

Pulmonary capillary blood volume in patients with probable pulmonary Kaposi's sarcoma

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Abstract

Background – An increase in pulmonary capillary blood volume secondary to angiogenesis has been described in Kaposi's sarcoma. The value of the pulmonary capillary blood volume as an early marker of pulmonary Kaposi's sarcoma was evaluated.

Methods – In a prospective study 45 HIV positive patients (nine asymptomatic for Kaposi's sarcoma, 29 with cutaneous or mucocutaneous Kaposi's sarcoma, and seven with pulmonary Kaposi's sarcoma), underwent pulmonary function tests and determination of transfer capacity for carbon monoxide (TLCO) with its components, pulmonary capillary volume and membrane factor.

Results – Total lung capacity (TLC), TLCO, and its components were similar in the three groups. TLCO was normal in patients with pulmonary Kaposi's sarcoma and no changes in membrane factor or pulmonary capillary volume were observed.

Conclusion – Pulmonary function tests and pulmonary capillary volume alone are not useful for identifying patients with pulmonary Kaposi's sarcoma.

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Keywords: pulmonary Kaposi's sarcoma, HIV, pulmonary capillary blood volume.

Pulmonary Kaposi's sarcoma is the most common non-infectious pulmonary manifestation of the acquired immunodeficiency syndrome (AIDS). Its frequency is uncertain because diagnosis requires histopathological proof. It has been estimated to occur in 20% but necropsies have shown pulmonary Kaposi's sarcoma in 55% of patients with AIDS and systemic Kaposi's sarcoma.¹

Clinical symptomatology, chest radiographs, and computed tomographic (CT) scans are helpful for diagnosing pulmonary Kaposi's sarcoma but are not specific. Fibreoptic bronchoscopy remains the most sensitive technique available.

An increase in pulmonary capillary blood volume (Vc) has been measured in some patients with AIDS and cutaneous Kaposi's sarcoma including two who had probable pulmonary involvement.² Histological studies have shown an increase in the number of capillary vessels in patients with pulmonary Kaposi's sarcoma suggestive of angiogenesis.³ Given the vascular nature of the tumour proliferation in Kaposi's sarcoma, we reasoned that even occult

pulmonary localisations of Kaposi's sarcoma might cause an increase of Vc, irrespective of the overall value of transfer factor for carbon monoxide (TLCO).

It is important to diagnose pulmonary Kaposi's sarcoma early because it may respond to chemotherapy. The aim of this study was to evaluate TLCO and its components – that is, pulmonary capillary blood volume (Vc) and membrane factor (Dm) – as an early marker of pulmonary Kaposi's sarcoma in HIV infected men.

Methods

PATIENTS

Forty five men from the Hôpital Bichat-Claude Bernard infected with HIV were included in a prospective study between January and August 1993. The study was approved by the ethics committee of our institution and all the patients gave their written informed consent.

The following patients were not eligible for inclusion: intravenous drug abusers, patients with a history of *Pneumocystis carinii* pneumonia or with concomitant bronchopulmonary infection, and patients who had received more than 120 mg bleomycin.

The patients were divided into three groups. Control patients were divided into groups 1 and 2 according to the following criteria: group 1 – nine asymptomatic patients with HIV infection and no manifestation of Kaposi's sarcoma, and group 2 – 29 patients with cutaneous Kaposi's sarcoma and no documented pulmonary involvement (normal chest radiograph, normal high resolution CT scan, and normal appearance at fibreoptic bronchoscopy). Group 3 consisted of seven patients with proven or probable pulmonary Kaposi's sarcoma on the basis of (1) proven pulmonary Kaposi's sarcoma diagnosed by open biopsy or trans-bronchial biopsies, or (2) probable pulmonary Kaposi's sarcoma in whom histological confirmation could not be obtained for ethical reasons but with the following criteria:

- (i) other lesions of Kaposi's sarcoma (cutaneous and/or mucosal);
- (ii) characteristic chest radiographic features including peribronchial infiltrates and/or disseminated nodules, and characteristic high resolution CT scans;
- (iii) characteristic endobronchial lesions with erythematous patches and raised purpuric lesions at bronchoscopy; and
- (iv) elimination of other pulmonary diseases (*Pneumocystis carinii* pneumonia by the induced sputum technique or broncho-alveolar lavage (BAL); mycobacterial

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infections by negative cultures of gastric secretions or BAL fluid; pulmonary cryptococcal infection by negative testing for soluble antigen in blood; lymphoma by normal bone marrow biopsy examination and the clinical course).

PULMONARY FUNCTION TESTS

Spirometric tests were performed using a water-sealed spirometer (Pulmonet III, Godart, Bithoven, The Netherlands). Forced expiratory volume in one second (FEV₁) and vital capacity (VC) were measured and the FEV₁/VC ratio was calculated. Functional residual capacity (FRC) was determined by the helium dilution method. Total lung capacity (TLC) was expressed as a percentage of predicted values in terms of sex, age, and stature (ECCS, 1983).

Blood gas tensions were measured with an ABL 500 (Radiometer, Copenhagen, Denmark) and haemoglobin was measured by spectrophotometry using an arterial blood sample (OSM3 Radiometer). The alveolar arterial difference for PO₂ (A-aPO₂) was either calculated using the Rahn equation or measured using a rapid oxygen analyser (OM-11, Sensor-medics, California, USA) during sampling.

The transfer capacity for carbon monoxide (TLCO) was measured by the single breath method of Ogilvie and coworkers as modified by Cotes (Masterlab Jaeger, Germany)⁴ and the transfer coefficient (Kco) – that is, TLCO corrected for alveolar volume – was calculated.

The two components of the transfer factor were determined using the equation originally used by Roughton and Forster⁵:

$$1/\text{TLCO} = 1/\text{Dm} + 1/\theta \cdot \text{Vc}$$

where Dm (mmol/min/kPa) is the diffusing capacity of the alveolar capillary membrane and Vc (ml) is the capillary blood volume. θ is the reaction rate of carbon monoxide with oxyhaemoglobin.

TLCO values were corrected for the concentration of haemoglobin according to the method of Cotes.⁶ TLCO and its components were measured in nine healthy young men and the results confirmed the predicted values of Cotes:

$$1/\text{Dm pred} = -0.054 \text{ h} + 0.0036 \text{ a} + 0.035$$

$$1/\text{Vc pred} = -0.0201 \text{ h} + 0.047$$

where h is height (in metres) and a is age (in years). Values are valid for men.

Bronchoscopy with BAL and endobronchial biopsies were performed in patients when possible (n = 36).

STATISTICAL ANALYSIS

Statistically significant differences (p < 0.05) were identified by using analysis of variance.

Results

TLC, TLCO and Kco values were within the normal range and did not differ between the three groups (table 1). FEV₁/VC was significantly lower in patients in group 2 than in control group 1. Dm and Vc, expressed as a percentage of predicted values, were lower in patients in group 3 but there was no significant difference between the three groups.

The clinical, radiological, and pulmonary function tests results of patients in group 3 are summarised in table 2.

Discussion

In this study values of pulmonary function tests and, specifically, Vc were evaluated as potential early markers of pulmonary Kaposi's sarcoma in three groups of HIV infected patients. Patients receiving more than 120 mg bleomycin were excluded although Vc values do not significantly change between 0 and 150 mg.⁷

Spirometric parameters, apart from FEV₁/VC, were normal in all the patients, contrary to previous data.⁸ In particular, FEV₁/VC showed similar small alterations in patients in groups

