Acta Orthopaedica et Traumatologica Turcica 51 (2017) 142–145

Contents lists available at ScienceDirect

Acta Orthopaedica et Traumatologica Turcica

journal homepage: https://www.elsevier.com/locate/aott

Association between phantom limb complex and the level of amputation in lower limb amputee

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A R T I C L E I N F O

Article history:
Received 17 November 2015
Received in revised form
20 April 2016
Accepted 17 November 2016
Available online 27 February 2017

Keywords:
Level of amputation
Lower limb amputation
Phantom limb pain
Phantom sensation
Stump pain

A B S T R A C T

Objective: The aim of this study was to evaluate the natural course of phantom limb complex without any treatment after lower limb amputation.

Methods: The study design was consisted of a combination of retrospective review and cross-sectional interview. 101 patients with lower limb amputation were included into the study. Patients were divided into three groups according to the amputation level: i) from hip disarticulation to knee disarticulation (including knee disarticulation) (25 patients, mean age: 55.9, 19 males, 6 females) ii) transtibial amputation (below knee to ankle including ankle disarticulation) (41 patients, mean age: 58.6, 33 males, 8 females) iii) below ankle to toe amputation (35 patients, mean age: 58.7, 26 males, 9 females). The patients were evaluated on both early postoperative period (EPP) and sixth months after the surgery (ASM). The data related amputation including amputation date, level, cause, stump pain (SP), phantom limb pain (PLP), components of PLP, phantom sensation (PS) were recorded based on the information obtained from patients' and hospital files.

Results: Statistically significant differences were found for pain intensity (VAS) between groups for SP and PLP at EPP ($p < 0.001$, $p = 0.036$; respectively). The mean VAS score in Group I for SP and PLP was higher than other groups. This differences for SP and PLP did not continue at ASM assessment ($p = 0.242$, $p = 0.580$; respectively).

Conclusion: VAS scores for SP in above knee amputations and VAS scores for PLP in above knee amputations and below ankle amputations were higher at EPP. But these high scores had disappeared over time. Management strategies have to be considered particularly in the early postoperative period in patients who had undergone above knee amputation.

Level of Evidence: Level III Prognostic study.

Phantom limb phrase has always been used to define illusion of presence of a limb after it has been amputated.[1] Phantom limb complex includes 3 different terms: phantom sensation (PS), stump pain (SP), and phantom limb pain (PLP).[2] Although PS and SP are considered normal condition, PLP is not evaluated as normal status. Cerebral changes, as well as peripheral and spinal factors, have been suggested as pathophysiological factors of PLP. Peripheral nerve damage causes increase in ectopic activity and loss of inhibitory control at the dorsal horn. Furthermore, PLP corresponds to maladaptive reorganization of the thalamus and body representations in somatosensory and motor cortices.[3]

Incidence of PLP ranges from as low as 2%–80%. PLP has been described as shooting, boring, squeezing, throbbing, and burning sensations.[4] PLP begins immediately following amputation, within the first 24 h, for about half of patients, and within a week for another 25%.[2,5] It has been reported that PLP persists over time.[6,7]

Occurrence of PLP seems to be independent of age in adults, as well as gender, level, and side of amputation.[2] PLP generally occurs distally to missing limb.[6–8] There are conflicting data regarding relationship between level of amputation and presence of PLP. Some studies emphasize that there was no association found between PLP and level of amputation.[6,7] In contrast, Dijkstra et al have reported that PLP was more common in proximal site of limb.[9] Aim

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Peer review under responsibility of Turkish Association of Orthopaedics and Traumatology.

http://dx.doi.org/10.1016/j.aott.2017.02.007
1017-995X/

of the current study was to investigate relationship between level of amputation and occurrence of phantom limb, and whether any change was observed 6 months after amputation in patients who did not have any treatment for phantom limb.

Patients and methods

Design of this hospital-based study was combination of retrospective review and cross-sectional interview. Clinical trial was performed at the Department of Physical Medicine and Rehabilitation and Department of Orthopedics of Cukurova University Faculty of Medicine. Study protocol was approved by the institutional review board of Cukurova University.

