INDIAN JOURNAL OF ORTHOPAEDICS
July 2006
*Volume 40 : Number 3 : P. 160-163*

# A reliable and simple method for identifying at start patients with tuberculosis of the spine suitable for ambulatory chemotherapy

**K Sriram, PR Somasundaram, R Parthasarathy, V Chandrasekaran**

*Tuberculosis Research Centre, Chennai*

**Background** : Ambulatory chemotherapy is very effective in the treatment of spinal tuberculosis, involving vertebral bodies, without paraplegia. However, some patients with thoracic disease could develop worsening of kyphosis. It would be helpful to predict which patients were unlikely to develop severe kyphosis.

**Methods** : Step-wise discriminant analysis on the 10-year data of 79 patients treated with ambulatory chemotherapy showed that the angle of kyphosis on admission and the site of the lesion were associated with an angle of 50 $^0$ or less at 10 years. An equation based on these factors was evolved to give a discriminant function (D) value.

**Results :** Of 51 patients with an angle of 50 $^0$ or less at 10 years, 47 had a D value of 0.499 or less, giving a predictive accuracy of 92%. Of 28 patients who had an angle of more than 50$^0$ at 10 years, 5 had a D value of 0.499 or less (false-negativity of 18%). Considering the initial angle, which was much more important ($p<0.0001$) than the site of the lesion ($P<0.03$), 46 of the patients with an angle of 50$^0$ or less at 10 years had an initial angle of 30$^0$ or less (predictive accuracy of 90%); 3 of the patients who had an angle of more than 50$^0$ at 10 years had an initial angle of 30$^0$ or less (false-negativity of 11%).

**Conclusion :** If the angle of kyphosis on admission is 30$^0$ or less, ambulatory chemotherapy could be confidently prescribed. The method is reliable and simple.

**Key-words :** Spinal tuberculosis; Choice of treatment method; Ambulatory chemotherapy; Out-patient treatment; Angle of kyphosis; Discriminant analysis.

## Introduction

Spinal tuberculosis is a common disease, especially in developing countries such as India. Ambulatory chemotherapy is very effective in patients having tuberculosis of the spine without paraplegia [1,2,3]. However, approximately 20% of patients on ambulatory chemotherapy develop severe deterioration of kyphosis [4]. This could lead to serious complications such as late–onset paraplegia [4,5,6] or cardio-respiratory failure [7]. It is therefore important to identify, at the start of treatment, patients unlikely to develop severe kyphosis. We have done extensive analyses of the data of a 10-year report on short-course chemotherapy for tuberculosis of the spine [1], to evolve a reliable method to identify at start patients who could be successfully treated with ambulatory chemotherapy.

Dr K Sriram c/o Dr PR Narayanan, Director, Tuberculosis Research Centre, Mayor V.R.Ramanathan Road, Chennai 600 031. Phone 044 28369600; E mail; mnraadha@gmail.com

## Patients and Methods

The subjects were 79 patients with tuberculosis involving the first thoracic to the second lumbar ($T_1$-$L_2$) vertebral bodies [1]. They were treated with ambulatory chemotherapy alone, namely, daily isoniazid and rifampicin, given for either 6 months (41 patients) or 9 months (38 patients). Of the 79 patients, 43 were males and 36 were aged less than 15 years. The site of the lesion was thoracic in 57 and thoraco-lumbar or lumbar (up to $L_2$) in 22. The number of vertebrae affected was 2 or less in 54 and the total vertebral body loss was 1.0 or less in 50. The angle of kyphosis on admission was 30 ° or less in 62 %; none had more than 60°. A kyphosis of 50 $^0$ or less is considered to be acceptable deformity for this study as the upper limit of normal thoracic kyphosis [8,9] is 50$^0$.

