4], subjects reported that their osteoarthritic knee pain interfered significantly with their recreation, social, and family activities, keeping them from participating for more than 30 days. Long periods of inactivity are common among individuals with LEAs. Consequently, weight gain is normal and increases the forces placed on weight bearing joints. Prosthetic componentry, alignment and fit all play an important role in equalizing force distribution across both the residual and intact limbs. However, problems in these areas are common and as a result, prosthesis compliance decreases. These issues can be fixed through routine checkups. Prosthetic limbs typically need to be updated every 3 years, however, this is not possible for all amputees as accessibility and cost can deter individuals from receiving the treatment they need [4].

Hip Osteoarthritis

Previous studies have shown that persons with LEA have a 6-fold higher risk of developing radiographic osteoarthritis in the ipsilateral hip and a 2-fold risk of developing radiographic osteoarthritis in contralateral hip. After a TFA, there is a 3-fold increased risk of developing radiographic osteoarthritis in the ipsilateral hip when compared with a TTA [19] Amanatullah., *et al.* [19] found that 55% of the ipsilateral hips and 18% of the contralateral hips studied had OA. Eighty-eight percent of the persons with LEA had radiographic evidence of osteoporosis in the ipsilateral limb after TTA and patients with an ipsilateral TFA had lower bone mineral densities than those with an ipsilateral TTA [19] This has been directly linked to higher metabolic demand for ambulation of a TFA. Chang., *et al.* [20] found that hip OA has been associated with larger hip abduction moments and increased bone mineral density (BMD) in the femoral neck than healthy controls. Amanatullah., *et al.* additionally found that patients with an ipsilateral amputation or a TTA progress to THA faster than those with a contralateral amputation or TFA, respectively. Ipsilateral hip degeneration is often increased as a result of the hip flexors, extensors, and external rotators compensating for the lack of ankle function during gait. Progression to THA after a TTA was statistically shorter (6.4 ± 6.1 years) than the mean after TFA (15.6 ± 15.4 years) for either hip. The mean time progression after contralateral LEA was more than double (12.2 ± 12.8 years) the time to THA after an ipsilateral LEA (5.4 ± 6.0 years) [19].

Knee Pain and Osteoarthritis

For individuals with LEAs, the prevalence of OA in their intact limb is up to 10 times higher than in able-bodied individuals and onset ages are younger [15]. Recent reviews have indicated a rising incidence of idiopathic knee OA in service members with limb loss and, in general, veterans have a prevalence of knee OA that is 30%–90% greater in the intact limb compared to veterans without limb loss [7,4,21]. Norvell., *et al.* reported that the prevalence of knee pain among amputees and nonamputees was 40.3% and 20.2%, respectively [4]. The authors also determined that the prevalence of knee pain among TFAs was 50% and 36.4% among TTAs [4]. Symptomatic knee OA prevalence among amputees and nonamputees was 16.1% and 11.7%, respectively [4]. The age and average weight-adjusted prevalence ratio of knee pain among amputees, compared with nonamputees, was 2.2 and the identically adjusted prevalence ratio of symptomatic knee OA was 1.5 [4].

In a study of military service members with unilateral LEA, Donias., *et al.* found 14 (7%) had documented new contralateral knee pain. Of those 14, only three (21%) underwent surgical intervention, while six (43%) had evidence of knee OA on their radiographs. All three of the service members who underwent surgical intervention had radiographic evidence of knee OA [17]. Two of the service members who underwent surgical intervention sustained TFAs, while the other sustained a TTA [17]. Despite improving care and rehabilitation, only 13% of all service members with an amputation are able to return to active duty status, and only 2% are able to return to their original occupation [17].