The patients included in the study had amputation of lower limb extremity between 6 months and 3 years before interview. Hospital database records of computer-based pre- and postoperative files from years 2010 through 2012 were analyzed and interviews were conducted with the patients who fulfilled criteria. Patients were evaluated in both early postoperative period (EPP) and 6 months after surgery (ASM). Data related to amputation: amputation date, level, cause, PS, PLP, SP, components of PLP (i.e., intensity of pain and number of attacks) were recorded based on information obtained from the patients and hospital files. EPP data were obtained from hospital database and patients' preoperative and postoperative files. ASM data were obtained from face-to-face interviews.

Patients were classified into 3 groups according to amputation level. Group I included those patients with hip disarticulation to knee disarticulation (including knee disarticulation), Group II comprised patients with transtibial amputation (below knee to ankle, including ankle disarticulation), and Group III was made up of patients with below ankle to toe amputation. Patients were excluded from the study if there were missing data concerning amputation or records of follow-up period. In addition, patients were excluded if there was systemic malignancy or musculoskeletal malignancy, patient was in active chemotherapy treatment, receiving analgesic medication, there were severe psychological problems, patient was younger than 18 years of age, or patient received medical treatment for PLP.

All analyses were performed using SPSS version 20.0 statistical software (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as numbers and percentages, and continuous variables were summarized as mean and standard deviation, or as median and minimum-maximum, where appropriate. Chi-square test was used to compare categorical variables between groups. For comparison of continuous variables between 2 groups, Student's t-test was used. For comparison of 2 related (paired) continuous variables, Wilcoxon signed-rank test was used. For comparison of more than 2 groups, one-way analysis of variance or Kruskal–Wallis test was used, depending on whether or not statistical hypothesis was fulfilled. For normally distributed data regarding homogeneity of variances, Bonferroni, Scheffe, and Tamhane tests were used for multiple comparisons of groups. For non-normally distributed data, Bonferroni-adjusted Mann Whitney U-test was used for multiple comparisons of groups. p value of <0.05 was considered statistically significant.

Results

Records of 317 patients with lower limb amputation were evaluated. In all, 101 patients were included in the study. Thirteen of the original 317 patients had died, hospital records of 51 patients were inadequate, ASM interview could not performed with 52 patients due to contact failure, and 100 patients were excluded as result of treatment for PLP.

Group I, above-knee amputation (including knee disarticulation) comprised 25 patients; Group II, transtibial amputation to ankle (including ankle disarticulation) consisted of 41 patients; and Group III, below ankle to toe amputation was made up of 35 patients. Although there was no significant difference in terms of age or gender among 3 groups ($p = 0.088$, $p = 0.632$, respectively), mean age of patients in Group I was younger than other groups (Table 1). There was no significant difference regarding preoperative visual analog scale (VAS) scores between 3 groups ($p = 0.803$; Table 1). Additional demographic and baseline clinical data are provided in Table 1.

SP was observed in all patients at EPP, and there were no significant difference in number of patients with SP at EPP and ASM assessments. Statistically significant differences were found for SP intensity between all groups at EPP ($p < 0.001$). This difference was due to Group I, as mean VAS score at EPP in Group I was higher than other groups. However, this difference was not seen at ASM assessment ($p = 0.242$; Table 2).

All patients in Group I ($n = 25$) had PLP at EPP, while 35 of 41 patients in Group II, and 31 of 35 patients in Group III had PLP at EPP. No significant difference was found between number of patients and PLP at EPP ($p = 0.112$; Table 3). Approximately 50% decrease in number of patients with PLP was observed in all groups at ASM. There was significant difference in PLP VAS scores among 3 groups at EPP ($p = 0.021$), with Group I scoring higher than other groups. This significance was due to difference between Group I and Group II ($p = 0.038$). However, this difference did not persist at ASM assessment ($p = 0.580$). Number of PLP attacks was higher in Group I than other groups and there were statistically significant

Table 1
Patient demographic and clinical data.

