Original Article

Reversal of digital clubbing in surgically treated lung cancer patients*,**

Regressão do hipocratismo digital em pacientes com câncer de pulmão tratados cirurgicamente

José da Silva Moreira[1], Marlene Hass[2], Ana Luiza Schneider Moreira[3], James de Freitas Fleck[4], José de Jesus Peixoto Camargo[5]

Abstract

Objective: To objectively evaluate the reversal of digital clubbing (DC) in a series of surgically treated lung cancer patients, and to review the literature on the subject. **Methods:** Sixty-one patients with non-small cell lung cancer—40 with and 21 without DC—were treated by pulmonary resection. Eleven (18%) received additional postoperative radiation therapy. Preoperatively, as well as on postoperative days 7, 18, and 90, the hyponychial angle (HA) and the distal phalangeal depth/interphalangeal depth (DPD/IPD) ratio were determined on profile shadow projections of the index fingers. A review of the literature on reversal of DC (1954-2007) was also performed. **Results:** From the preoperative period to postoperative day 90, HA decreased from 200.5 ± 5.0° to 193.3 ± 6.8° ($p < 0.001$), and the DPD/IPD ratio decreased from 1.014 ± 0.051 mm to 0.956 ± 0.045 mm ($p < 0.001$) in the group of 40 patients with DC. The HA and the DPD/IPD ratio decreased in 33 (82.5%) but remained the same in 7 (1.7%), 6 with unfavorable evolution. In the 21 patients without DC, HA (184.5 ± 5.5°) and the DPD/IPD ratio (0.937 ± 0.046 mm) remained unchanged after surgery. In the literature (1954-2007), we found 52 cases, 5 of which were lung cancer cases, in which reversal of DC, observed in several clinical conditions, was explicitly reported. **Conclusion:** In most lung cancer patients, DC resolves after effective surgical treatment of the tumor, as can occur in patients with other conditions.

Keywords: Osteoarthropathy, secondary hypertrophic; Lung neoplasms; Pulmonary surgical procedures.

Resumo

Objetivo: Estudar, por meio de avaliações objetivas, a ocorrência de regressão do hipocratismo digital (HD) em pacientes com câncer de pulmão, tratados cirurgicamente, e revisar a literatura sobre o assunto. **Métodos:** Sessenta e um pacientes com câncer de pulmão não-pequenas células—40 com e 21 sem HD—foram tratados por cirurgia de ressecção pulmonar. Onze deles (18%) também receberam radioterapia pós-operatória. No período pré-operatório e no 7º, no 18º e no 90º dia pós-operatório, o ângulo hiponiquial (AH) e a relação entre as espessuras falangeana distal e interfalangeana (EFD/EIF) foram determinados sobre imagens da sombra dos dedos indicadores em perfil. Uma revisão da literatura sobre regressão do HD (1954-2007) também foi efetuada. **Resultados:** Do período pré-operatório ao 90º dia pós-operatório, o AH diminuiu de 200,5 ± 5,0° para 193,3 ± 6,8° ($p < 0,001$), e a relação EFD/EIF, de 1,014 ± 0,051 mm para 0,956 ± 0,045 mm ($p < 0,001$) no grupo de 40 pacientes com HD. Em 33 (82,5%), o AH e a relação EFD/EIF diminuíram, mas, em 7 (1,7%), 6 com evolução desfavorável, esses valores não se reduziram. Nos 21 pacientes sem HD, tanto o AH (184,5 ± 5,5°) como a relação EFD/EIF (0,937 ± 0,046 mm) permaneceram inalterados após a cirurgia. Na literatura (1954-2007) foram encontrados 52 casos em que a regressão do HD, observada em diversas condições clínicas, foi explicitamente referida, 5 dos quais eram casos de câncer de pulmão. **Conclusões:** O HD em pacientes com câncer de pulmão regride na maioria dos casos após tratamento cirúrgico efetivo do tumor, o que pode também ocorrer em pacientes com outras condições.

Descritores: Osteoartropatia hipertrófica secundária; Neoplasias pulmonares; Procedimentos cirúrgicos pulmonares.

---

* Study carried out at the Pereira Filho Ward of the Porto Alegre Santa Casa Hospital, Postgraduate Program in Respiratory Sciences of the *Universidade Federal do Rio Grande do Sul* – UFRGS, Federal University of Rio Grande do Sul – Porto Alegre, Brazil.

1. Professor in the Postgraduate Program in Respiratory Sciences. *Universidade Federal do Rio Grande do Sul* – UFRGS, Federal University of Rio Grande do Sul – Porto Alegre, Brazil.
2. Clinician at the Moinhos de Vento Hospital, Porto Alegre, Brazil.
3. Clinician at the Pereira Filho Ward of the Porto Alegre Santa Casa Hospital, Porto Alegre, Brazil.
4. Professor in the Department of Internal Medicine. *Universidade Federal do Rio Grande do Sul* – UFRGS, Federal University of Rio Grande do Sul – Porto Alegre, Brazil.
5. Professor in the Department of Surgery. *Fundação Faculdade Federal de Ciências Médicas de Porto Alegre* – FFFCMPA, Federal Foundation School of Medical Sciences of Porto Alegre – Porto Alegre, Brazil.