Gait mechanics and compensatory measures

The vast majority of people with amputation who use a prosthesis walk with at least one gait deviation as a result of improper prosthetic fit or alignment, lack of proper gait training, development of poor habits, or compensation for a secondary physical limitation [6]. Sansam., *et al.* stated that the majority of studies reported better walking ability, longer walking distances and greater domestic activity levels after distal and unilateral amputations compared with more proximal or bilateral amputations [12]. Regardless, when looking at gait temporal and loading parameters, persons with LEA tend to walk asymmetrically with more time spent and load exerted on the intact limb [22]. Amputees with a higher mobility grade tend to load their sound limb more extensively during activities of daily living as well as to relieve the residual side [8,21].

A common gait compensation of people with amputation is moving the intact limb toward midline while slightly increasing the external rotation of the lower limb. This posture, combined with increased stance time on the intact limb, may be used to improve medial/lateral stability [6]. Gait characteristics highly dependent on the intact limb tend to induce secondary disorders and may lead to degenerative arthritis at weight-bearing joints [20].

Unilateral amputees commonly walk using passive prosthetic feet on their residual llimb, which cannot perform net positive work. This results in compensations from other muscles to provide body support and propulsion. Differences created in walking mechanics as walking speed increases may influence the joint loads that develop in amputees [23]. Typically, larger impulses to the intact limb result from insufficient power in the trailing prosthetic limb for lifting and propelling the body's center of mass [16]. This reduced prosthetic limb push-off power leads to increased effort of the intact limb to maintain walking balance [24]. Increased net joint moments and power output of the intact limb result in adaptation mechanisms that affect the ankle, knee, and hip of the intact limb [6].

Temporal and loading asymmetries are associated with several comorbidities: increased falls, OA of the sound limb, osteoporosis of the contralateral limb and back pain [22]. Temporal asymmetry is typically measured based on step or stance duration; loading asymmetry based the magnitude of the first peak of the vertical GRF, and the impulse of GRF [22-26]. In their systematic review, Gailey., *et al.* [6] reported that people with unilateral amputation have up to 23% force asymmetry depending on the type of prosthesis, while people without amputation have < 10% force asymmetry. Pruziner., *et al.* believe peak vertical GRF may not be as important to onset and progression of arthritis as the rate at which that load is applied [16]. Lloyd., *et al.* found that knee muscle strength asymmetry, specifically in the sagittal plane, was most closely related to loading rates, which, in their study, had a moderate relationship with OA risk [25]. Presently, there are no longitudinal studies investigating baseline joint loading and the initiation of knee OA in the limb loss population [21].

Various biomechanical gait studies have closely examined joint contact forces in an attempt to identify which contribute more substantially to the onset and progression of OA. Karimi., *et al.* [27] defined joint contact force as the combination of all forces applied on a joint while walking including ground reaction force, muscle force, ligament and surrounding tissue forces of a joint. Peak contact forces have routinely been greater in limb loss groups than matched controls [7,16,21]. Larger knee adduction moments (KAM) have been found to have a significant relationship with the presence and severity of knee OA [15,16,20,25] Farrokhi., *et al.* [7] reported that elevated peak KAM during walking is strongly associated with severity of medial compartment knee OA. Additionally, internal KAM was shown by Chang., *et al.* [20] to reflect the force distribution at the knee joint, where larger internal KAMs were associated with greater loads on the medial knee compartment.

Peak external knee adduction moment (EKAM) has been the most frequently used surrogate measure for medial knee joint loading relating to OA and multiple studies have shown that amputees have larger EKAMs [7,17,26,28] Peak EKAM values not normalized to body mass are a more sensitive indicator of knee OA progression than normalized values, as they represent the magnitude of the load [15]. In conjunction with peak EKAM, its angular impulse can assess joint loading across the gait cycle [26]. The external knee flexor moment (EKFM) is related to the overall load on the knee and large EKFMs have been shown to increase the frontal plane moment. EKFM has a major influence on the shape, magnitude, and medial/lateral ratio of joint contact forces, and should be considered when assessing joint loading in gait [29]. EKFMs represent the overall load on the knee and large EKFMs are related to greater EKAMs [15].