	Group I (n = 25)	Group II (n = 41)	Group III (n = 35)	p
Age (mean) (min/max) (SD)	55,9 (18/73) (19.4)	58.6 (18/85) (13.7)	58.7 (21/80) (13.7)	0.088
Gender (M/F)	19/6	33/8	26/9	0.632
Occupation (n)				
Laborer	1	13	9	
Retired	3	2	7	
Office worker	7	4	2	
Craftsman	8	14	9	
Housewife	3	6	6	
Other	3	2	5	
Reason for amputation (n)				
Trauma	13	17	7	
DM	2	12	25	
Vascular disease	6	5	1	
Cancer	4	2	0	
Infection	0	3	1	
Other	0	2	1	
Method of amputation				
Hip disarticulation	2			
Transfemoral	15			
Knee disarticulation	8			
Transtibial		39		
Ankle disarticulation		2		
Chopart			17	
Lisfranc			17	
Toe			1	
Patients with preoperative pain (n)	10/25	23/41	9/35	
Preoperative VAS (mean) (SD)	5.5 (1.2)	5.5 (1.7)	5.2 (1.8)	0.803

Group I: Hip disarticulation to knee disarticulation (including knee disarticulation); Group II: Transtibial amputation (below knee to ankle, including ankle disarticulation); Group III: Below ankle to toe amputation.
DM: Diabetes mellitus; VAS: visual analog scale.

Table 2
Stump pain frequency and intensity in 3 patient groups.

	Group I (n = 25)	Group II (n = 41)	Group III (n = 35)	p
Stump pain (EPP) (n)	25/25	41/41	35/35	
Stump pain (ASM) (n)	13/25	6/39	8/37	
Stump pain VAS score (EPP) (SD)	7.12 (0.73)	5.79 (1.28)	5.54 (1.41)	<0.001
Stump pain VAS score (ASM) (SD)	3.46 (1.4)	4.20 (1.30)	3.44 (1.01)	0.242

Group I: Hip disarticulation to knee disarticulation (including knee disarticulation); Group II: Transtibial amputation (below knee to ankle, including ankle disarticulation); Group III: Below ankle to toe amputation.
ASM: Six months postamputation; EPP: Early postoperative period; VAS: visual analog scale.

Table 3
Phantom pain frequency and intensity in 3 patient groups.

	Group I (n = 25)	Group II (n = 41)	Group III (n = 35)	p
Phantom pain (EPP) (n)	25	35	31	0.112
Phantom pain (ASM) (n)	17	16	12	0.201
Phantom pain VAS score (EPP) (SD)	7.12 (0.83)	6.51 (1.03)	6.90 (0.70)	0.036
			PI-II	0.038
			PI-III	0.999
			PII-III	0.198
Phantom pain VAS score (ASM) (SD)	3.79 (0.90)	3.79 (1.04)	3.44 (1.00)	0.580
Phantom pain attack (EPP) (n)				
Permanent	24	18	19	
Everyday, on and off	1	17	12	
Once in 3 days	0	0	0	
Once a week	0	0	0	
Once in 10 days	0	0	0	0.001
Once in 15 days	0	0	0	
Once a month	0	0	0	
Phantom pain attack (ASM) (n)				
Permanent	0	0	0	
Everyday on and off	0	0	0	
Once in 3 days	0	2	1	
Once a week	2	2	3	0.495
Once in 10 days	3	5	2	
Once in 15 days	6	6	3	
Once a month	6	1	3	

Group I: Hip disarticulation to knee disarticulation (including knee disarticulation); Group II: Transtibial amputation (below knee to ankle, including ankle disarticulation); Group III: Below ankle to toe amputation.
ASM: Six months postamputation; EPP: Early postoperative period; VAS: visual analog scale.

differences between all groups at EPP (p = 0.001; Table 3). Total of 24 of 25 patients in Group I had PLP all during the day. This difference was not present at ASM (p = 0.495; Table 3).

All patients had PS at EPP and there were no statistically significant differences between groups at ASM assessment (p = 0.627; Table 4).

Discussion

Phantom limb complex includes PLP, PS, and residual limb pain. This phenomenon has been known since ancient times. It has been suggested that phantom limb occurs in between 90% and 98% of patients after amputation.[10] Pathophysiological background of phantom limb-related phenomena, especially PLP, is still unclear. Some hypotheses have been suggested to account for its development, including peripheral generators and changes to spinal cord excitability or brain plasticity.[1]

In this study, we aimed to investigate prognosis of patients with phantom limb who had not had any therapeutic intervention for PLP. We found that patients with higher pain intensity scores at EPP had higher level of amputation, but all patients had SP at EPP. This was an expected condition at EPP. However, there was no SP in majority of patients at ASM evaluation. Although VAS score of Group I was higher than other groups at EPP, it was similar for all 3 groups at ASM. Most common etiology of amputation in Group I was trauma, and this may account for higher initial VAS score. In a review, it was reported that SP was quite frequent at EPP, which was consistent with our study, but persisting pain was reported in 5%–10% of patients with SP, and it was thought might get worse with time. Authors also suggested relationship between SP onset and prognosis with etiology of amputation.[2] In another report, the authors indicated SP occurrence rate of 74%, which was lower than that seen in our study.[11] Patients, especially those who have above-knee amputation, should be informed about prognosis of SP. Furthermore, physicians should be aware of this condition and arrange treatment plan in order to prevent or treat SP.

