Incidence of LE due to treating cutaneous melanoma

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Abstract

Background: Lymphoedema after lymphadenectomy for breast cancer has been extensively studied, but more studies concerning lymphadenectomy for melanoma are needed. *Aim:* To assess the incidence of lymphoedema and other postoperative complications in patients undergoing radical lymphadenectomy for melanoma. *Methods:* Eighty-four patients who had undergone axillary, inguinal or ilio-inguinal lymphadenectomy for the treatment of cutaneous melanoma at AC Camargo Hospital in Brazil were evaluated. Patients' data were obtained by tape measurement, medical records and questioning. *Results:* The incidence of lymphoedema in the postoperative period was 17.5% and 59.1% for the upper and lower limbs, respectively. The incidence of other postoperative complications of axillary, inguinal and ilioinguinal lymphadenectomies were: seroma, 37.5%, 38.1% and 34.8%; surgical site infections (SSIs), 17.5%, 33.3% and 47.8%; scar dehiscence, 5%, 66.7% and 26.1%; cellulitis and/or erysipelas occurring up to one year postoperatively, 20%, 14.3% and 26.1%. *Conclusions:* Inguinal and ilio-inguinal lymphadenectomy showed a higher prevalence of lymphoedema in comparison to axillary lymphadenectomy. In addition to lymphoedema, skin numbness, infection and scar dehiscence were the most frequent morbidities. *Declaration of interest:* None.

Key words

Melanoma
Lymphadenectomy
Morbidity
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The rates of morbidity associated with lymphadenectomy as a treatment for cutaneous melanoma, as reported in the literature, vary due to the different methods used in the studies. As a result, it is difficult to compare data from different research (Kretschemer et al, 2008). Assessing the incidence of lymphoedema and other morbidities in patients with melanoma is important, as over time the risk of developing lymphoedema increases.

Healthcare professionals need to know the incidence of lymphoedema and other morbidities in patients with melanoma to assess if methods of prevention and treatment are being effective, or if they should be improved (Burmeister et al, 2002; Moffatt et al, 2003; Ballo et al, 2006; McLaughlin et al, 2008).

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Lymphoedema is a chronic lymphatic disorder and is thought to be the most common morbidity after axillary and inguinal lymphadenectomies (Serpell et al, 2003; Wrightson et al, 2003; de Vries et al, 2005, 2006; McLaughlin et al, 2008). The objectives of the study discussed in this paper were to determine the incidence of lymphoedema and other morbidities from the treatment of cutaneous melanoma by lymphadenectomy (lymph

node dissection) among patients at the Hospital AC Camargo, Brazil.

Patients and methods

A retrospective study was conducted on patients diagnosed with cutaneous melanoma, admitted to the Department of Skin Oncology of AC Camargo Cancer Hospital, Brazil between 1990 and 2008, who had undergone surgery six months before the onset of symptoms of lymphoedema and other morbidities. Patients who did not agree with the terms of consent, who had had a limb amputated, or who had bilateral lymph node dissection were excluded from the study.

The study was a random sample of convenience, consisting of 84 patients. Patients were assessed during routine consultations. Those who were not being followed up, were recruited by telephone and given transportation to the hospital. Ethical approval was given by the Research Ethics Committee of the AC Camargo Cancer Hospital, Brazil.

The authors performed manual perimetry using a tape measure. For

the upper limbs, measurements were taken 14 and 7cm above the elbow's interarticular line and 7, 14 and 21cm below (Bergmann et al, 2005). The lower limbs were measured every 10cm from the ground up to the seventh measurement, this being the most commonly used method with the truncated frustum formula (Casley-Smith, 1994; Karges et al, 2003). One researcher undertook all measurements to prevent differences of tension in the tape.

The data were placed in the truncated cone formula:

$$V = h \frac{(C1^2 + C1 \times C2 + C2^2)}{12\pi} \text{ where,}$$

V = volume of the final segment of the limb, C1 and C2 = circumference measured between the points, h = distance between the circles (C1 and C2 in each segment); all measures were done in centimetres.

Upper limb lymphoedema was diagnosed when the difference between the volumes of the two limbs was larger than 10% (Bass et al, 1992; Kosir et al, 2001; Haid et al, 2002; de Vries et al, 2005), and for lower limbs greater than 6.5% (Ballo et al, 2006; de Vries et al, 2006).

The values for the upper and lower limbs were based on studies that measured volume by water displacement, because there were no studies that gave a value for diagnosing lymphoedema based on the limb volume through the truncated cone.

The degree of upper limb lymphoedema was classified according to Stillwell (1969), as cited by de Vries et al (2005). Lymphoedema was classified as follows:
▸ 0–10% = normal
▸ 10.1–20% = mild
▸ 20.1–40% = moderate
▸ 40.1–80%= marked
▸ >80.1% = severe.