Transfemoral mechanics

Individuals with TFA tend to become increasingly sedentary in the years following amputation [15] and less than 30% of TFAs achieve independent mobility outside of the home environment [8]. As previously discussed, the absence of mechanical loading in the limb tends to lead to changes in articular cartilage. In the initial stages of gait training, all amputees favor their sound limb and overload it, as they are unable to fully trust their prosthesis. Morgenroth., *et al*. [28] found that the KAM peak, impulse, and loading rate were all significantly correlated with the degree of knee structural abnormality present in the intact limb of middle-aged adults (mean age 56 years) with unilateral TFAs. However, studies examining the biomechanics of TFAs during gait are not always in agreement, alluding to the elusiveness of degenerative diseases.

In the study conducted by Chang., *et al.* [20] the step length ratio of TFAs during level walking showed more gait asymmetries than the control group. Transfemoral amputee's step width (18.27 ± 3.17cm) was about 2-fold greater than healthy persons' (9.84 ± 2.38cm). The joint moment of experimental group was larger than that of the control group, in spite of the slower gait speed compared to matched controls. This may be indicative of overloading of the sound side knee joint which results from the observed loading asymmetry. Chang., *et al.* [20] also noted that the ankle power in sound limb (1.23 ± 0.62W/kg) was 8-folder greater than that in affected limb (0.15 ± 0.11W/kg) at terminal stance. This result implies the intact knee joint of TFAs easily tends to be exposed to excessive loads in the course of walking forward at terminal stance.

Chang and co-workers found that the intact KAM of TFA's increased by 32% compared to the prosthetic side and more than twice compared to the control group at terminal stance [20]. The peak value of the intact KAM moment was 0.41Nm/kg at terminal stance, with the matched control group having approximately 0.19Nm/kg. The most relevant finding of Chang., *et al.* [20] study is that the peak value of the intact hip adduction moment (HAM) was larger than that of prosthetic side but was 9% smaller than control group (0.67Nm/kg vs 0.73Nm/kg). Additionally, the peak HAM appeared in the terminal stance, which is contrary to previous studies findings. At loading response, there was no significant difference in HAM within the TFA group, however, the intact limb had a 21% smaller peak value than the control [20]. At terminal stance, HAM of the intact limb was 31% larger than HAM of the prosthetic side in TFAs and 9% smaller than that of the control group [20] Higher KAM on the intact side may predispose TFAs to comorbidities, but the peak HAM results of their study were not indicative of a correlation to hip OA.

Cutti., *et al.* [22] examined three populations in their study; TFAs using mechanical knees (TFM), TFAs using microprocessor knees (TFC) and TTAs. They examined impulse symmetry and found that 25% of TFCs and 43% of TTAs had a higher impulse on the prosthetic side. If only considering impulse symmetry, 100% of TFM's overload the sound side. If only looking at first peak symmetry, 41% of TFAs load more on the sound side. The first peak symmetry results showed 59% of TFAs and 30% of TTAs loaded more the prosthetic side. In general, all TFAs spent more time on the sound side: TFM's have the highest asymmetry (median asymmetry of 22%), which is twofold the TFC's (11%), and 16 times that of TTA's [22] Previous studies have attributed this force distribution to the greater ability of the sound limb to advance step and maintain balance until the prosthesis can sustain the body's weight [30] Hof., *et al.* [31] explained this as the "extrapolated center of mass" adaptation that TFAs adopt in order to gain the stability lost to the amputated ankle.

Pruziner., *et al.* [16] investigated vertical GRFs and found that intact limb mean and peak vertical GRF loading rates were 40-50% larger in subjects with transfemoral limb loss with less than 6 months and greater than 2 years of experience ambulating with a prosthesis versus control subjects. Similarly, intact limb vertical GRF impulses were also larger among TFA subjects versus control subjects [16] The larger GRF impulses occurred at both early and late time points in the sound side gait cycle versus control subjects [16]. These increased vertical ground reaction force impulses could be attributed to longer stance times and increased loading rates [16]. On the contrary, Pruziner and colleagues found that, in calculating peak EKAM, TFAs did not experience greater medial compartment knee joint loads than the control group at self-selected walking velocities [16].