PS is accepted as generally normal condition.[3] Casale et al reported that rate of PS was 90% after 6 months and 60% 1 year after lower limb amputation.[1] Results of this study at ASM were consistent with the findings of our study. Nearly 80% of patients in the current study had PS at ASM.

PLP was first introduced by Ambrose Pare, who was a military surgeon in the mid-16th century.[5] Since that time, numerous studies have been performed on epidemiology, pathophysiology, and clinical outcomes of PLP. Despite the difficulties, theories on pathophysiological mechanisms of PLP are growing. Central sensitization and peripheral factors, including ectopic discharge from neuroma, wound infection, osteomyelitis, and poor prosthetic fit, are generally suggested as primary causes. Cortical reorganization has been reported to be responsible for peripheral and central changes in chronic PLP. Cortical reorganization affects perceptual, motor, and autonomic systems, which are related to PLP. In addition, psychological factors have also been reported to evoke and modulate PLP.[12]

Table 4
Number of patients reporting phantom sensation in 3 patient groups.

	Group I (n = 25)	Group II (n = 41)	Group III (n = 35)	p
Phantom sensation (EPP) (n)	25	41	35	
Phantom sensation (ASM) (n)	21	31	30	0.627

Group I: Hip disarticulation to knee disarticulation (including knee disarticulation); Group II: Transtibial amputation (below knee to ankle, including ankle disarticulation); Group III: Below ankle to toe amputation.
ASM: Six months postamputation; EPP: Early postoperative period.

PLP consists of 4 domains, including intensity, frequency of episodes, duration of each episode, and description of pain.[13] We only evaluated intensity and frequency of episodes in the current study as result of retrospective design. There are many studies regarding prognosis, characteristics, and clinical features of PLP in the literature. It has been reported that postamputation period and cause of amputation were important predictive factors for prognosis of PLP, yet it was also reported that there was no difference in development of PLP between patients with and without diabetes mellitus (DM).[14] More severe PLP generally occurs due to peripheral vascular disease after amputation. Intensity of PLP has been reported to decrease after 6 months.[15–17] This result is consistent with the present study. Etiology of amputation has been reported to have no effect on PLP.[2,5] Unfortunately, we did not evaluate influence of etiology on PLP in present study.

There have been conflicting results regarding association between preoperative pain and PLP.[5,6,18,19] There was no difference between 3 groups in the current study with regard to pre-amputation pain. Results of our study demonstrate no relationship between preoperative pain and PLP.

Conflicting results regarding correlation between level of amputation and PLP have been reported in the literature.[13,6,20,21] We found statistically significant difference in PLP between all groups, but in one-by-one analysis significant difference was found only between Groups I and II. However, pain scores decreased in all groups at ASM, and no significant difference was found at that point. Also, it was observed that pain attacks were more intense in all groups at EPP. It was reported that painful attacks decreased over time.[2] These results indicated that above-knee amputation and distal amputation were predictive factors for PLP. Furthermore, additional factors may trigger PLP, such as weather changes, stump massage, and stress, and these factors may complicate studies of PLP.[2,22] Patients should also be informed of effects of psychological factors on development of PLP, especially patients with above-knee and distal amputation.

Limitations of our study include relatively small number of patients in all groups; lack of etiological comparison because primary etiology was trauma in Group I, while DM was most common cause in group III; and retrospective design of study, which meant many patients were excluded due to insufficient data.

In conclusion, we found that intensity and attacks of untreated PLP were higher at EPP in patients who had above-knee amputation. There were no significant differences in long-term follow-up between groups. SP and PS were observed in all patients at EPP. SP intensity was higher in patients with above-knee amputation at EPP. Further studies with large sample size and with long-term follow-up assessments could provide new data about prognosis and clinical features of PLP.

Conflicts of interest

None declared.