Table 1 Mean (SD) results of pulmonary function tests

	Control group 1 (n = 9) HIV without KS	Control group 2 (n = 29) Cutaneous or mucocutaneous KS	Group 3 (n = 7) Pulmonary KS	p
Age (years)	35.4 (6.3)	37.8 (9.3)	35.9 (4.9)	NS
CD4/mm ³	290 (285)	85.8 (102)	11.0 (7.1)	0.001
TLC (% pred)	96.7 (10.1)	91.4 (11.3)	90.7 (10.7)	NS
FEV ₁ /VC (%)	81.9 (5.6)	77.3 (7.4)	69.1 (5.9)	<0.005
Kco (% pred)	83.4 (6.2)	85.2 (9.5)	87.4 (11.0)	NS
A-aPO ₂ (kPa)	1.70 (1.2)	1.70 (0.7)	3.20 (1.8)	0.005
Vc (% pred)	101.9 (9.1)	89.9 (18.3)	83.2 (12.6)	NS
Dm (% pred)	86.9 (13.6)	80.0 (16.9)	76.6 (18.5)	NS

CD4 = counts for lymphocytes CD4 cells; TLC = total lung capacity; FEV₁/VC = forced expiratory volume in one second reported on vital capacity; Kco = transfer lung factor corrected for alveolar volume; A-aPO₂ = alveolar arterial gradient for PO₂; Vc = capillary blood volume; Dm = membrane factor; KS = Kaposi's sarcoma.

Table 2 Characteristics of patients with pulmonary Kaposi's sarcoma

Patient no	Clinical H C D	CD4 (/mm ³)	Bronchoscopy	HRCT	TLC (% pred)	FEV ₁ /VC	Kco (% pred)	Vc (% pred)	Dm (% pred)	Tobacco (pack/years)
1	+ +	7	—	Disseminated nodules + PBVT	81.4	69.0	67.5	68.0	48.3	12
2	0 0 0	4	OLB + 1 lesion	Nodules	92.1	73.0	90.7	77.0	76.4	0
3*	+ 0 0	43	1 tracheal lesion	Disseminated nodules	102.2	75.0	92.8	101.8	91.6	0
4*	0 + +	11	Diffuse lesions	Parenchymatous condensations	87.0	67.0	101	68.0	73.2	22
5*	0 + 0	15	Unilateral diffuse lesions	Disseminated nodules	97.0	71.0	87.4	88.0	74.5	0
6*	0 + 0	26	Diffuse lesions	Disseminated nodules + PBVT	75.0	57.0	79.0	90.2	65.5	13
7	0 0 0	10	Unilateral localisations	Disseminated nodules	100.0	72.0	93.5	89.4	106.4	0

H = haemoptysis; C = cough; D = dyspnoea; OLB = open lung biopsy; HRCT = high resolution computed tomography; TLC = total lung capacity; Kco = transfer lung factor corrected for alveolar volume; Vc = capillary blood volume; Dm = membrane factor; PBVT = peribronchial vascular thickening.

* Bleomycin (<120 mg cumulative value).

2 and 3. This may be related to smoking habits which were similar in the two groups. Nevertheless, in the few smokers in group 3 (patients 1, 4, 6) relatively severe airways obstruction could not be related only to smoking. Peribronchial lesions of pulmonary Kaposi's sarcoma may induce obstruction. High resolution CT scanning showed that airway diameter was not altered by peribronchovascular thickening but scans were performed at full inspiration and airways may be more collapsible during expiration. Moreover, patients with pulmonary Kaposi's sarcoma were evaluated at the beginning of pulmonary involvement in order to evaluate pulmonary capillary volume as a marker of pulmonary Kaposi's sarcoma. This explains why no cases of restrictive lung function were observed in our population. For the same reasons, KCO was within the normal range in patients in group 3. Contrary to previous findings,² the pulmonary capillary blood volume in the patients with pulmonary Kaposi's sarcoma was normal. The preliminary results of Similowski *et al* were not sufficiently documented with regard to pulmonary Kaposi's sarcoma. Histologically characteristic lesions of pulmonary Kaposi's sarcoma depict an increase in the number of capillary vessels. Such vessels were found either near an intact surface epithelium or situated more deeply.⁹ In one patient in whom the diagnosis of pulmonary Kaposi's sarcoma was confirmed by open lung biopsy similar histological lesions were seen. The increase in the number of capillary vessels could induce an increase in capillary blood volume. However, the ability of these new blood vessels to participate in gas exchange is unknown. Cotes' method allows pulmonary capillary blood volume, a factor involved in gas exchange, to be determined. Our findings suggest that angiogenesis does not contribute to capillary blood volume augmentation as measured by the method of Cotes. Indeed, histological studies have shown that capillaries are often wide or filled with crushed endothelial cells in pulmonary Kaposi's sarcoma.