Correspondence to: José da Silva Moreira. Pavilhão Pereira Filho (Santa Casa), Rua Annes Dias, 285, CEP 90020-090, Porto Alegre, RS, Brasil.
Tel 55 51 3228-2789. E-mail: moreirapneumo@bol.com.br

Submitted: 23 June 2007. Accepted, after review: 24 September 2007.

**A versão completa em português deste artigo está disponível em www.jornaldepneumologia.com.br

Introduction

Digital clubbing (DC) is a clinical sign that is of diagnostic value,[1] typically indicating pulmonary[2] or cardiac[3] disease. It can also be related to chronic liver diseases,[4] bowel diseases,[5] and thyroid diseases,[6] or it can be hereditary.[7] It can occur in isolation or as a result of hypertrophic osteoarthropathy (HOA, or Marie-Bamberger syndrome), which can also produce prominent skin manifestations. Most of the HOA cases are correlated with a non-small cell type of intrathoracic neoplasms.[8]

Although the causes of DC and HOA are unknown, some theories have attempted to define them.[9] It has recently been postulated that growth factors, such as hormones or megakaryocytes that secrete cytokines, which accumulate at the sites of abnormalities, might be involved in the pathogenic process.[10] In cases associated with pulmonary or cardiac shunts, the diverted blood, which should be handled by the normal lung, returns to the periphery transporting the possible promoting factors for the DC or HOA anatomical changes.[11] Neurogenic components might also be involved in the whole mechanism contributing to the formation of pulmonary vascular shunt or to its maintenance, as suggested by the HOA symptom relief observed after vagotomy in patients with inoperable lung cancer.[12] Traumatic or nontraumatic lesions of the vascular-nerve bundle of a limb can establish extrapulmonary vascular communications or cause neurogenic changes resulting in distal blood stasis and in longer duration of the factors involved, thereby explaining the occurrence of asymmetrical DC.[13] Furthermore, some primary pulmonary lesions, particularly neoplasms, can produce substances that affect the distant peripheral tissues.[14]

The diagnosis of DC is clinical, and it is not difficult in cases of evident anatomical changes in the fingertips. However, it may not be so easy when the changes are incipient and the abnormalities are still undetected. Objective evaluation criteria can help the assessment in such cases, additionally allowing a better follow-up evaluation of the changes in the fingers over time, with advantages over the subjectivity of the clinical judgment.

Among the objective criteria currently used for the evaluation of DC, the most reliable are the profile angle (PA) of index fingers or thumbs,[5,15] the hyponychial angle (HA) of index fingers,[16] and the ratio of distal phalangeal depth to interphalangeal depth (DPD/IPD) of index fingers.[17] For the application of such criteria, however, profile images[18,19] or rigid casts of the fingers[20] have currently been used. In adult individuals, some normal values of such measurements found in index fingers are as follows:

- for PA: 168.3 ± 3.6°,[22] 166.3 ± 4.3°,[5] and 172.8 ± 5.3°[21]
- for HA: 180.1 ± 4.2°,[18] 178.9 ± 4.7°,[19] 177.9 ± 4.6°,[5] 181.5 ± 4.8°,[21] and 186.0 ± 2.0°[16]
- for the DPD/IPD ratio: 0.904 ± 0.029 mm[21] and 0.903 ± 0.043 mm[22]

In normal children, such values are not significantly different.[17] In individuals with clinically established DC, however, they are considerably higher.[19,21]

Improvement of paraneoplastic manifestations, reversal of DC, or relief of HOA symptoms after treatment of the underlying condition have been reported in the medical literature.[23] Most publications point to alleviation or disappearance of HOA joint symptoms immediately after surgical resection of a thoracic tumor,[8] but later reversal of bone abnormalities is less frequently documented.[24] References specific to reversal of DC are less common, usually appearing in the form of case reports based on clinical impression,[25-27] rather than being based on objective documentation.[5,20,28]

The objective of the present study was to investigate, through objective evaluations, the occurrence of reversal of DC in a series of surgically treated lung cancer patients, and to review the literature on the subject.

Methods

This study investigated a series of surgically treated lung cancer patients in order to objectively document, using known measurement criteria, the occurrence of reversal of DC after treatment of the underlying condition. In addition, a review of the literature on the subject was performed.

Sixty-one adult patients with non-small cell lung cancer treated by pulmonary resection were studied. Upon clinical examination, 40 of them were found to have DC (DC group), whereas 21 had normal fingers (control group).

All patients in the DC group (34 males and 6 females; 58.9 ± 12.9 years) had been smokers for 15 to 60 years (mean, 25 cigarettes per day).

Twenty-six had squamous cell carcinoma, 11 had adenocarcinoma, and 3 had large cell carcinoma. Peripheral lesions predominated (60%), and 82.4% of the tumors were staged as IA-IIB, according to the international classification. The most prevalent symptoms in this group were cough (67%) and weight loss (47.5%). Six patients (15%) presented HOA. The duration of symptoms in 38 patients was 4.7 ± 3 months, and 2 had no symptoms. The general clinical condition was good in 29 (72.5%)

Table 1 - Cases of reversal of digital clubbing after treatment of the underlying disease (1954-2007).

