

# Clinical observation on pericardiocentesis and glucocorticoid in the treatment of tuberculous pericarditis

H. LI, F.-Y. LIU, X.-L. LI, L. ZHU, H. ZHOU

Department of Cardiovascularology, Xiangyang Hospital Affiliated to Hubei University of Medicine, Xiangyang, Hubei, China

**Abstract. – OBJECTIVE:** To investigate pericardiocentesis and glucocorticoids in the treatment of the clinical curative effect of tuberculous pericarditis.

**PATIENTS AND METHODS:** Choose 128 cases of our hospital diagnosed as tuberculous pericarditis patients as the research object, according to the treatment, were divided into group A (pericardium puncture + anti-tuberculosis (anti-TB) treatment of 26 cases) and group B (pericardium puncture +anti-tuberculosis (anti-TB) + glucocorticoid treatment of 30 cases), group C (anti-tuberculosis (anti-TB) + glucocorticoid therapy of 24 cases, and group D anti-tuberculosis (anti-TB) treatment of 48 cases, in the treatment of 8 weeks, 3 months, 6 months, 9 months, 12 months, 18 months by B ultrasonic and CT examination to observe the efficacy of treatment.

**RESULTS:** At 8 weeks after treatment in group A, group B and group C and group D efficient were 61.54%, 93.33%, 54.17%, and 68.75%, respectively, group B, respectively, compared with group A, group C, and group D, had obvious statistical significance difference ( $p < 0.05$ ); Groups of early and late treatment comparison difference have no statistical significance ( $p > 0.05$ ).

**CONCLUSIONS:** Tuberculous pericarditis in anti-TB treatment on the basis of using pericardiocentesis and sugar cortical hormone treatment, can achieve an ideal effect.

## Key Words

Pericardiocentesis, Glucocorticoids, Tuberculous pericarditis, Clinical curative effect

## Introduction

Tuberculous pericarditis is severe tuberculosis and also a common critical disease in the Department of Cardiology. It is mainly resulted from the direct extension of trachea, peribronchial and mediastinal scrofula, or primary pulmonary tuberculosis, and hematogenous spread of pleural

tuberculosis. In the early stage, it is fibrinous and hemorrhagic pericarditis. With the development of disease, it would gradually develop into hydropericardium, then into cardiac hypertrophy, and finally convert to subacute stage or chronic stage or develop into pericardial constriction<sup>1,2</sup>. Tuberculous pericarditis possesses a high proportion of pericarditis diseases, accounting for 21.3%-35.8% of pericardial diseases, for 90% of constrictive pericarditis, and 19% of bloody pericardial effusion<sup>3</sup>. In clinic, anti-tuberculosis (anti-TB) therapy and operative treatment are the major treatment methods. In the early stage, triple anti-TB chemotherapy comprising isoniazid, rifampicin, and streptomycin or ethambutol could effectively reduce mortality, but operative treatment is still in need to reduce the occurrence of constrictive pericarditis<sup>4,5</sup>. In our study, we have selected 128 patients and investigated the curative effects of pericardiocentesis and glucocorticoid in the treatment of tuberculous pericarditis.

## Patients and Methods

### Patients

One hundred and twenty-eight patients, who were diagnosed with tuberculous pericarditis in our hospital from January 2009 to December 2014, were enrolled, all of whom complied with the following criteria: 1) confirmed with medium hydropericardium under B ultrasonography (10 mm  $\leq$  width of anechoic area  $<$  20 mm, and without pericardium incrassation), course of disease  $<$  1 month; 2) with focus in the lung, and confirmed as positive under mycobacterium culture on sputum, pleural effusion, pericardial effusion, urine, and lymph gland secretion; 3) diagnosed with tuberculosis under pathological diagnosis on percutaneous lung puncture, lymph node biopsy, peri-

cardial biopsy; 4) culture result of mycobacterium smear was negative, Purified Protein Derivative (PPD Mantoux) test result (+++), ADA > 45  $\mu$ /L. Among the 128 patients were 74 cases of male and 54 cases of female, being aged from 17-60 years old, on average 33.8 years old; all of the 128 patients were accompanied with pleural effusion, 46 patients combined with peritoneal dropsy, 6 patients combined with renal tuberculosis, 21 patients combined with lymph gland; clinical performances include 79 cases of coughing, 55 cases of mild fever, 39 cases of night sweat, 50 cases of chest pains, 95 cases of increasing heart rate, 13 cases of dyspnea, and 38 cases of abdominal distension.