Results from a study conducted by Russell Esposito., *et al.* corroborated these findings [26]. The authors found that individuals with TFA did not demonstrate biomechanical risk factors for high medial compartment knee joint loads, but the increased loading rates could place the sound knee at greater risk for cartilage or other tissue damage, even if not localized to the medial compartment [15]. Peak GFR force was larger and maximal loading rates (normalized and nonnormalized) were significantly greater (50-60%) in the TFA group than control across all walking velocities. Loading rates, however, were not normalized BMI. Normalized peak EKAM and EKAM impulses were significantly lower in TFAs (25.7%) than control (27.1%) across all velocities. As an explanation for their results, Russell Esposito., *et al.* [15] suggested that gait characteristics such as increased step width and frontal plane trunk lean can redirect and reduce peak values of both EKAM and vertical GRF.

Transtibial mechanics

Transtibial amputee's typically employ compensatory mechanisms due to limitations in ankle kinematics resulting from the selected prosthetic ankle joint [27]. The lack of power generation may increase the loads in the joints of the sound side [27]. Norvell., *et al.* [4] discovered that the knee of a TTA is 5 times less likely to be painful than the corresponding knee of a nonamputee. The authors suggested this connotes a compensatory mechanism where TTA's shift most of their weight away from the prosthesis and to the intact limb instead [4]. While some studies have shown that subjects with TTA are at an increased risk of secondary complications in their intact limbs, others have noted that TTAs do not consistently exhibit risk factors for knee OA in their sound limb [15,20,25-27].

Cutti., *et al.* [22] believe an increased peak force at loading response is due to the reduced ankle plantar flexion, which has direct consequences on stance duration, increasing sound side work overall. In their study, TTAs clearly demonstrated asymmetric loading with higher values on the sound side (70% of patients) seen especially in first peak symmetry [22]. Seventy-five percent of TTA subjects spent more time on their affected side [22].

In the study conducted by Fey and Neptune, knee abduction moment impulse was significantly lower in the intact knee compared to control subjects at 0.6 and 0.9 m/s. KFM and knee external rotation moment impulse were larger in the intact knee than the residual knee. Intact knee extension moment impulse increased as speed increased in the intact limb. Similarly, posterior force impulse significantly increased with walking speed in the intact limb [23] There was also an increased knee flexor moment impulse in the intact knee compared to the residual knee [23].

GRFs in TTAs are a controversial subject and it is unclear whether or not they differ significantly on the contralateral side of the amputee from those in matched able-bodied subjects. Karimi., *et al.* [27] found that while some average maximum values were slightly higher at certain peaks of the antero-posterior force, the overall GRF components of TTAs did not differ substantially from those in the reference group. Interestingly, Pruziner., *et al.* [16] found that mean and peak vertical GRF loading rates were larger in the intact limb for TTAs with less than 6 months of experience ambulating with a prosthesis compared with control limbs, but not for TTAs with greater than 2 years of experience ambulating with a prosthesis. When examining the effects of specific ankle prostheses, Russell Esposito and Wilken [26] found that loading rates in the sound limb were increased (12%) in subjects using an ESR foot and were significantly reduced (7%) when subjects used a powered ankle prosthesis.

Gailey., *et al.* [6] reported vertical GRFs were approximately 12% greater and the horizontal forces approximately 19% greater for the group with amputation than the control group. Silverman and Neptune [14] found that the intact and non-amputee peak forces and impulses were larger than in the residual leg in the axial and medial-lateral directions. The peak anterior force in the intact leg was also larger than the residual leg. These results agree that there are greater GRFs occurring through the intact leg relative to the residual leg. Norvell., *et al.* [4] emphasized that vertical GFRs increase in magnitude, particularly on the intact limb, and that magnitude intensity is often linked to discomfort or pain felt in the joint.