Reference	Disease	N	Treatment
Wierman WH et al. JAMA 1954; 155(17):1459-63.	Bronchiectasis	1	Resection
Mellins RB, Fishman AP. Circulation 1966; 33(1):143-5	Fallot's tetralogy	1	Surgical correction
Yamamoto H et al. Kyobu Geka 1970; 23(3):177-83	Lung cancer	1	Resection
Fielding JF & Cooke WT. Gut 1971, 23(6):442-4.	Regional enteritis	3	Resection/medical treatment
Mullins GM & Lanhard RE. J Hopk Med J 1971; 128(3):153-7	Hodgkin's disease	1	Radiotherapy
Silk DBA et al. Gastroenterology 1975; 68(4):790-4	Laxative abuse	1	Discontinuation of laxative use
Kuritzky P et al. JAMA 1975; 234(11):1166-7.	Hodgkin's disease	1	Chemotherapy
Herbst JJ et al. Am J Dis Child 1976; 130(11):1256-8.	Gastroesophageal reflux	3	Surgical correction
Ferguson R et al. Br Med J 1978; 1(6106):151-2.	Leiomyoma of the ileum	1	Resection
Gold AH et al. J Hand Surg 1979; 4(1):60-6.	Palmar aneurysm	1	Resection
Kitis G et al. Br Med J 1979; 2(6194): 825-8.	Crohn's disease	13	Resection
Prabhu R et al. Chest 1980; 78(6):883-5.	Lymphomatoid granulomatosis	1	Chemotherapy
Stoller JK et al. Hepatology 1990; 11(1):54-8.	Hepatic cirrhosis	1	Liver transplantation
Gossman HH & Hilger H. Rofo 1990; 152(6):734-5	Thyroid disease	1	Spontaneous
Pujol JL et al. Ver Pneumol Clin 1991; 47(1):57-8	Lung cancer	1	Chemotherapy
Fukumoto H et al. Nippon Kyobu Geka; 1992; 40(7):1161-5	Lung cancer	1	Resection
Bhandari S et al. Postgrad Med J 1994; 70(824): 457-8	Myeloid leukemia	1	Chemotherapy
Agnihotri MS & Goel MK. Ind J Tub 1994; 41(3):177-9.	Tuberculous spondylitis	1	Antituberculosis drugs
Sansores RH et al. Chest 1995; 107(1):283-5.	Pulmonary fibrosis	1	Lung transplantation
Ghoshal UC et al. Indian J Gastroenterol 1995; 14(3):112	Esophageal stenosis	1	Endoscopic dilatation
Ikeda S et al. Transpl Int 1996; 9(6):596-9.	Hepatic cirrhosis	1	Liver transplantation
Rabast U. Dtsch Med Wochenschr 1997; 122(40):1207-12	Sarcoma of the stomach	1	Resection
Abe K et al. Angiology 1999; 50(1):69-73.	Palmar aneurysm	1	Resection
Urschel JD et al. Chest 1999; 115(6):1735-7	Pleural mesothelioma	1	Resection
Rena O et al. Eur J Cardiothorac Surg 2001; 19(2):185-9	Fibrous tumor of the pleura	3	Resection
Augarten A et al. Pediatr Pnaumonol 2002; 34(5):378-80.	Cystic fibrosis	3	Lung transplantation
Yang WC et al. Kaoshiung J Med Sci. 2003; 19(4):183-7	Lung cancer	1	Resection/chemotherapy
Lamme B et al. Ned Tjdschr Geneeskd. 2003; 147(25):1216.	Lung cancer	1	Resection
Andrés R et al. J Clin Oncol 2003; 21(18):3540-1	Metastatic leiomyoma	1	Chemotherapy
Pichler G et al. Scand J Rheumatol 2004; 33(3):189-91	Pulmonary pseudotumor	1	Resection
Harish K et al. Indian J Gastroenterol 2005; 24(4):183-4	Esophageal stricture	1	Dilatation
Asai S et al. Intern Med 2005; 44(12):1307-11	Gingival hyperplasia	1	Dental extraction
Present series -----	Lung cancer	33	Resection[a]

[a]82.5% of 40 cases.

and regular in 11 (27.5%) of the patients. Good respiratory function was observed in most patients, with forced expiratory volume in one second (FEV_1) of 2.23 ± 0.56 L and arterial oxygen tension (PaO_2) of 77.3 ± 9.22 mmHg. Three patients had FEV_1 of less than 1.5 L, and 3 had PaO_2 of less than 60 mmHg. The most frequent associated condition in this group was chronic obstructive pulmonary disease, identified in 11 cases (27.5%).

In the control group (18 males and 3 females; 59.9 ± 10.3 years), there were 11 cases of squamous cell carcinoma, 8 cases of adenocarcinoma, and 2 cases of large cell carcinoma, 71.4% of which were peripheral lesions and 61.9% of which occurred in the right lung. Seventeen patients were staged as IA-IIB, and 4 were staged as IIIA. Cough (66.7%) and weight loss (61.9%) were also the most common symptoms in this group. Seven (33.3%) of the patients presented comorbid chronic obstructive pulmonary disease. The FEV_1 was 2.10 ± 0.59 L, and PaO_2 was 74.5 ± 12.7 mmHg. Two patients presented FEV_1 and PaO_2 values of less than 1.5 L and 60 mmHg, respectively.

