ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2014;95:1710-3

ORIGINAL ARTICLE

Heterotopic Ossification in Civilians With Lower Limb Amputations

Mary E. Matsumoto, MD, Mohammed Khan, MD, Prakash Jayabalan, MD, PhD, Jessica Ziebarth, DO, Michael C. Munin, MD

From the Department of Physical Medicine and Rehabilitation, University of Pittsburgh, Pittsburgh, PA.

Abstract

Objectives: To report the incidence of symptomatic heterotopic ossification (HO) in a defined civilian amputee population, describe its characteristics, and compare these findings to published data in military amputees.

Design: Retrospective chart analysis from July 1998 to July 2009.

Setting: Ambulatory amputee clinic within a large university medical center.

Participants: Adults with lower limb amputation (N = 158).

Interventions: Not applicable.

Main Outcome Measure: Patients with symptomatic HO confirmed by radiographs.

Results: A total of 261 patients were evaluated; 158 met inclusion criteria, with 59% having traumatic etiology, 18% vascular etiology, 22% infection, and 1% tumor. Symptomatic HO was diagnosed in 36 (22.8%) patients, and 94% patients had mild HO on radiographic scoring. Rate of HO in amputations related to trauma was not increased compared with those of other etiologies. Surgical resection of the ectopic bone was required in 4 (11%) patients.

Conclusions: HO is seen commonly after civilian lower limb amputation regardless of etiology. The prevalence was less than that observed in previous reports from military populations. This is the first report estimating the prevalence of HO in adult civilian amputees.

Archives of Physical Medicine and Rehabilitation 2014;95:1710-3

Heterotopic ossification (HO) is the formation of mature lamellar bone in soft tissue. This condition has been documented in patients with spinal cord injuries, burns, fractures, traumatic brain injury, and limb amputations.[1] The pathogenesis of HO is related to the activation of osteogenic precursor cells in response to humeral, neural, and local factors.[2]

In lower limb amputation, HO has been implicated as a factor in poorly fitting prostheses and postamputation pain.[3-5] It may result in skin perforation and pressure ulcers.[6,7] Treatments include range of motion and stretching; bisphosphonates; nonsteroidal anti-inflammatory drugs; radiation therapy; and surgical excision and prosthetic modification, including the addition of liners, hard socket modifications, and fabrication of new sockets.

Until recently, HO as a complication of amputations had been best studied in the pediatric population, in which the prevalence ranged anywhere from 5% to 86% depending on the study.[6,8,9] HO was seen more commonly in traumatic amputations,[6,10] and it was seen less commonly in patients older than 12 years.[7,9]

Recent reports describe the development of HO in an adult military amputee population, with a reported prevalence of approximately 64%.[11,12] However, information regarding HO in civilian amputees is limited to case reports.[3,4,13] A single case report described the development of HO in a civilian nontraumatic amputee,[3] and there are no reports estimating the prevalence of HO or risk factors for its development in this population. One objective of this retrospective analysis was to report for the first time the prevalence and clinical characteristics of HO in a cohort of adult civilians with lower limb amputation.

Methods

The study protocol was approved by the institutional review board of the University of Pittsburgh Medical Center. A retrospective review of medical charts of all patients consecutively treated at the University of Pittsburgh Medical Center Amputee Clinic from July

Presented to the University of Pittsburgh School of Medicine, May 24, 2012, Pittsburgh, PA.
Disclosures: None.

0003-9993/14/$36 - see front matter © 2014 by the American Congress of Rehabilitation Medicine
http://dx.doi.org/10.1016/j.apmr.2014.03.010

1998 to July 2009 was performed. Subjects were included in the study if they (1) were at least 18 years old at initial review, (2) had a lower limb amputation (subtalar, transtibial, or transfemoral) or hip disarticulation, and (3) had radiographs of the amputated limb performed. Three independent reviewers (M.E.M., P.J., J.Z.), blinded to clinical data, diagnosed the presence or absence of HO on limb radiographs. The severity of HO in the radiographs was quantified using the methodology described in military amputees.[11] Medical charts were reviewed for each patient, and the following data were recorded: age, sex, cause of amputation, presenting symptoms, and presence of comorbidities. Charts of patients with HO were also reviewed for the treatment of HO, including pharmacotherapy, surgical revision, and prosthetic modifications at the time of the radiograph that diagnosed HO. *Phantom limb pain* and *residual limb pain* were defined as persistent pain in the area of the missing limb and persistent pain from the remaining limb documented on multiple office visits, respectively.

