

Finger clubbing in cystic fibrosis

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SUMMARY Finger clubbing was measured in 73 of 105 patients with cystic fibrosis undergoing full assessment. The sign correlated well with the chest x ray score and indices of pulmonary function and infection but not with weight, height, age, liver function, or degree of fat malabsorption. The presence of clubbing suggests appreciable pulmonary involvement. Most probably its progression indicates a deterioration in pulmonary state. In both instances increased efforts should be made to treat the infection.

The aetiology of finger clubbing is still poorly understood, despite being fairly common, but its clinical associations are well known. For some time it has been recognised as a feature of cystic fibrosis, together with the rarer hypertrophic pulmonary osteoarthropathy.¹ Cystic fibrosis is a multisystem disorder and produces many pathological processes. Primarily these involve the lung, with recurrent infection, airway obstruction, bronchiectasis, fibrosis, and ultimately respiratory failure. In addition, there is malabsorption due to pancreatic dysfunction, liver cirrhosis, and portal hypertension. All of these separate processes can be individually associated with finger clubbing.

Two methods of quantifying the degree of clubbing have been reported. One requires the production of a finger cast to measure the ratio of depths of the distal phalanx at the nail fold and the distal interphalangeal joint.^{2 3} The other involves measurement of the hyponychial angle obtained from the projected lateral shadow of the finger.⁴

In this report the degree of clubbing in patients with cystic fibrosis is compared with other clinical and laboratory variables to evaluate the relation between the sign and the other features of the disease.

Method

Patients with cystic fibrosis referred to this hospital undergo a comprehensive assessment to determine their present condition and as a guide to planning future management.⁵ This is repeated at intervals to monitor treatment and progress. In this report information from the first assessment of each patient has been used.

Clubbing was correlated with the age at assess-

ment and at diagnosis, growth, respiratory function, infection, liver function, and malabsorption. Details of the methods used are described below.

Clubbing. A modified version of the shadowgram method described by Bentley⁴ was used with an overhead projector.⁶ The hyponychial angle rather than the profile angle was taken as this is more reliable.⁴ A second simple clinical score of clubbing was also recorded by the examiner and graded from 0 to 3 according to severity.

Growth. The weight and height were assessed as standard deviation scores.^{7 8}

Respiratory function. Forced expiratory volume in one second and forced vital capacity were recorded using a Vitalograph dry spirometer and then expressed as a percentage of the mean value predicted for height.⁹ The chest x ray was scored from 0 to 38 according to the method of Chrispin and Norman.¹⁰

Infection. The serum immunoglobulin (IgG) concentration was chosen as a single objective measurement of the response to pulmonary infection. In our own series of patients there is a strong relation between high serum immunoglobulin concentrations and other measures of pulmonary infection not enumerated here, which is supported by other reports.^{11 12}

Liver function. The alanine aminotransferase activity was taken as a sign of hepatocellular injury.

Malabsorption. Dietary fat balance was measured from a two day faecal fat collection, which followed a five day run in period using ingested polyethylene

glycol as a marker.¹³ Dietary assessment of fat intake was made over the same period. The results were expressed as percentage fat absorption. During this time patients were on their usual pancreatic enzyme supplements.

All patients were understood to be in a reasonably steady clinical state and were seen on an outpatient basis.

Results

At the time of this survey 105 patients had had a full assessment; a satisfactory shadowgram permitting an accurate measurement of the hyponychial clubbing angle was recorded in 73. The median hyponychial clubbing angle was 192 degrees (range 176 to 213). The median age at assessment was 8.0 years (range 1.1 to 25.6 years) and at diagnosis was 0.4 years (range 0 to 13 years).

Variables for each individual were measured and

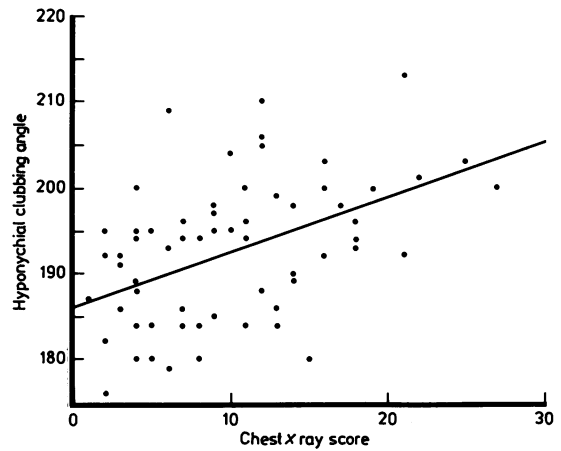


Figure Relation between the measured angle of clubbing and the Chrispin-Norman chest x ray score¹⁰ in patients with cystic fibrosis

Table 1 Median values and ranges for clubbing angle and clinical variables taken from first assessment for each child

Variable	n	Median	Range
Weight standard deviation score	73	-1.07	-3.56 to +2.83
Height standard deviation score	73	-0.93	-4.29 to +1.64
% Expected forced expiratory volume in one second	40	60	15-105
% Expected forced vital capacity	40	68	27-102
Chest x ray score*	72	8	0-27
Immunoglobulin IgG (g/l)	70	13	6-30
Alanine aminotransferase activity (IU/l)	67	29	3-76
% Fat absorption	52	71	21-100