All 61 patients were treated by pulmonary resection. Of the 40 patients in the DC group, 20 underwent lobectomy or bilobectomy, 11 underwent pneumonectomy, and one underwent segmentectomy. Of the 21 patients in the control group, 17 underwent lobectomy, 2 underwent bilobectomy, and 2 underwent pneumonectomy. Eight (20 %) of the patients in the DC group and 3 (14.3%) of those in the control group also received postoperative radiotherapy.

In the immediate preoperative period, each of the 61 lung cancer patients had their fingers clinically evaluated by two trained physicians, who ought to be in agreement about either the presence or absence of DC. Cases in which there was no consensus were excluded.

Immediately after the clinical examination, the preoperative HA (PRE-HA) and the preoperative DPD/IPD ratio (PRE-DPD/IPD) were determined on profile shadow images of the right index finger of all patients. The finger shadow images were projected through a flat glass pane onto a sheet of common white paper.[21] Length measurements were performed using a Vernier caliper calibrated to 0.05 mm, and angle measurements were performed using a protractor calibrated to 0.5°. The images and measurements were obtained by one main investigator, and the values were checked by a second one.

The HA and DPD/IPD ratio measurements were repeated in the postoperative period by day 7 (POST-HA-1 and POST-DPD/IPD-1), by day 18 (POST-HA-2 and POST-DPD/IPD-2), and after day 90 (POST-HA-3 and POST-DPD/IPD-3), and these values were compared with those found in the preoperative period. The first postoperative measurement was performed in 32 patients with DC and in 16 patients without DC, the second one was performed in 33 patients with DC and in 17 without DC, and the last one was performed in all 40 patients with DC and in 21 patients without DC. The most common causes interfering with the measurements in the immediate postoperative days were tremor and hand edema. Clinical examination was also repeated postoperatively in all patients. Four patients had their fingers photographed before and after surgery.

Table 2 - Preoperative and postoperative hyponychial angle and distal phalangeal depth/interphalangeal depth ratio in the 40 surgically treated lung cancer patients with digital clubbing.*

PRE-HA	POST-HA-1	POST-HA-2	POST-HA-3	PRE-DPD/IPD	POST-DPD/IPD-1	POST-DPD/IPD-2	POST-DPD/IPD-3
(40)	(32)	(33)	(40)	(40)	(32)	(33)	(40)
200.5 ± 5.0[a]	200.0 ± 6.1	197.0 ± 7.7	193.3 ± 6.8[a]	1.014 ± 0.051[a]	0.992 ± 0.057	0.987 ± 0.060	0.956 ± 0.045[a]
(192.0-214.0)			(183.0-216.0)	(0.917-1.103)			(0.866-1.129)

PRE-HA: preoperative hyponychial angle; POST-HA-1: immediate postoperative hyponychial angle; POST-HA-2: recent postoperative hyponychial angle; POST-HA-3: late postoperative hyponychial angle; PRE-DPD/IPD: preoperative distal phalangeal depth/interphalangeal depth ratio; POST-DPD/IPD-1: immediate postoperative distal phalangeal depth/interphalangeal depth ratio; POST-DPD/IPD-2: recent postoperative distal phalangeal depth/interphalangeal depth ratio; and POST-DPD/IPD-3: late postoperative distal phalangeal depth/interphalangeal depth ratio. [a]Significant differences between PRE-HA and POST-HA-3 ($p < 0.0001$), as well as between PRE-DPD/IPD and POST-DPD/IPD-3 ($p < 0.0001$). *Hyponychial angle expressed in degrees and distal phalangeal depth/interphalangeal depth ratio expressed in millimeters.

Table 3 - Data related to the 40 surgically treated lung cancer patients with digital clubbing.[a]