*Statistical methods:* Step-wise linear discriminant analysis [10], using the Statistical Package for Social Sciences (SPSS) software (release 4.0), was undertaken to determine the best combination of pre-treatment factors that could identify patients unlikely to have a kyphosis angle of more than 50$^0$ by 10 years. The pre-treatment factors considered were sex, age, site of lesion, number of vertebrae involved, total vertebral body loss, kyphosis angle and duration of chemotherapy. In the discriminant function equation, the appropriate pretreatment values were substituted for each patient to arrive at the discriminant function (D) value. An equation based on the angle of kyphosis on admission (A: p

<0.0001) and the site a of the lesion (a : coded as 1 for thoracic and 2 for thoraco-lumbar or lumbar) (S: $p < 0.03$) gave the best discrimination. The discriminant function equation was as follows:

$$D = 0.104 \times A + 0.743 \times S - 3.982$$

Using the theoretical critical D value of 0.500, the patients were classified as those predicted to have a kyphosis angle not exceeding $50^0$ at 10 years (D=0.499 or less) and those predicted to have a 10-year angle exceeding $50^0$ (D=0.500 or more). Considering an observed angle of $50^0$ or less at 10 years, the prediction was correct if the 10-year predicted angle was also $50^0$ or less; it was incorrect (false-positive) if the predicted angle was more than $50^0$. In the case of an observed angle of more than $50^0$ at 10 years, the prediction was correct if the 10-year predicted angle exceeded $50^0$; it was incorrect (false-negative) if the predicted angle was less than $50^0$.

## Results

Of the 79 patients, the observed angle at 10 years was $50^0$ or less in 51 patients and more than $50^0$ in 28 patients. Table I gives the prediction results based on discriminant function values. A D-value of 0.499 or less had a prediction accuracy of 92 % (95 % confidence limits: 84.8-99.5%). The false-negativity rate was 18 %.

**Table 1.** Prediction results of discriminant (D) function values based on the initial kyphosis angle (A) and the site of the lesion (S) with reference to the observed angle at 10 years

| Discriminant (D) function value | Persons having the following observed angle at 10 years : | | | |
|---|---|---|---|---|
| | $50^0$ or less | | More than $50^0$ | |
| | No | % | No | % |
| 0.499 or less [a] | 47 | 92 | 5 | 18[b] |
| 0.500 or more [c] | 4 | 8[d] | 23 | 82 |
| Total | 51 | 100 | 28 | 100 |

[a]: Corresponds to a predicted angle of $50^0$ or less at 10 years
[b]: False-negative
[c]: Corresponds to a predicted angle of more than $50^0$ at 10 years
[d]: False-positive

Since the initial angle of kyphosis was a much more important factor ($p<0.0001$) than the site of the lesion ($p< 0.03$), analyses were undertaken to assess the prediction accuracy of the angle of kyphosis on admission when considered by itself. The distribution of various initial angles with reference to an observed angle of $50^0$ or less at 10 years were scrutinized. For example (Table II), an initial angle of $25^0$ or less had a prediction accuracy of 61% only; an initial angle of $35^0$ or less had a false-negativity rate of 25 % .

**Table II.** Prediction results of different angles of kyphosis on admission with reference to the observed angle at 10 years

| Angles of kyphosis on admission [a] | Persons having the following observed angles at 10 years | | | |
|---|---|---|---|---|
| | $50^0$ or less (Correct prediction) | | More than $50^0$ (False negative) | |
| | No. | % | No. | % |
| $25^0$ or less | 31 | 61 | 2 | 7 |
| $35^0$ or less | 49 | 96 | 7 | 25 |
| Total | 51 | 100 | 28 | 100 |

[a] Corresponds to a predicted angle of $50^0$ or less at 10 years

An initial angle of $30^0$ or less gave the best overall results (Table III). Thus, it had a prediction accuracy of 90 % (95 % confidence limits: 82.0-98.4 % ) and false-negativity of 11%.

**Table III.** Prediction results of kyphosis angles on admission with reference to observed angles at 10 years

| Angles of kyphosis on admission [a] | Persons having the following observed angles at 10 years | | | |
|---|---|---|---|---|
| | $50^0$ or less | | More than $50^0$ | |
| | No. | % | No. | % |
| 30 or less [a] | 46 | 90 | 311[b] | |
| More than 30[c] | 5 | 10[d] | 25 | 89 |
| Total | 51 | 100 | 28 | 100 |

[a]: Corresponds to a predicted angle of $50^0$ or less at 10 years
[b]: False-negative
[c]: Corresponds to a predicted angle of more than $50^0$ at 10 years
[d]: False-positive