References

1. Casale R, Alaa L, Mallick M, Ring H. Phantom limb related phenomena and their rehabilitation after lower limb amputation. *Eur J Phys Rehabil Med*. 2009;45:559–566.
2. Nikolajsen L, Jensen TS. Phantom limb pain. *Br J Anaesth*. 2001;87:107–116.
3. Giummarra MJ, Moseley GL. Phantom limb pain and bodily awareness: current concepts and future directions. *Curr Opin Anaesthesiol*. 2011;24:524–531.
4. Wolff A, Vanduynhoven E, van Kleef M, Huygen F, Pope JE, Mekhail N. 21. Phantom pain. *Pain Pract*. 2011;11:403–413.
5. Weeks SR, Anderson-Barnes VC, Tsao JW. Phantom limb pain: theories and therapies. *Neurologist*. 2010;16:277–286.
6. Nikolajsen L, Ilkjaer S, Kroner K, Christensen JH, Jensen TS. The influence of preamputation pain on postamputation stump and phantom pain. *Pain*. 1997;72:393–405.
7. Jensen TS, Krebs B, Nielsen J, Rasmussen P. Immediate and long-term phantom limb pain in amputees: incidence, clinical characteristics and relationship to pre-amputation limb pain. *Pain*. 1985;21:267–278.
8. Bosmans JC, Geertzen JH, Post WJ, van der Schans CP, Dijkstra PU. Factors associated with phantom limb pain: a 31/2-year prospective study. *Clin Rehabil*. 2010;24:444–453.
9. Dijkstra PU, Geertzen JH, Stewart R, van der Schans CP. Phantom pain and risk factors: a multivariate analysis. *J Pain Symptom Manage*. 2002;24:578–585.
10. Ramachandran VS, Hirstein W. The perception of phantom limbs. The D. O. Hebb lecture. *Brain*. 1998;121:1603–1630.
11. Hsu E, Cohen SP. Postamputation pain: epidemiology, mechanisms, and treatment. *J Pain Res*. 2013;6:121–136.
12. Le Feuvre P, Aldington D. Know pain know gain: proposing a treatment approach for phantom limb pain. *J R Army Med Corps*. 2014;160:16–21.
13. Sherman RA, Sherman CJ. Prevalence and characteristics of chronic phantom limb pain among American veterans. Results of a trial survey. *Am J Phys Med*. 1983;62:227–238.
14. Clark RL, Bowling FL, Jepson F, Rajbhandari S. Phantom limb pain after amputation in diabetic patients does not differ from that after amputation in nondiabetic patients. *Pain*. 2013;154:729–732.
15. Hunter JP, Katz J, Davis KD. Stability of phantom limb phenomena after upper limb amputation: a longitudinal study. *Neuroscience*. 2008;156:939–949.
16. Hunter JP, Katz J, Davis KD. Dissociation of phantom limb phenomena from stump tactile spatial acuity and sensory thresholds. *Brain*. 2005;128:308–320.
17. Richardson C, Glenn S, Nurmikko T, Horgan M. Incidence of phantom phenomena including phantom limb pain 6 months after major lower limb amputation in patients with peripheral vascular disease. *Clin J Pain*. 2006;22:353–358.
18. Hanley MA, Jensen MP, Smith DG, Ehde DM, Edwards WT, Robinson LR. Preamputation pain and acute pain predict chronic pain after lower extremity amputation. *J Pain*. 2007;8:102–109.
19. Richardson C, Crawford K, Milnes K, Bouch E, Kulkarni J. A clinical evaluation of postamputation phenomena including phantom limb pain after lower limb amputation in dysvascular patients. *Pain Manag Nurs*. 2015;16:561–569.
20. Kooijman CM, Dijkstra PU, Geertzen JH, Elzinga A, van der Schans CP. Phantom pain and phantom sensations in upper limb amputees: an epidemiological study. *Pain*. 2000;87:33–41.
21. Schley MT, Wilms P, Toepfner S, et al. Painful and nonpainful phantom and stump sensations in acute traumatic amputees. *J Trauma*. 2008;65:858–864.
22. Mac Iver K, Lloyd D. Management of phantom limb pain. In: Murray C, ed. *Amputation, Prosthesis Use, and Phantom Limb Pain. An Interdisciplinary Perspective*. New York: Springer; 2010:157–173.