Case	Age	Gender	HIST	Surgical procedure	PRE-HA	POST-HA-3	PRE-DPD/IPD	POST-DPD/IPD-3	POSTOP	EVOL
1	39	M	Sq	Right pneumonectomy	195.0	187.5	0.954	0.905	90	G
2	54	M	Sq	Left pneumonectomy	192.5	190.0	0.966	0.962	179	F
3	57	M	Ad	Left upper lobectomy	192.0	186.0	1.003	0.933	150	G
4	46	M	Sq	Right pneumonectomy	202.0	189.0	0.993	0.933	327	G
5	58	M	Ad	Left pneumonectomy	201.5	194.5	1.000	0.943	90	G
6	64	F	Sq	Upper and middle bilobectomy	192.0	188.0	0.931	0.921	845	G
7	43	M	Sq	Left upper lobectomy[b]	195.0	197.0	0.935	0.950	306	G
8	42	F	Sq	Right lower lobectomy	201.5	190.5	1.036	0.980	90	G
9	70	M	Sq	Right pneumonectomy[b]	199.0	203.0	1.014	0.989	92	F
10	63	M	Sq	Left pneumonectomy	201.0	189.0	0.987	0.948	118	G
11	56	M	Sq	Left lower lobectomy	194.0	193.0	1.085	0.993	92	G
12	39	M	Lc	Left upper lobectomy	208.5	204.0	1.000	0.940	330	G
13	61	M	Lc	Upper and middle bilobectomy[b,c]	203.0	216.0	1.005	1.129	132	G[d]
14	58	M	Ad	Left upper lobectomy	214.0	193.5	0.941	0.930	278	F
15	74	M	Sq	Middle lobectomy + Upper segmentectomy	196.5	191.5	1.001	0.943	462	G
16	55	M	Ad	Right middle lobectomy	197.5	189.5	1.055	0.971	253	G
17	54	M	Ad	Right upper lobectomy[b]	195.0	194.0	0.917	0.924	96	G
18	46	M	Sq	Left upper lobectomy[b,c]	209.0	212.0	1.000	1.000	210	F
19	61	M	Sq	Left upper lobectomy[c]	201.0	192.0	0.968	0.920	397	G
20	66	M	Sq	Left upper segmentectomy	198.0	192.5	1.000	0.965	323	G
21	64	M	Sq	Lower and middle bilobectomy[b]	206.5	205.0	1.062	0.985	180	F
22	59	F	Sq	Left pneumonectomy[c]	198.0	193.5	1.076	1.000	139	F
23	56	M	Sq	Left lower lobectomy	195.5	190.5	0.944	0.943	270	G
24	39	F	Ad	Right upper lobectomy	197.0	183.0	0.933	0.866	182	G
25	48	M	Sq	Lower left lobectomy + lingulectomy	205.0	198.0	1.055	1.000	167	G
26	69	M	Sq	Left pneumonectomy[c]	199.0	189.0	0.994	0.943	270	G
27	70	M	Sq	Right lower lobectomy	207.5	189.0	1.060	0.940	215	G
28	69	M	Ad	Right lower lobectomy	207.5	188.5	1.055	0.945	212	G
29	69	M	Sq	Left pneumonectomy[c]	203.0	190.5	1.085	0.930	190	G
30	67	M	Sq	Right pneumonectomy[c]	198.0	192.0	0.969	0.950	192	G
31	53	M	Sq	Left upper lobectomy	204.0	190.0	1.103	0.956	92	G
32	61	F	Ad	Left upper lobectomy	203.5	193.5	1.067	1.000	137	G
33	60	M	Ad	Left upper lobectomy	198.0	192.0	0.986	0.935	116	G
34	64	M	Sq	Right upper lobectomy	197.0	186.0	1.052	0.966	193	G
35	62	M	Sq	Right lower lobectomy	202.0	191.0	1.044	0.940	160	G
36	67	M	Ad	Right upper lobectomy	200.5	189.0	1.008	0.916	165	G
37	63	F	Lc	Left pneumonectomy[b,c]	203.0	202.0	1.068	1.072	110	G
38	67	M	Ad	Right upper lobectomy	204.0	194.4	1.066	0.933	138	G
39	59	M	Sq	Left lower lobectomy	198.5	190.0	1.022	0.940	162	G
40	66	M	Sq	Right lower lobectomy	203.5	193.0	1.043	0.923	144	G

HIST: histology of the tumor (Sq = squamous; Ad = adenocarcinoma; and Lc = large cells); PRE-HA: preoperative hyponychial angle; POST-HA-3: late postoperative hyponychial angle; PRE-DPD/IPD: preoperative distal phalangeal depth/interphalangeal depth ratio; POST-DPD/IPD-3: late postoperative distal phalangeal depth/interphalangeal depth ratio; POSTOP: postoperative day of assessment; and EVOL: postoperative evolution (G = good and F = fair). [a]Hyponychial angle (HA) expressed in degrees, and distal phalangeal depth/interphalangeal depth ratio (R) expressed in millimeters. [b]No reversal of digital clubbing. [c]Postoperative radiotherapy. [d]late postoperative death.

Numerical variables with homogeneity of variance were compared using mean tests (t test or ANOVA), whereas proportions were compared using the chi-square test or Kruskal-Wallis H-test. Pearson's correlation test was used to evaluate HA and DPD/IPD. A significance level of 5% was adopted.

In our review of the literature (1917-2007), we examined 87 references, in which 248 patients were studied (246 treated and 2 untreated). Of those 248 patients, 170 had lung cancer. In the collective sample of those 87 references (n = 248), there were 197 cases of improvement of HOA, 45 cases of reversal of DC, and 6 cases of HOA symptoms and disappearance of DC. The 52 cases (collected from 32 references) in which reversal of DC was explicitly reported between 1954 and 2007 are listed in Table 1. Only 5 of them were lung cancer cases.[25-27,29,30]

The study was approved by the Postgraduate Program Committee of the institution, and written informed consent was obtained from all patients.

Results

The preoperative and postoperative HA and DPD/IPD in the 40 patients with DC and lung cancer are presented in Table 2, and the characteristics of those 40 patients are presented in Table 3. The level of inter-rater reliability of the measurements in the preoperative and in the late postoperative periods was high (p = 0.953). In comparison to the preoperative measurements, there was a significant decrease in HA and DPD/IPD in the late postoperative period (after day 90), and this is also photographically illustrated in one case (Figure 1).