High resolution CT scans revealed characteristic features of pulmonary Kaposi's sarcoma including scattered pulmonary macro-

nodules with spindle-shaped outlines associated with peribronchial vascular thickening. The involvement of pulmonary Kaposi's sarcoma was depicted as 50% for maximal peribronchial vascular thickening, 25% for distal peribronchial vascular thickening, and 83% for nodules (unpublished data). The disease process of pulmonary Kaposi's sarcoma appeared to be both interstitial and interlobular.

Clinical features of pulmonary Kaposi's sarcoma may be not specific and could resemble those of pulmonary infection. In group 3 pulmonary capillary volume and membrane factor were slightly decreased. Murray *et al*¹⁰ have reported a decrease in pulmonary capillary blood volume associated with a profound decrease in KCO and membrane factor in patients with AIDS and *Pneumocystis carinii* pneumonia. This infection was not involved in the deterioration of transfer factor parameters in our study as the BAL fluid was negative and both pulmonary capillary volume and membrane factor were only slightly decreased.

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- 1 Meduri GU, Stover DE, Lee M, Myskowski PL, Caravelli JF, Zaman MB. Pulmonary Kaposi's sarcoma in the acquired immune deficiency syndrome. *Am J Med* 1986;**81**:11-18.
- 2 Zetter BR. Angiogenesis. State of the art. *Chest* 1988;**93**:159-66S.
- 3 Similowski T, Regnard J, Dinh Xuan AT, Lockhart A. Increased pulmonary capillary volume during AIDS-related Kaposi's sarcoma (KS). *Vth International Conference on AIDS*. Montreal, June 1989, Abstract WBO22.
- 4 Ogilvie CM, Forster RE, Blakemore WS, Morton JW. A standardized breath holding technique for the clinical measurement of the diffusing capacity of the lung for carbon monoxide. *J Clin Invest* 1957;**36**:1-17.
- 5 Roughton FJW, Forster RE. Relative importance of diffusion and chemical reaction rates in determining rate of exchange of gases in human lung, with special reference to true diffusing capacity of pulmonary membrane and volume of blood in the lung capillaries. *J Appl Physiol* 1957;**11**:290-302.
- 6 Cotes JE. *Lung function*. 4th edn. Boston: Blackwell Scientific Publications, 1979.
- 7 Luursemma PB, Star-Kroesen MA, Van Der Mark ThW, Sleyfer DT, Schraffordt Koops H, Peset R. Bleomycin-induced changes in carbon monoxide transfer factor of the lungs and its components. *Am Rev Respir Dis* 1983;**128**: 880-3.
- 8 Miller RF, Tomlinson MC, Cottrill CP, Donald JJ, Spittle MF, Semple SJG. Bronchopulmonary Kaposi's sarcoma in patients with AIDS. *Thorax* 1992;**47**:721-5.
- 9 Fourret PJ, Touboul JL, Mayaud CM, Akoun GM, Roland J. Pulmonary Kaposi's sarcoma in patients with acquired immunodeficiency syndrome: a clinicopathological study. *Thorax* 1987;**42**:262-8.
- 10 Sankary RM, Turner J, Lipavsky A, Howes EL, Murray JF. Alveolar-capillary block in patients with AIDS and *Pneumocystis carinii* pneumonia. *Am Rev Respir Dis* 1988;**137**:443-9.