## **Methods**

### *Material Grouping*

Patients, after acquiring basic understanding of the various therapies, chose therapies on their own. And according to different therapies, they were divided into Group A, Group B, Group C, and Group D. Group A contained 26 patient that were administrated with pericardiocentesis + anti-TB therapy, Group B contained 30 patients that were administrated with pericardiocentesis + anti-TB + glucocorticoid therapy, Group C contained 24 patients that were administrated with anti-TB + glucocorticoid therapy, Group D contained 48 patients that were administrated with anti-TB therapy. Differences on general materials among groups had no statistical significance ( $p > 0.05$ ) with comparability. Dosage for glucocorticoid therapy was dependent on the condition of the patient. Normal dosage: prednisone tablets 30-50mg/day, administered at draught in the morning for 4 weeks, then reduced by 5mg every month, for a total of 9-13 weeks; patients that can not tolerate were required to quit the experimental group.

### *Treatment Methods*

Forty-eight patients in Group D were treated with simple standardized anti-TB chemotherapy, which lasted for 12-18 months. Drugs were chosen according to the principle of efficient, sensitive, and harmfulness. Triple anti-TB chemotherapy comprising isoniazid, rifampicin, and streptomycin or ethambutol was implemented. Chemotherapy regimen was personalized based on whether excreted bacteria existed in the patients' sputum and whether they had a history of

anti-TB therapy or not. Treatment duration was decided according to the patients' condition of illness and its improvement. Chemotherapy process was divided into two periods: strengthened bacteria killing period and continuous bacteria killing period. The first two or three months belong to strengthened bacteria killing period, during which at least four kinds of anti-TB drugs were combined. Continuous bacteria killing period followed strengthened bacteria killing period and its duration was decided according to the patients' conditions. Methods for medication include daily medication during the whole course of treatment, daily medication during strengthened period and intermittent medication during continuous period, intermittent medication during the whole course of treatment. The 26 patients in Group A were administrated with pericardiocentesis + anti-TB therapy while the 30 patients in Group B were administrated with pericardiocentesis + anti-TB + glucocorticoid therapy. The 24 patients in Group C were administrated with anti-TB + glucocorticoid therapy.

### *The Handling of Ineffective Therapies*

Specific measures were adopted to deal with specific ineffectiveness, for example, in the case that Mycobacterium tuberculosis culture was positive and drug-sensitive test showed drug tolerance, anti-TB therapy shall be adjusted promptly; in the case that hydropericardium increased significantly to a large amount during treatment, paracentesis therapy shall be reselected; in the case that constrictive pericarditis occurred and accompanied with significant pericardium incrasation, returned blood volume shall be reduced and venous pressure be lessened, if necessary, turn to implement pericardium decollement or fenestration pericardium. For patients with abnormal liver function, treatment shall be focused on liver protection; for patients with hyperuricemia, treatment shall be focused on alkalifying urine and reducing uric acid.

### *Efficacy Determination*

Conducting B ultrasonography and CT examination on all patients to check and judge their hydropericardium and pericardium thickness. Assessing their curative effects after treatment for 8 weeks, 3 months, 6 months, 9 months, 12 months, and 18 months and dividing curative effects into three levels: excellent, effective, ineffective. Excellent: without hydropericardium under B ultrasonography, without symptoms or positive

**Table I.** Curative effects on patients after treatment for 8 weeks in all groups (n, %).

Group	Excellent	Effective	Ineffective	Effective rate
A (n = 26)	9, 34.62	7, 26.92	10, 38.46	16, 61.54*
B (n = 30)	17, 56.67	11, 36.67	2, 6.67	28, 92.34 <sup>§</sup>
C (n = 24)	6, 25.00	7, 29.17	11, 45.83	13, 54.17 <sup>§</sup>
D (n = 48)	18, 37.50	15, 31.25	15, 31.25	33, 68.75 <sup>§</sup>