In 33 (82.5%) of the patients in the DC group, late postoperative HA and DPD/IPD

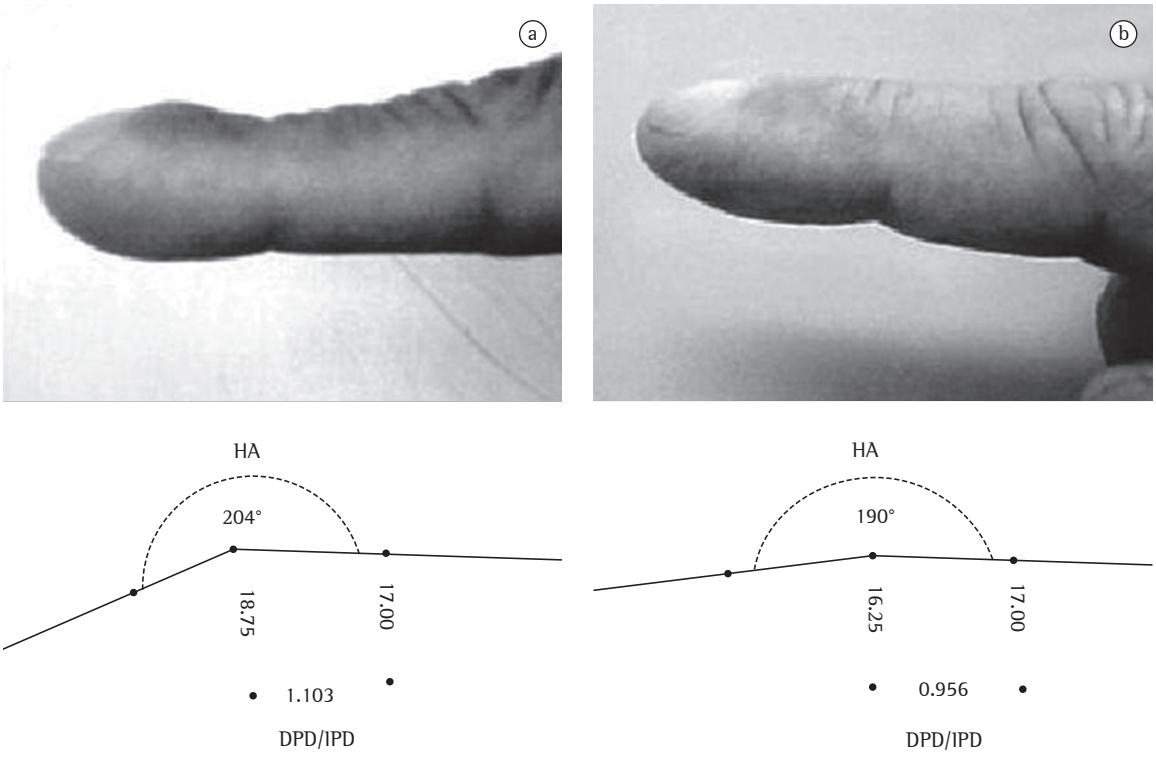

Figure 1 - a) Clinically evident clubbing observed in the index finger; and b) significant reversal of the clinical sign found 92 days after resection of a lung cancer (case 31). Note the corresponding hyponychial angle (HA) and distal phalangeal depth/interphalangeal depth (DPD/IFD) ratio measurements of the index finger (shadow images). HA expressed in degrees; and DPD/IFD ratio expressed in millimeters.

decreased, and, in 23 of those 33, HA levels decreased to normal (183.0-191.5°). In 7 patients (cases 7, 9, 13, 17, 18, 21 and 37)—6 with an unfavorable post-treatment evolution—HA and DPD/IPD either did not change or increased. Of those 7 patients, 3 also received postoperative radiotherapy. Excluding these 7 cases in which no reversal of DC was observed, in the remaining 33 cases, POST-HA-3 (191.1 ± 3.8°) and POST-DPD/IPD-3 (0.946 ± 0.030 mm) were much different ($p < 0.0001$) from the corresponding higher preoperative values.

The late postoperative measurements (after day 90) in the DC group showed a weak correlation with the moment in which they were performed ($r = -0.13$ for POST-HA-3; and $r = -0.27$ for POST-DPD/IPD-3). However, a good correlation ($r = 0.72$) between HA and DPD/IPD was observed.

No significant late postoperative changes (after day 90) were detected in the control group: PRE-HA was 184.5 ± 5.5° and POST-HA-3 was 185.5 ± 5.8° ($p = 0.643$); PRE-DPD/IPD was 0.937 ± 0.046 mm and POST-DPD/IPD-3 was 0.952 ± 0.049 mm ($p = 0.310$).

Figure 2 illustrates the preoperative and postoperative HA and DPD/IPD found in the DC group and in the control group.

No age- or gender-related differences were found in the postoperative HA or DPD/IPD. Nor were there any differences related to preoperative symptoms, tumor histology, clinical staging, or site of the pulmonary lesion.

It was of note, however, that, for clinical comparisons, recollection of pre-treatment finger aspect, particularly in the late postoperative period, presented difficulties to the observer who worked in both moments.