From these data, the prevalence of HO in this cohort of civilian amputees was calculated, and the presenting symptoms, severity of HO, cause of amputation, and treatment with medications, surgical excision, or prosthetic modifications were described. The association of age with HO was tested by using an unpaired Student *t* test, and the association of sex was tested by using the chi-square test. Chi-square test or Fischer exact test, where appropriate, was performed to evaluate the cause of amputation (corrected *P* value for multiple comparisons = .012); comorbid illnesses (corrected *P* value for multiple comparisons = .005); or the presence of symptoms of residual or phantom limb pain in patients who developed HO. Chi-square analysis was used to test whether differences in symptoms were due to traumatic versus nontraumatic causes. The rate of HO in our sample was compared to that reported in the military population[11,12] using a 1-sample *t* test. Unless otherwise indicated, a *P* value of $<.05$ was considered statistically significant.

Results

Of the patients evaluated during this study period, 158 subjects met inclusion criteria of having radiographs performed in the symptomatic residual limb. The reasons for amputation in the study cohort were trauma (59%), infection (22%), vascular insufficiency (18%), and tumor (1%).

HO was diagnosed radiographically in 36 of 158 subjects, as judged by 3 blinded raters (M.E.M., P.J., J.Z.) with 100% interrater reliability, yielding a prevalence of 22.8% in this cohort. Of note, radiographs were not routinely ordered but were most often ordered by the treating physiatrist or surgeon in cases of ongoing symptoms or problematic prosthetic fit. The prevalence of HO found in this population was significantly different than the rate of 64% found by Potter et al[11,12] in the military population ($t = -12.31$; $P < .001$). The mean age of these subjects was 45±13.6 years, and 78% were men. There were no significant associations detected between the presence of HO and age or sex. The prevalence of diabetes mellitus, hypertension, hyperlipidemia, hemiparesis, and smoking was not associated with the presence of HO (table 1).

Of the patients with HO, 64% had received amputations secondary to trauma, 17% secondary to infection, and 19% secondary to vascular insufficiency (fig 1). We found no significant associations between the presence of HO and the etiology of amputation ($\chi^2 = 1.33$; $df = 3$; $P = .72$). Surprisingly, rates of HO were not significantly different between patients who had amputation secondary to trauma (25%) compared with those with amputation secondary to other etiologies (20%) ($\chi^2 = .26$; $df = 1$; $P = .61$).

The radiographic severity of HO was mild in 34 (94%) patients, moderate in 1 (3%) patient, and severe in 1 (3%) patient (fig 2). The etiology of amputation was infectious in the moderate case and traumatic in the severe case. There was no significant difference in the presenting symptoms of either residual limb or phantom limb pain between those with HO and those without ($\chi^2 = 2$; $df = 1$; $P = .16$; $\chi^2 = .005$; $df = 1$; $P = .95$), although both groups reported high levels of postamputation pain (>60% in both groups had phantom limb pain).

In this cohort, 9 (25%) patients with HO were treated with nonsteroidal anti-inflammatory drugs, 3 (8%) patients with bisphosphonates, and 4 (11%) patients with surgical resection of the ectopic bone formation in the residual limb. In patients with HO, 18 (50%) patients had prosthetic modifications at the time of the radiograph. Four (11%) patients had selective padding added to the socket; 6 (17%) patients had modifications of the hard socket to relieve contact pressure points; and 8 (22%) patients had fabrication of a new socket.

Discussion

HO is a known complication of lower limb amputation. It has been studied in the military population, in which it occurs with high prevalence (64%) after traumatic and combat-related

Table 1 Subjects' demographic and clinical characteristics

Characteristic	Patients Without HO (n = 122)	Patients With HO (n = 36)	Statistics
Age at amputation (y), mean±SD	46.4±17.5	45.6±13.6	$T = -0.2849$, $P = .78$
Sex (%)			
Male	75	78	$\chi^2_1 = 0.03$, $P = .87$
Female	25	22	
Etiology (%)			
Vascular	18	19	$\chi^2_1 = 0.003$, $P = .72$
Trauma	57	64	$\chi^2_1 = 0.26$, $P = .61$
Tumor	2	0	$P = 1$ (Fischer exact)
Infection	23	17	$\chi^2_1 = 0.33$, $P = .57$
Symptoms (%)			
Residual limb pain	46	61	$\chi^2_1 = 2$, $P = .16$
Phantom limb pain	61	64	$\chi^2_1 = 0.005$, $P = .95$
Comorbidities (%)			
DM	29	17	$\chi^2_1 = 1.51$, $P = .22$
HTN	45	42	$\chi^2_1 = 0.03$, $P = .86$
HLD	25	19	$\chi^2_1 = 0.17$, $P = .68$
Smoking	34	36	$\chi^2_1 = 0.002$, $P = .96$
Hemiparesis	1	3	$P = .40$ (Fischer exact)

Abbreviations: DM, diabetes mellitus; HLD, hyperlipidemia; HTN, hypertension.

List of abbreviations:

HO heterotopic ossification