For legs, the classification was based on Bass et al (1992) and were as follows:
▸ 0–6.5% = normal
▸ 6.6–20% = mild

▸ 20.1–40% = moderate
▸ >40.1% = severe.

Postoperative complications were analysed and included:
▸ Seroma
▸ Surgical site infections (SSIs)
▸ Scar dehiscence
▸ Cellulitis and/or erysipelas occurring up to one year postoperatively
▸ Skin sensitivity (occurring up to six months postoperatively with persistence).

The statistical analysis of risk factors for the onset of lymphoedema after surgery was performed by univariate analysis via Pearson's chi-square test or Fisher's exact test. Adherence to normality was verified using the Kolmogorov-Smirnov test. All statistical tests were accepted at a significance level of 5%.

Results
Of the 84 patients, 40 (47.6%) had axillary lymph node dissection, 21 (25%) had inguinal lymphadenectomy and 23 (27.4%) had ilioinguinal lymphadenectomy. The average time elapsed since lymphadenectomy was 44 months (standard deviation 56.1).

The majority of patients were female (48 cases, corresponding to 57.1%) and white (73 cases, 86.9%). The average age of patients at surgery was 47.2 years (SD 16.7), with a range from 5 to 80 years.

At assessment, the average age was 52.5 years (SD 16), with a range from 10 to 81 years. Three participants were under 18 years old (3.6%).

The incidence of lymphoedema in the upper and lower limbs was 17.5% and 59.1%, respectively (42.9% in inguinal and 73.9% in ilioinguinal lymphadenectomy).

The mean total volumes were as follows: the affected upper limb 2028.7 litres (SD 414), the upper control 1911.9 l (SD 383.1), the affected leg 8602.3 l (SD 2569.4) and the lower unffected 7170.6 l (SD 1838.8).

There were differences in lymphoedema (p <0.001), infection (p=0.037) and scar dehiscence (p<0.001) between the types of lymphadenectomy (*Table 1*). The relationship of the location and extent of lymphadenectomy for lymphoedema (mild or moderate) was statistically significant (p<0001). Patients who had undergone ilioinguinal lymphadenectomy presented with more light and moderate lymphoedema than those who had axillary or inguinal procedures. Lymphatic drainage of the limb is extremely difficult with the ilioinguinal group, since there is significant reduction in alternative routes of drainage, hence the higher incidence of lymphoedema. In the patient sample, there were no cases of severe lymphoedema (*Table 2*).

Table 1

Number and percentage of patients by type of postoperative complication and local lymphadenectomy: axillary (AL), inguinal (IL) and ilioinguinal (IIL)

Postoperative complication	AL (n=40)		IL (n=21)		IIL (n=23)		P value
	n	%	n	%	n	%	
Lymphoedema	7	17.5	9	42.9	17	73.9	<0.001
Seroma	15	37.5	8	38.1	8	34.8	0.969
Infection	7	17.5	7	33.3	11	47.8	0.037
Scar dehiscence	2	5.0	14	66.7	6	26.1	<0.001
Cellulitis and/or erysipelas within last year	8	20.0	3	14.3	6	26.1	0.686
Skin sensitivity	37	92.5	19	90.5	21	91.3	1.000

Table 2

Relationship between location of axillary (AL), inguinal (IL) or ilio-inguinal lymphadenectomy (IIL) and the degree of lymphoedema

Degree of lymphoedema	AL (n=40)		IL (n=21)		IIL (n=23)		P value
	n	%	n	%	n	%	
None	33	82.5	12	57.1	6	26.1	
Light	5	12.5	8	38.1	9	39.1	
Moderate	2	5	1	4.8	8	34.8	<0.001

Table 3

Relationship of lymphoedema (tape measurement) to postoperative complications

Postoperative complication	No (n=51)		Yes (n=33)		P value
	n	%	n	%	
Seroma	21	41.2	10	30.3	0.313
Infection	10	19.6	15	45.5	0.011
Scar dehiscence	14	27.5	8	24.2	0.744
Cellulitis and/or erysipelas within last year	7	13.7	10	30.3	0.065
Skin sensitivity	46	90.2	31	93.9	0.699

Surgical site infections (SSIs) (p=0.011) were the only postoperative complication that occurred more frequently in patients with lymphoedema (19.6% versus 45.5%, p=0.011) (*Table 3*). There was no difference between both groups according to other surgical complications, such as seroma, cellulitis and/or erypsipelas (within the last year), and skin sensitivity.