EKAM is believed to be an indicator of the distribution of loads between the medial and lateral sides of the knee joint and has been strongly associated with the incidence and progression of OA in the able-bodied population [25]. Kesikburun., *et al.* [24] found EKAM in the intact knees of patients with TTA to be higher than in the amputated knee. On the contrary, Russell Esposito and Wilken [26] found that TTAs do not exhibit greater peak EKAMs or EKAM impulses than able-bodied individuals across a range of standardized velocities. In fact, they found a 35% reduction in peak EKAM at the slowest walking speed in subjects who wore an ESR foot [26]. Miller., *et al.* [21] noted that TTAs tended to have greater peak KFM than the TFAs. Likewise, Russell Esposito and Wilken found that the sound limb's peak EKFM was significantly greater than controls, specifically when subjects wore an ESR foot and increased speed [26].

In a study using predictive simulations of gait, Koelewijn and van den Bogert [32] found that TTAs can walk with more symmetry in the joint moments at the cost of increased effort and abnormal kinematics. In some simulation, the authors found that joint moment asymmetry could be reduced by 70% with little increase in effort or metabolic cost [32]. Koelewijn and van den Bogert [32] found a lower peak extension moment in the hip and knee reduced joint moment asymmetry and yielded a lower JCF in both joints. High JCFs are correlated with higher incidence rates of OA so in decreasing the JCF, it is likely that it would decrease the incidence rate.

Musculoskeletal patterns

A significant portion of the biomechanical differences observed in amputees pertains to their functional anatomy. Individuals with amputations have weaker quadriceps bilaterally compared to nonamputees, which were highly correlated with increased rates of vertical impact loading of the lower limb during gait [7]. The quadriceps play a protective role to the joint as a shock absorber to dampen the rate of knee loading, such as decreasing the heel strike transient during the loading response phase of gait [7]. Similarly, hip muscle weakness has been attributed to knee OA [7]. Chang., *et al.* [20] reported that greater hip adductor strength is associated with a reduced likelihood of medical compartment knee OA progression. Farrokhi., *et al.* [7] agreed, stating that by strengthening the hip musculature, individuals with LEA can significantly improve pain and function despite virtually no change in KAM.

It is well known that that the medial compartment of the tibiofemoral joint bears a larger portion of loading than the lateral, as several studies have shown the medical compartment of the sound knee to be affected in individuals with LEA [15] A lower frequency of knee joint loading due to decreased activity levels post-amputation can lead to the reduction in cartilage resiliency [7]. Loading of the knee joint is inherently linked to maintenance of the articular cartilage. Adequate levels of mechanical stimulation are essential for maintaining articular cartilage tissue homeostasis through balancing solid matrix synthesis and degeneration [7]. Kesikburun and colleagues' ultrasonographic measurements of individuals with traumatic LEA's sound side medial and lateral condyles showed early and significant femoral articular cartilage loss [24]. Additionally, they found medial narrowing of the tibiofemoral joint space, increased bone mineral density at the proximal tibia, and patellofemoral degeneration in patients' intact limbs [24].

Transfemoral patterns

TFAs tend to have decreased hip extension range of motion due to their level of amputation. This decreased range is typically due to iliopsoas tightness. In their systematic review, Gailey., *et al.* [6]

mentioned a lack of iliopsoas flexibility can also result in gait deviations such as difficulty initiating swing phase. This consequentially promotes hip hiking, or increased posterior rotation of the pelvis. Additionally, Gailey., *et al.* [6] stated a compensatory anterior pelvic tilt of 10° has been described in people with TFA as it permits the prosthetic limb to achieve the 15° of hip extension needed for normal step length. Posture of maximum anterior pelvic tilt does significantly increase the depth of lumbar lordosis [6].

Transtibial patterns

TTAs have significant muscle strength discrepancies between their intact and sound sides which implies they employ a gait compensation mechanism which relies heavily on the intact limb despite the importance of the prosthetic side musculature [25]. Muscular strength and strength symmetry in the knee extensors, knee flexors, and hip abductors have been shown to correspond to improved gait function and symmetry in TTAs [25].