Remark: comparing <sup>§</sup> with \*, <sup>§</sup>, <sup>§</sup>, respectively,  $\chi^2$  value was 6.701, 9.150, 5.349,  $p < 0.05$ ; comparing \* with <sup>§</sup>,  $\chi^2 = 0.040$ ,  $p > 0.05$ ; comparing \* with <sup>§</sup>,  $\chi^2 = 0.136$ ,  $p > 0.05$ ; comparing <sup>§</sup> with <sup>§</sup>,  $\chi^2 = 0.911$ ,  $p > 0.05$ .

signs, without hydropericardium or pericardiac incassation under chest CT scanning; effective: hydropericardium  $\leq 1$  cm under B ultrasonography, without symptoms or positive signs, without hydropericardium but with certain pericardiac incassation under chest CT scanning; Ineffective: not up to the effective standard, including the re-appearance of the disappeared hydrops. Patients with long-term use of hormones might have hypercortisolism, drug-induced diabetes, infection, osteoporosis, etc. in our study, there was no record of the number of cases with cortisol.

### Statistical Analysis

SPSS15.0 software package (IBM Company, New York, NJ, USA) was adopted to make computer processing, result was presented by enumeration data, Pearson  $\chi^2$  test was used to make comparisons among groups, and test criterion = 0.05,  $p < 0.05$  was considered statistically significant.

## Results

### Curative Effects on Patients After Treatment for 8 Weeks in all Groups

After treatment for 8 weeks, Group B had the most ideal curative effect among the four groups, and comparison difference between Group B and Groups A, C, and D had statistical significance ( $p < 0.05$ ). Comparisons among Groups A, C, and D had no statistical significance (Table I).

### Curative Effects on Patients after Treatment for 3, 6, 9, 12 Months in All Groups

Curative effects on patients after treatment for 3, 6, 9, 12 months in all groups (Table II).

### Curative Effects on Patients After Treatment for 18 Months in All Groups

After treatment for 18 months, Group B had the most ideal curative effect among the four groups,

and comparison difference between Group B and Groups A, C, and D had statistical significance ( $p < 0.05$ ) (Table III).

## Discussion

### Pathogenesis of Acute Tuberculous Pericarditis

Tuberculous pericarditis is severe tuberculosis and also a common critical disease in the Department of Cardiology. It is mainly resulted from the direct extension of trachea, peribronchial and mediastinal scrofula, or primary pulmonary tuberculosis, and hematogenous spread of pleural tuberculosis. Tuberculosis focus of tuberculous pericarditis is generally incurred by the invasion of tuberculosis focus in other parts of the body. The most common invasion channels include the following: firstly, Mycobacterium tuberculosis lymph-vessel retrogrades to pericardium and leads to pericarditis; secondly, tuberculosis focus invades through hematogenous spread, which is based on miliary tuberculosis or combined tuberculous polyserositis; thirdly, spread and extension of tuberculosis focus in adjacent tissues and results in pericarditis<sup>6,7</sup>. Young people are more vulnerable to this disease, and in clinic, it is more often seen in males. It is characterized by slow onset and nonspecific constitutional symptoms, accompanied with clinical manifestations including fever, chest pain, palpitation, cough, dyspnea, anorexia, emaciation, lacking in strength, and night sweat. Main signs include tachycardia, enlargement of heart border, distant heart sounds, pericardial friction sound, pleural effusion, so on and so forth<sup>8,9</sup>. Among the patients in our study were 57.81% of male, on average 33.8 years old; among the 128 patients, 61.72% were accompanied with coughing, 42.97% with mild fever, 74.22% with increasing heart rate, and 29.67% with abdominal distension.