Rates of skin sensitivity near the site of lymphadenectomy were high among the various types of lymphadenectomies: 92.5% in the axillary, 90.5% in the inguinal and 91.3% in the ilioinguinal. Cellulitis and/or erysipelas occuring within the first year postoperatively was seen in 20% of axillary lymph node dissections and 14.3% and 26.1% of inguinal and ilioinguinal lymph node dissections.

Five patients (12.5%) with mild lymphoedema were referred for axillary lymph node dissection, eight (38.1%) for inguinal and nine (39.1%) for ilio-inguinal. Two patients (5%) with moderate lymphoedema were referred for axillary lymph node dissection, one (4.8%) to inguinal and eight (34.8%) to ilioinguinal. These data were statistically significant (p<0001), with those patients undergoing ilioinguinal lymphadenectomy presenting with a greater percentage of moderate lymphoedema than the other types. For mild lymphoedema, the rate in the lower limbs was not significantly different between the inguinal and ilioinguinal lymphadenectomy groups. However, there was a greater difference in the axillary lymph node dissection group. Patients with inguinal or ilioinguinal lymphadenectomies have higher rates of lymphoedema than patients with axillary lymphadenectomy.

Body mass index (BMI) was classified as follows:
- Low weight (<18.4)
- Normal (18.5 to 24.9)
- Overweight (25 to 29.9)
- Obesity (>30).

On the day of surgery, most patients were overweight (36 patients, 48%), followed by normal (24, 32%) and obese (15, 20%) patients. For nine patients, there was no data on body mass and/or stature in the medical record. At assessment in hospital, during the transversal analysis of this study for prospective collection of data, the number of overweight patients was also greater (39 cases, 46.4%), followed by obesity (23, 27.4%), normal weight (21, 25%) and low weight (1, 1.2%). There were no differences between patients with and without lymphoedema in relation to BMI (p=0.790). Patients without lymphoedema had an average BMI of 26.8 (SD 3.6) and patients with lymphoedema had a BMI mean of 28.1 (SD 6.9).

The average drainage at withdrawal of the drain was 68.9ml (SD 81.1), although 47 patients did not have a record of this in their notes. The mean time of drainage for axillary lymphadenectomy was 12.5 days (SD 5.2), for inguinal 15.3 (7.3) and ilioinguinal 16.6 (10.8), with a range of 3 to 46 days for all of the various types of lymphadenectomy.

Clark, Breslow and ulceration are prognostic factors for melanoma (Balch et al, 2001). Breslow is the thickness of the tumour. There are five levels of Clark and they are obtained by comparing the level of tumour invasion through layers of skin. Mean Breslow was 3.1mm (SD 4.6). Clark III was the most prevalent (33 patients, 49.3%), followed by Clark IV (25, 29.8), Clark V (5, 6%) and Clark II (4, 4.8%). Regarding ulceration, 17 (20.2%) patients had evidence of ulceration.

Primary melanoma was more often located in the lower limbs (38 cases, 45.2%), followed by the upper limbs (22, 26.2%) and the trunk (19, 22.6%). Five patients (6%) had an unknown location.

As for recurrence, only one patient had local recurrence (1.2%), two had lymph node involvement (2.4%), three were in transit metastatic melanoma (3.6%), six had lymph node involvement and in transit (7.1%), and 11 had distance metastasis (13.1%).

Melanoma stage III was the most prevalent (74 cases, 88.1%), followed by stage II (2, 3.6%), stage I (2, 2.4%) and stage IV (1, 1.2%). Four patients (4.8%) had a nondescript stage.

Discussion

This study had some limitations; namely, that it was a retrospective study. However, due to the relatively low incidence of melanoma and the fact that the aggressive nature of the disease results in death shortly after diagnosis, a prolonged monitoring period is difficult. For this reason, most studies of patients with melanoma are of a small sample size.

Another limitation was the differences in time between the postoperative patients. Some patients had recently undergone surgery (i.e. within the last year), while for others it was 10 years since they had had their surgery. Moreover, the surgical treatment of melanoma has changed during the 18 years this study examined.

Understanding the complications related to radical lymphadenectomy is important, especially in relation to lymphoedema, which affects quality of life with physical, social and emotional consequences (Moffatt et al, 2003; Cormier et al, 2005).

There are few studies concerning the epidemiology of lymphoedema in patients and its impact on health services, as it is a problem poorly recognised by professionals in the area (Moffatt et al, 2003). Different methodologies have been employed in studies of lymphadenectomies for treatment of melanoma, which has resulted in the diversity of rates of lymphoedema, with a range from 2 to 19% in the upper limbs (Lawton et al, 2002; Wrightson et al, 2003; Staritt et al, 2004; de Vries et al, 2005; van Akkooi et al, 2007; Kretschemer et al, 2008), and from 18 to 64% in the lower limbs (Bass et al, 1992; Lawton et al, 2002; Wrightson et al, 2003; de Vries et al, 2006; van Akkooi et al, 2007; Sabel et al, 2007; Allan et al, 2008; Kretschemer et al, 2008; Spillane et al, 2008) (*Table 4*).