Lloyd., *et al.* performed an in-depth investigative study into the musculoskeletal patterns of individuals with TTAs. A more extended hip and knee on the prosthetic side is a common gait adaptation for reducing moments at the stump/socket interface [25]. Gait alteration like this one, aimed at avoiding large moments at the stump/socket interface, are responsible for creating the relationship between strength asymmetry and loading rates. Lloyd., *et al.* [25] found that knee extension strength asymmetry was significantly related to KAM load rate asymmetry and knee flexion strength asymmetry was moderately related to the vertical GRF on the intact limb. Additionally, knee extensor strength asymmetry was correlated with frontal plane knee moment load rate asymmetry, while knee flexion strength asymmetry correlated with the intact side ground reaction force load rate [25].

With the gastrocnemius removed completely on the affected side, there is a resulting lack in push-off. Koelewijn and van den Bogert [32] hypothesized that the iliopsoas force may consequently increase on the prosthesis side during late stance in order to initiate swing phase and compensate for the activation of the hamstrings, which now flex the knee instead of the gastrocnemius. An increase in residual hamstring may increase hip extensor moments and have a smaller effect at the knee [14,23]. This increased activity may also help compensate for the lack of plantarflexors; knee extensors now play an important role in producing forward progression [14,25]. In the absence of plantar flexors, the prosthesis contributes largely to loading rates and the differences observed between residual, intact and non-amputee legs [14] If a reduction in prosthetic side quadricep and hamstring strength were to occur, this may impair the ability of the prosthetic side to produce adequate propulsion and consequently, the intact limb must produce the force to propel the body forward and absorb the impact as the center of gravity falls downwards [25] Quadricep strength would then act to reduce residual knee flexion moment and provide more adequate body weight support in the absence of plantar flexors [23].

Preventative measures

There are several non-systemic risk factors associated with the development and progression of knee OA. Farrokhi., *et al.* [7] study proposed factors included chronic knee pain, obesity, abnormal knee joint mechanics, muscle weakness, previous knee trauma and altered physical activity levels. Evidence exists in literature pertaining to sports participation for individuals with LEA and its protective and/or therapeutic effects on pathological knee conditions like OA [18]. Obesity is closely linked with the onset and progression of several secondary health conditions. A weight increase of 1 kg can result in a four-fold (4 kg) increase in compressive knee joint loads per step during activities of daily living [7] Comparatively, weight loss can reduce the risk for knee OA by 50%. An increase in adipose tissue has been associated with a combination of both biomechanical and metabolic risk factors and has been specifically associated with the development and progression of knee OA [7]. Unfortunately, there are high rates of body fat reported in individuals with TTA (21%) and TFA (23%) compared with age-matched controls (13%) [7]. As much as a three-fold increase in risk for future knee OA development has been reported for young men, 20-29, with BMI values between 24.7-37/6 kg/m2 [7].

In the systematic review by Gailey., *et al.* [6] there was a mention of therapeutic interventions such as balance, strength and gait training as well as other movement strategy interventions to help LEA clients equalize force distribution across both legs and minimize the stress placed on their contralateral side. Trunk stabilization is essential to reduce back pain and maintain an active lifestyle [6]. Femoral muscle strengthening, particularly focused on the quadriceps, can be an effective strategy for prevention and treatment of symptoms of knee OA [13,15]. Miller., *et al.* [21] suggest that long periods of unloading should be avoided as much as possible. Even the smallest changes in limb loading (5-7%) have been clinically relevant when accounted for long-term [26]. Orthopedic interventions such as laterally wedged orthotics and valgus bracing help redistribute a portion of the load borne through the tibiofemoral surface to decrease risk for knee OA [15].