Discussion

In this study, through the use of objective measurements, we documented reversal of DC in patients with lung cancer treated by pulmonary resection. Most of the cases of reversal reported in the literature are cases of clinically observed improvement of osteoarthropathy symptoms.[8,24] In the review of the 52 cases of several treated diseases in which reversal of DC was explicitly mentioned, we found that the reports usually refer to clinically verified cases, with few studies presenting an objective evaluation of the changes in clinical signs.[14,20,28]

In the present series, it was found that a significant decrease in the anatomical changes in the fingers occurred in most of the patients in the DC group, which was documented by the lower HA and DPD/IPD found in the late postoperative period (after day 90). This is in agreement with previous reports on the subject, in which patients with extrathoracic[4,5] or pulmonary lesion, particularly lung cancer,[26,29] were found to present post-treatment reversal of DC. However, no postoperative changes were detected in the patients in the control group, as expected.

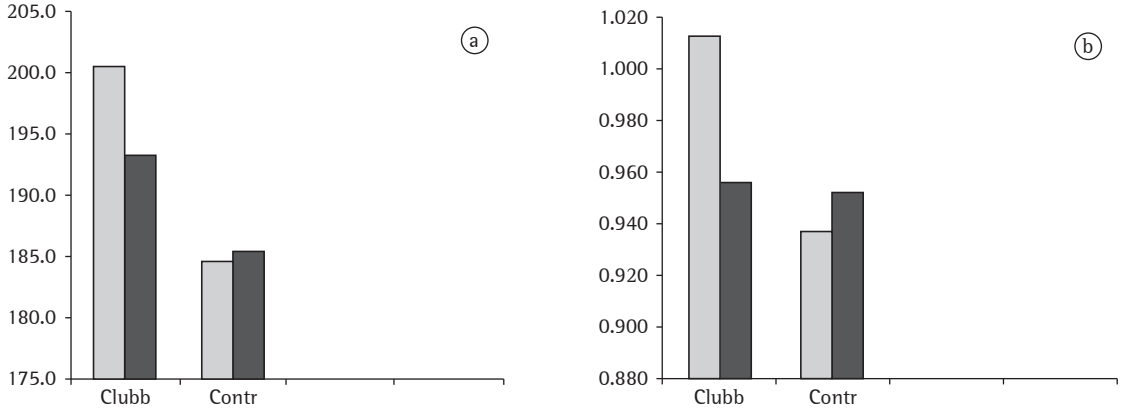

Figure 2 - a) Preoperative (□) and postoperative (■) hyponychial angle (expressed in degrees); and b) Preoperative (□) and postoperative (■) distal phalangeal depth/interphalangeal depth ratio (expressed in millimeters). Significant differences ($p < 0.001$) in the clubbing group (Clubb); no differences in the control group (Contr).

The use of tested objective measurement criteria[1,16] certainly is an advantage over the subjective clinical impression, with its inherent difficulties for comparisons of the late postoperative appearance of the fingers with their preoperative aspect. The method employed for the production and registration of images of the fingers,[21] exploring the shadow projection, similar to others previously reported,[18] is also very simple and easy to perform.

The reversal changes in the fingers of the patients in the DC group were not observed in the immediate (by day 7) or recent (by day 18) postoperative periods, but only later, after day 90. It must be considered, however, that no measurements were performed between postoperative days 30 and 90. These non-immediate postoperative changes in DC have also been reported by others.[25] Nevertheless, it is possible that the most significant anatomical reversal changes in the fingers can occur earlier, before postoperative day 90, as occurred in 2 of the 3 cases of transplanted cystic fibrosis patients reported by Augarten et al.[28] This is also suggested in the present series by the lack of correlation between the values measured and the moment of their verification in the late postoperative period. Being mainly associated with hand edema and tremor, the difficulties in performing the measurements during the early postoperative phases must also be stressed, and they certainly hinder the premature evaluations.

The reversal of DC occurred in most (82.5%) of the 40 patients who had the clinical sign. In 23 cases, the HA returned to normal values. However, in 7 patients, 6 of whom presented an unfavorable postoperative evolution, the changes in DC progressed or remained unchanged. The absence of improvement of HOA symptoms or change in DC is registered in cases of treated tumors when the underlying condition is not controlled or if it returns,[29] which can mean poor post-treatment prognosis.

Age, gender, preoperative symptoms, tumor histology, clinical staging, and site of the pulmonary lesion did not appear to influence the reversal of DC.

In addition, the good correlation between HA and DPD/IPD indicates that either one or the other of these objective criteria can be used for objective evaluation of reversal of DC.