It will be of interest to know the proportion of patients having an observed kyphosis angle of $50^0$ or less at different time points after the start of treatment (Table IV). Of 49 patients having an angle of $30^0$ or less on admission, the proportion having an observed angle of $50^0$ or less was 94 % at1½ years; this figure remained steady till 10 years. Considering 30 patients with an initial angle greater than $30^0$, the proportion of patients who had an observed angle of $50^0$ or less was

**Table IV.** Percentages of patients having an observed angle of $50^0$ or less at different time points related to the kyphosis angle on admission

| Angles of kyphosis on admission [a] | Percentage of patients having an observed angles at $50^0$ or least at (years) | | | |
|---|---|---|---|---|
| | 1½ | 3 | 5 | 10 |
| 30 or less [a](n=49) | 94% | 90% | 92 % | 94 % |
| More than 30 [b] (n=30) | 53 % | 43 % | 40 % | 17 % |

[a]: Corresponds to a predicted angle of $50^0$ or less at 10 years
[b] : Corresponds to a predicted angle of more than $50^0$ at 10 years

53% at 1½ years, 40% at 5 years and 17 % at 10 years. Thus the proportion of patients with an observed angle of more than $50^0$ increased from 60% at 5 years to 83% at 10 years (McNemar test - $p<0.01$).

Considering patients with complications initially, there were 12 patients who had clinically evident abscess/sinus. The lesions resolved in all 12 on the prescribed chemotherapy. In all, 9 patients had paraparesis (but able to walk across a room) on admission. This condition resolved in all 9 patients—in 6 on the scheduled treatment and in the remaining 3 with surgery.

## Discussion

Detailed analyses of the pre-treatment factors had shown that the angle of kyphosis on admission was the most important factor ($p < 0.0001$) for predicting which patients were likely to have a kyphosis of $50^0$ or less at 10 years. Thus if the angle on admission was $30^0$ or less, the angle at 10 years was likely to be $50^0$ or less. This correctly identified 46 out of 51 (90 %) patients who had an observed angle of $50^0$ or less at 10 years. The result achieved with the angle alone was not improved by using a discriminant equation (which required calculation) involving the site of the lesion in addition to the initial angle. It was also observed that 90-94% of patients having a kyphosis angle of $30^0$ or less on admission had an observed angle not exceeding $50^0$ between 1½ and 10 years. Therefore, if a patient has a kyphosis angle of $30^0$ or less initially, he could be prescribed ambulatory chemotherapy provided he has no complications such as neurological deficit.

This is in conformity with an earlier recommendation that "patients with an initial kyphosis angle of $30^0$ or less should be started on ambulant chemotherapy"[1]. This observation was based on mean angles and the present analysis, based on discriminant analysis, confirms the earlier observation. To our knowledge, no other workers have undertaken detailed statistical analyses and derived a basis for prescribing ambulatory chemotherapy with confidence.

There were 3 patients who had an initial angle of $30^0$ or less but an observed angle exceeding $50^0$ at 10 years. It would be undesirable to continue these 3 patients on ambulatory chemotherapy. Hence, we recommend that all patients who are started on ambulatory chemotherapy be monitored and suitable action taken if there is progression of kyphosis[11] (or any other complication).

It was observed that among patients having a kyphosis angle exceeding $30^0$ initially, 43 % had an observed angle of more than $50^0$ at 1½ years and 83 % at 10 years. Hence, it is advisable that for all patients with an initial kyphosis angle of more than $30^0$, a decision on the appropriate method of treatment is taken on an individual basis.

Rajasekaran and Shanmugasundaram[12] reported that the angle of gibbus deformity at 6 years was predictable with 90% accuracy by using a linear regression equation based on the initial vertebral body loss. But this finding was not confirmed in a Chennai study [1], in which the agreement ($\pm 10^0$) between the predicted and observed 10-year angles was 34 to 43 %. Furthermore, predicting the actual angle likely is not necessary. What is required is to predict whether a patient considered for ambulatory chemotherapy is likely to develop severe kyphosis after the start of treatment.