Prosthetic considerations

Several studies have been conducted to analyze prosthetic componentry for optimal effectiveness and patient compliance. Prosthetic fit an alignment (flexion and extension of the socket) are integral to distributing the forces action across the joints, minimizing back pain and postural changes, mitigating leg-length discrepancies, and deferring general deconditioning [6]. If a good prosthetic fit is not preserved throughout an amputee's lifetime, even the slightest compensations, over time, can predispose the contralateral limb to premature DJD [6]. Gailey.,., *et al.* [6] reported that a prosthesis that is 5 mm shorter in people with TTA and 10 mm shorter in people with TFA led to problems such as functional scoliosis, chronic back pain, and knee or hip pain in the intact limb. They also noted that in a previous study, only 15% of the subjects with LEA wore a prosthesis equal in length to the intact limb, while 34% had an unacceptable leg-length discrepancy of > 20 mm [6].

Prosthetic foot selection is arguably the most important component of a prosthetic design. Prosthetic feet with dynamic properties generate an aft shear impulse on the prosthetic limb which reduces the resultant GRF vector on the intact side during initial contact and increase the knee flexion moment during loading response [6]. Increased push-off from the prosthetic limb has been shown to reduce the magnitude of the peak EKAM in the sound limb [26,28]. The Karimi.,., *et al.* [27] study demonstrated that subjects with TTA wearing a flex foot had decreased peaks of GRF in their sound side limbs. Passive feet that store and release energy via microprocessor control are better able to mimic the function of a biological ankle and therefore can reduce the loads on the intact limb, normalizing them to those of able-bodied individuals [26,27, 32].

For TFAs specifically, Chang.,., *et al.* [20] recommended clinicians design quadrilateral sockets that take into consideration the weight placed on the ischial tuberosity. The results from the Cutti.,., *et al.* [22] study demonstrate that more advanced knees and their ability to improve temporal and loading symmetry. For TTAs Cutti.,., *et al.* [22] proposed improved socket design that does not limit knee extension and a selection of a prosthetic feet with improved push-off, roll-over shape and range of motion to lessen the first peak at loading response.

Conclusion

The current body of literature does not demonstrate enough knowledge of degenerative changes in the sound limb of persons with unilateral LEA. It is still unclear which features of joint loading contribute to disease onset and which are adaptations resulting from disease onset and progression. Presently, there are no longitudinal or prospective studies investigating risk factors and the effectiveness of their proposed interventions. Further and more sophisticated studies are required in order to determine the extent to which various gait abnormalities correlate with the onset and progression of OA and how effective various intervention strategies are post lower limb amputation. At this time, clinicians should focus on retraining undesirable biomechanics and addressing non-systematic risk factors in order to preserve the integrity of persons with unilateral LEA's intact limbs.

Recommendations

To improve quality of life for persons with unilateral LEA there is a desperate need for research to understand the mechanisms associated with the development and onset of DJD. A clear understanding of the etiology of this disease along with advancements in prosthetic componentry and socket design can more effectively mitigate the contributory joint contact forces. Studies that examine the relationship between cause of amputation (trauma, tumor, vascular, infection) and incidence of OA are important to predetermining populations that are at greater risk. The determination of baseline loading variables and their causal links to development of DJD can help clinicians better understand the long-term risks of knee OA. Force distribution patterns and how they vary across individuals is another important area in need of investigation. Longitudinal studies that determine the mechanisms most highly associated with DJD and their thresholds could prove effective for determining more preventative measures. Modeling studies can quantify the involvement of joint tissues on contact forces to determine which loads contribute to DJD over time. Rehabilitation protocols need to focus on proper identification and correction of modifiable gait abnormalities that have been associated with OA. Since vascular related amputations make up a large percentage of LEA, it is important for future research to identify how vascular insufficiency can affect the onset or progression of OA as well.

Disclosures

Contents of the manuscript represent the opinions of the authors and not necessarily those of the Department of Defense, Department of the Army, or the Department of Veterans Affairs or any academic or healthcare institution. Authors declare no conflict of interests.

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