This study obtained values consistent with previous literature (17.5% in upper limbs and 59.1% in lower limbs). Lawton et al (2002) also diagnosed lymphoedema by tape measurement and found similar values, 13% and 62%, respectively.

The incidence of seroma varies from 12–43.8% in studies that have examined axillary lymph node dissection for treatment of melanoma (Kretschemer et al, 2008; de Vries et al, 2005; Wrightson et al, 2003; Lawton et al, 2002; van Akkooi et al, 2007; Guggenheim et al, 2008), and 7–56.8% in inguinal or ilioinguinal lymphadenectomies (Bass et al, 1992; Lawton et al, 2002; de Vries et al, 2005; van Akkooi et al, 2007; Sabel et al, 2007; Guggenheim et al, 2008; Kretschemer et al, 2008), which corresponds with the values obtained in this study (i.e. axillary lymph node dissection in 37.5% and inguinal lymphadenectomy in 36.4%).

Wound infection rate after surgery has ranged from 6–45.8% (axillary lymph node dissection) in the literature (Lawton et al, 2002; de Vries et al, 2005; van Akkooi et al, 2007; Guggenheim et al, 2008; Kretschemer et al, 2008), and 9–64% (inguinal lymphadenectomy) (Coit et al, 1991; Bass et al, 1992; Lawton et al, 2002; de Vries et al, 2006; van Akkooi et al, 2007; Sabel et al, 2007; Guggenheim et al, 2008; Kretschemer et al, 2008; Poos et al, 2008). The rate of infection in axillary (17.5%) and inguinal lymph node dissections (40.9%) in this study was consistent with the literature.

Wound complications are more severe in the axillary than in the inguinal lymphadenectomies. This may be due to the fact that axillary lymph node dissection does not result in devascularisation of the skin flap, when compared to inguinal or ilioinguinal dissection (Coit et al, 1991).

In the studies analysed, scar dehiscence in axillary lymph node dissection ranged from 0–9% (Lawton et al, 2002; van Akkooi et al, 2007; Guggenheim et al, 2008; Kretschemer et al, 2008), and for inguinal dissection from 3–29% (Bass et al, 1992; Lawton et al, 2002; de Vries et al, 2006; van Akkooi et al, 2007; Guggenheim et al, 2008; Kretschemer et al, 2008; Spillane et al, 2008). In the authors' study, the incidence of axillary dehiscence was found in 5%, while it was found in 45.4% for inguinal and ilioinguinal lymph node dissections.

This study showed the incidence of lymphoedema in one hospital, and found it to be higher in inguinal and ilioinguinal lymphadenectomies than in axillary dissections. In addition to lymphoedema, skin sensitivity, infection and scar dehiscence were the most significant morbidities. Further multicentre studies with larger sample sizes are needed to obtain more reliable values. Such research should also include the use of optoeletronic volumetry, which is capable of providing a more accurate volume of the limb than tape measurement.

The high rates of lymphoedema in the lower limbs draws attention to a problem that often goes unnoticed. Early diagnosis and the referral of patients for physical therapy are paramount to reduce these rates. JL

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Table 4

Lymphoedema rates in prospective and retrospective studies with melanoma patients

	Study	Number of patients	Diagnosis of lymphoedema	ULL	LLL
Bass et al, 1992	Retrospective	151 IL	Displacement of water		20%
Lawton et al, 2002	Retrospective	162 (106 AL, 56 IL)	Perimetry	13%	62%
Wrightson et al, 2003	Prospective	389 (262 AL, 127 IL)	History and physical examination	4.6%	31.5%
Starritt et al, 2004	Retrospective	107 AL	Displacement of water	10%	
de Vries et al, 2005	Retrospective	14 AL	Displacement of water	7%	
de Vries et al, 2006	Retrospective	14 AL	Displacement of water		64%
Akkooi et al, 2007	Retrospective	179 (50 AL, 129 IL)	Physiotherapy or MLD	2%	30%
Sabel et al, 2007	Retrospective	212 IL	Patients' complaints, physical examination		30%
Spillane et al, 2008	Retrospective	66 IL	Perimetry and perometer		18%
Kretschmer et al, 2008	Prospective	111 (66 AL, 45IL)	Patients' complaints	19%	63%
Allan et al, 2008	Retrospective	72 IL	Medical records		44%

AL = axillary lymphadenectomy, IL = inguinal lymphadenectomy, ULL = upper limb lymphoedema, LLL= lower limb lymphoedema, MLD = manual lymphatic drainage

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