References

1. Spicknall KE, Zirwas MJ, English JC 3rd. Clubbing: an update on diagnosis, differential diagnosis, pathophysiology, and clinical relevance. J Am Acad Dermatol. 2005;52(6):1020-8.
2. Dickinson CJ. Lung diseases associated with digital clubbing. Clin Exp Rheumatol. 1992;10(Suppl 7):23-5.
3. Garg N, Kandpal B, Garg N, Tewari S, Kapoor A, Goel P, et al. Characteristics of infective endocarditis in a developing country-clinical profile and outcome in 192 Indian patients, 1992-2001. Int J Cardiol. 2005;98(2):253-60.
4. Stoller JK, Moodie D, Schiavone WA, Vogt D, Broughan T, Winkelman E, et al. Reduction of intrapulmonary shunt and resolution of digital clubbing associated with primary biliary cirrhosis after liver transplantation. Hepatology. 1990;11(1):54-8.
5. Kitis G, Thompson H, Allan RN. Finger clubbing in inflammatory bowel disease: its prevalence and pathogenesis. Br Med J. 1979;2(6194):825-8.
6. Vanhoenacker FM, Pelckmans MC, De Beuckeleer LH, Colpaert CG, De Schepper AM. Thyroid acropachy: correlation of imaging and pathology. Eur Radiol. 2001;11(6):1058-62.
7. Fischer DS, Singer DH, Feldman SM. Clubbing, a review, with emphasis on hereditary acropachy. Medicine (Baltimore). 1964;43:459-79.
8. Stenseth JH, Clagett OT, Woolner LB. Hypertrophic pulmonary osteoarthropathy. Dis Chest. 1967;52(1):62-8.
9. Atkinson S, Fox SB. Vascular endothelial growth factor (VEGF)-A and platelet-derived growth factor (PDGF) play a central role in the pathogenesis of digital clubbing. J Pathol. 2004;203(2):721-8.
10. Atkinson S, Fox SB. Vascular endothelial growth factor (VEGF)-A and platelet-derived growth factor (PDGF) play a central role in the pathogenesis of digital clubbing. J Pathol. 2004;203(2):721-8.
11. Currie AE, Gallagher PJ. The pathology of clubbing: vascular changes in the nail bed. Br J Dis Chest. 1988;82(4):382-5.
12. Huckstep RL, Bodkin PE. Vagotomy in hypertrophic pulmonary osteoarthropathy associated with bronchial carcinoma. Lancet. 1958;2(7042):343-5.
13. Kaditis AG, Nelson AM, Driscoll DJ. Takayasu's arteritis presenting with unilateral digital clubbing. J Rheumatol. 1995;22(12):2346-8.
14. Mito K, Maruyama R, Uenishi Y, Arita K, Kawano H, Kashima K, et al. Hypertrophic pulmonary osteoarthropathy associated with non-small cell lung cancer demonstrated growth hormone-releasing hormone by immunohistochemical analysis. Intern Med. 2001;40(6):532-5.
15. Lovibond JL. Diagnosis of clubbed fingers. Lancet 1938;1:363-4.
16. Regan GM, Tagg B, Thomson ML. Subjective assessment and objective measurement of finger clubbing. Lancet. 1967;1(7489):530-2.
17. Waring WW, Wilkinson RW, Wiebe RA, Faul BC, Hilman BC. Quantitation of digital clubbing children. Measurements of casts of the index finger. Am Rev Respir Dis. 1971;104(2):166-74.
18. Bentley D, Moore A, Shwachman H. Finger Clubbing: A quantitative survey by analysis of the shadowgraph. Lancet. 1976;2(7978):164-7.
19. Husarik D, Vavricka SR, Mark M, Schaffner A, Walter RB. Assessment of digital clubbing in medical inpatients by

digital photography and computerized analysis. Swiss Med Wkly. 2002;132(11-12):132-8.
20. Mellins RB, Fishman AP. Digital casts for the study of clubbing of the fingers. Circulation. 1966;33(1):143-5.
21. Moreira JS, Porto NS, Moreira AL. Objective evaluation of clubbing on shadow images of index fingers. A study of patients with pulmonary disease and of normal individuals. J Bras Pneumol. 2004;30(2):126-33.
22. Sly RM, Ghazanshahi S, Buranakul B, Puapan P, Gupta S, Warren R, et al. Objective assessment for digital clubbing in Caucasian, Negro, and Oriental subjects. Chest. 1973;64(6):687-9.
23. Markman M. Response of paraneoplastic syndromes to antineoplastic therapy. West J Med. 1986;144(5):580-5.
24. Shih WJ. Pulmonary hypertrophic osteoarthropathy and its resolution. Semin Nucl Med. 2004;34(2):159-63.
25. Yamamoto H, Abe O, Yoneyama T, Ishikawa S, Honma H. [Disappearance of the symptoms of clubbing of fingers and toes following the surgery of lung cancer][Article in Japanese]. Kyobu Geka. 1970;23(3):177-83.
26. Fukumoto H, Nishimoto T, Morita H. [A case of hypertrophic pulmonary osteoarthropathy caused by adenocarcinoma of the lung][Article in Japanese]. Nippon Kyobu Geka Gakkai Zasshi. 1992;40(7):1161-5.
27. Lamme B, Spoelstra FO, Lastdrager WB. [Diagnostic image (144) A man with clubbing of fingers. Hypertrophic osteoarthropathy(Pierre-Marie-Bambergersyndrome)][Article in Dutch]. Ned Tijdschr Geneeskd. 2003;147(25):1216.
28. Augarten A, Goldman R, Laufer J, Szeinberg A, Efrati O, Barak A, et al. Reversal of digital clubbing after lung transplantation in cystic fibrosis patients: a clue to the pathogenesis of clubbing. Pediatr Pulmonol. 2002;34(5):378-80.
29. Yang WC, Lin SC, Liu TC, Chen CJ, Yen JH, Ou TT, et al. Clubbed fingers and hypertrophic osteoarthropathy in a patient with squamous cell carcinoma of the lung. Kaohsiung J Med Sci. 2003;19(4):183-7.
30. Pujol JL, Noyola A, Parrat E, Dan-Aouta M, Godard P. [Regression of hippocratic fingers during chemotherapy of bronchial cancer][Article in French]. Rev Pneumol Clin. 1991;47(1):57-8.