*Calculated according to Chrispin and Norman.¹⁰

Table 2 Correlation between clinical variables and hyponychial clubbing angle

Variable	n	Spearman's coefficient of correlation	p Value
Chest x ray score	72	0.56	<0.0001
Immunoglobulin IgG	70	0.47	<0.01
% Predicted forced expiratory volume in one second	40	-0.42	<0.01
% Predicted forced vital capacity	40	-0.47	<0.01
Age at diagnosis	72	0.33	0.01 > p > 0.05
Age at assessment	72	0.26	0.01 > p > 0.05
Height standard deviation score	72	0.26	0.01 > p > 0.05
Weight standard deviation score	73	-0.24	0.01 > p > 0.05
Alanine aminotransferase activity	67	-0.13	None
% Fat absorption	51	0.02	None

correlated against the degree of clubbing, the results being displayed in Tables 1 and 2. The Figure shows the relation between the measured angle of clubbing and the Chrispin-Norman chest x ray score. All correlations were performed using a non-parametric test, Spearman's rank correlation method corrected for ties. The most positive and significant factors were in the following order; Chrispin-Norman chest x ray score (coefficient of correlation (rs) 0.56, p<0.0001); IgG concentration (rs 0.47, p<0.01); % predicted forced vital capacity (rs -0.47, p<0.01), and % predicted forced expiratory volume in one second (rs -0.42, p<0.01). Less significant but positive correlation was shown with increasing age at diagnosis and of assessment, and negative correlations were shown with weight and height standard deviation scores (rs 0.34 or less, p<0.05). There was no correlation between clubbing and biochemical liver function or percentage fat absorption.

The simple score for degree of clubbing assessed by clinical examination had a positive correlation with the hyponychial nail fold angle of 0.55 (p<0.0001). In a larger series of 138 patients, including the 105 from which this survey derived, this simple clinical score of clubbing was compared with various factors and seemed to behave similarly to the smaller population. The correlation between degree of clubbing and the chest x ray Chrispin-Norman score was 0.64 (p<0.0001) for 136 pairs of observations.

Discussion

The data in this cross-sectional survey confirm the

conventional impression that finger clubbing indicates the presence and extent of chest involvement in cystic fibrosis. A definite positive correlation is shown between degree of finger clubbing and state of the disease, even with a crude simple clinical score. This conforms to previous accounts of clubbing in which the distribution of the hyponychial angle measurements is quite separate for normal children (mean (SD) angle 180 (4.1)) and those with cystic fibrosis (mean (SD) angle 195 (8.3)).⁴

One might infer that the degree of clubbing in the individual subject is a sign of progressive pulmonary deterioration. Early impressions from repeated measurement of some patients suggests that this is so, but further longitudinal observations are needed to validate the claim. Indeed, the degree of clubbing may possibly regress, together with clinical improvement, after intensification of treatment.

Possible mechanisms in the development of clubbing include circulating vasodilators,¹⁴ local tissue hypoxia,¹⁵ reflex stimulation of vagal pathways,¹⁶ and genetic factors.¹⁷ The final common pathway seems to be an increased blood supply to the nail bed and the distal part of the limb. Clubbing is a descriptive term, however, not a distinct pathological entity.¹⁸ In cystic fibrosis the most plausible mechanism for clubbing is a circulating vasodilator, normally removed by the lungs. This would also occur in any other condition in which systemic venous blood bypasses the pulmonary microcirculation. Prostaglandins F_{2α} and E have been suggested as possible vasodilators in cystic fibrosis.¹⁹

Hypertrophic pulmonary osteoarthropathy is not common in children with cystic fibrosis. In adults it has a variable relation with state of disease and finger clubbing. None of these patients were known to be affected. The mechanism involved may be different though related to that for clubbing. It has been suggested that hypertrophic pulmonary osteoarthropathy will be seen more as patients with cystic fibrosis achieve greater life spans.^{20 21}

There seems to be little evidence to invoke genetic factors for clubbing in this condition. The gene for cystic fibrosis is an autosomal recessive, whereas hereditary clubbing is passed on as an autosomal dominant and is very much rarer.¹⁶ There was no history of clubbing in unaffected close relatives of these patients. The state of blood gas was not assessed in these subjects so that any relation between hypoxia and finger clubbing remains conjectural. None of them were clinically cyanosed at the time of assessment, though this does not exclude such a possibility.

The evidence presented in this paper suggests that the pulmonary changes are responsible for the development of clubbing in cystic fibrosis, rather

than liver disease or pancreatic dysfunction. True differentiation of these factors is difficult as very few patients with cystic fibrosis (none in this series) are to be found with advanced liver problems or malabsorption without considerable chest disease. All these subjects were concurrently treated with enzyme and nutritional supplements, none apparently having intact pancreatic function. Apart from the biochemical disturbance measured by the alanine aminotransferase enzyme activity, none of these patients had clinically significant liver failure.

In conclusion, finger clubbing is a definite and easily observed physical sign of great clinical importance in cystic fibrosis. More widespread use of early and aggressive treatment promises a brighter future for these patients. The occurrence or progression of finger clubbing in a patient with cystic fibrosis strongly suggests suboptimal control of the chest infection and should prompt more detailed evaluation of the chest and more vigorous treatment.

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