Rajasekaran[13] has evolved a spinal instability score, based on radiological signs developing during the course of the disease in children under 15 years of age receiving chemotherapy. He reported that 89% of 37 patients with an instability score of 2 or less had a deformity of less than $30^0$ at 15 years. This supports our recommendation to prescribe ambulatory chemotherapy for those with an initial angle of $30^0$ or less on admission.

It is concluded that ambulatory chemotherapy could be confidently prescribed to spinal tuberculosis patients if the initial angle of kyphosis is $30^0$ or less. This method is reliable because it identifies 9 out of 10 patients fit for ambulatory chemotherapy; it is simple because it requires just one measurement- that of the kyphosis angle on admission. We believe that our method would be of great use to treatment providers who have to take quick decisions regarding the line of treatment for large numbers of patients with spinal tuberculosis.

## References

1. **Parthasarathy R, Sriram K, Santha T, Prabhakar R, Somasundaram PR, Sivasubramanian S**. Short Course Chemotherapy for tuberculosis of the spine. A comparison between ambulant treatment and radical surgery – Ten – year report. *J Bone Joint Surg (Br)* 1999; 81:464-71.
2. **Medical Research Council Working Party on Tuberculosis of the Spine**. A 10 - year assessment of controlled trials of inpatient and outpatient treatment and of plaster-of-Paris jackets for tuberculosis of the spine, in children on standard chemotherapy: studies in Masan and Pusan, Korea. *J Bone Joint Surg (Br)* 1985; 67:103-10
3. **Medical Research Council Working Party on Tuberculosis of the Spine.** A 15 – year assessment of controlled trials of the management of tuberculosis of the spine in Korea and Hong Kong. *J Bone Joint Surg (Br).* 1998; 80: 456 – 62.
4. **Leong JCY**. *Editorials*, Tuberculosis of the spine. *J Bone Joint Surg (Br).* 1993; 75: 173.

**5.** **Griffiths DL**. Tuberculosis of the spine: a review. *Adv Tuberc Res.* 1980; 20:92-110.

**6.** **Rajeswari R, Ranjani R, Santha T, Sriram K, Prabhakar R.** Late–onset paraplegia–a sequela to Pott's disease. A report on imaging, prevention and management. *Int J Tuberc Lung Dis.* 1997; 1(5): 468 – 473.

**7.** **Medical Research Council Working Party on Tuberculosis of the Spine.** A five – year assessment of controlled trials of in-patient and out-patient treatment and of plaster-of-Paris jackets for tuberculosis of the spine in children on standard chemotherapy: studies in Masan and Pusan, Korea. *J Bone Joint Surg (Br).* 1976*;* 58:399-411

**8.** **Fon GT, Pitt MJ, Theis AC** Jr. Thoracic kyphosis. Range in normal subjects. A J R. 1980, **134,** 979. Quoted by: **Hammerberg KW.** Kyphosis. In: Bridwell KH, DeWald RL, Ed. *The textbook of spinal surgery*, Vol 1, JB Lippincott Company, Philadelphia 1991; 501

9. **Stagnara P, De Mauroy JC, Drau G *et al*.** Reciprocal angulation of vertebral bodies in a sagittal plane: Approach to references for the evaluation of kyphosis and lordosis. *Spine*. 1982; 7, 335. Quoted by **Hammerberg KW**. Kyphosis. In: Bridwell KH, DeWald RL, Ed. *The textbook of spinal surgery,* Vol.1, JB Lippincott company, Philadelphia 1991;501

10. **Hand DJ.** *Discrimination and classification*. John Wiley & Sons, New York, 1981: 71

**11.** **Thilakavathi S, Fredrick JS, Fredrick KG, Parthasarathy R, Santha T, Somasundaram PR, Prabhakar R**. High coverage for long term follow-up of patients with spinal tuberculosis. *Ind J Tuberc.* 1993; 40 **:** 91-94

**12.** **Rajasekaran S, Shanmugasundaram TK.** Prediction of the angle of gibbus deformity in tuberculosis of the spine. *J Bone Joint Surg (Am).* 1987; 69-A: 503-9.

**13.** **Rajasekaran S.** The natural history of post – tubercular kyphosis in children: Radiological signs which predict late increase in deformity. *J Bone Joint Surg (Br).* 2001; 83-B:954–62.