**Table II.** Curative effects on patients after treatment for 3, 6, 9, 12 months in all groups (n).

Group	3 Months later			6 Months later			9 Months later			12 Months later		
	Excellent	Effective	Ineffective	Excellent	Effective	Ineffective	Excellent	Effective	Ineffective	Excellent	Effective	Ineffective
A (n = 26)	9	9	8	10	7	9	10	7	9	10	7	9
B (n = 30)	18	10	2	18	10	2	18	10	2	18	10	2
C (n = 24)	7	8	9	7	8	9	7	8	9	7	8	9
D (n = 48)	21	16	11	21	17	10	21	17	10	21	17	10

Remark: comparing with corresponding terms in Table I, differences had no statistical significance,  $p > 0.05$ .

### **Clinical Curative Effect of Pericardiocentesis Combined Glucocorticoid in Treating Tuberculous Pericarditis**

The result of our study showed that by combining pericardiocentesis with glucocorticoid therapy on the basis of anti-TB therapy, tuberculous pericarditis could achieve better curative effects. Dosage was dependent on the condition of the patient. Normal dosage: prednisone tablets 30-50 mg/day, administered at draught in the morning for 4 weeks, then reduced by 5mg every month, for a total of 9-13 weeks; patients that can not tolerate were required to quit the experimental group. Among the 128 patients, Group B had achieved the best curative effect after treatment for 8 weeks (pericardiocentesis + anti-TB + glucocorticoid therapy). Comparing Group B with Group A, C, D, differences had statistical significance ( $p < 0.05$ ). While comparisons among Group A (pericardiocentesis + anti-TB therapy), Group C (anti-TB + glucocorticoid therapy), and Group D (anti-TB therapy) showed that differences had no statistical significance ( $p > 0.05$ ). As treatment went on, except for Group B, the effective rate of the rest groups all had been improved, but not quite significantly. Difference between treatment for 8 weeks and for 18 months had no statistical significance ( $p < 0.05$ ). After treatment for 18 months, comparison differences between Group B and Group A, C, D had statistical significance ( $p < 0.05$ ), which indicated that by combining pericardiocentesis with glucocorticoid therapy on the basis of anti-TB therapy, tuberculous pericarditis could achieve not only better but also faster curative effects. Such result was consistent with the studying results of most domestic researchers<sup>10-12</sup>.

### **Conclusions**

Tuberculous pericarditis was often secondary to tuberculous lesions in other parts of the body. Mycobacterium tuberculosis, after invading the pericardium, would reproduce in large amount and result in pericardial congestion and exudation of pericardium viscerale and parietal layer; then, the body would produce a super sensitive reaction to Mycobacterium tuberculosis and metabolites, and the exudation would increase and become seroplastic seepage. Later, the absorption of liquid would lead a large number of fibrous cells to deposit and cover the pericardium, and the lesion

**Table III.** Curative comparison among all groups after treatment for 18 months (n, %).

Group	Excellent	Effective	Ineffective	Effective rate
A (n = 26)	10, 38.46	7, 26.92	9, 34.62	17, 65.38*
B (n = 30)	18, 60.00	10, 33.33	2, 6.67	28, 93.33 <sup>§</sup>
C (n = 24)	7, 29.17	8, 33.33	9, 37.50	15, 62.5 <sup>&amp;</sup>
D (n = 48)	21, 43.75	17, 35.42	10, 20.83	33, 68.75 <sup>§</sup>

Remark: comparing<sup>§</sup> with \*, <sup>&</sup>, <sup>§</sup>, respectively,  $\chi^2$  value was 6.701, 9.150, 5.349,  $p < 0.05$ ; compared with treatment effect after 8 weeks, effective rate among all groups after treatment for 18 months had no statistical significance ( $p > 0.05$ ); pairwise comparison among \*, <sup>&</sup>, <sup>§</sup> had no statistical significance ( $p > 0.05$ ).

progressed into the subacute phase, uring which pericardium had apparent tubercular injuries and granulomatous inflammation; after the lesion entered the chronic phase, fibroblasts would increase, fiber cells and collagen would replace granuloma, protein and fiber would form a band and result in partition inside pericardial cavity, fibrous tissues would deposit in the pericardial wall and the visceral layer to make them adhere. Finally, the pericardial cavity would block and lead to constrictive pericarditis; pericardium can be thickened for 3-5 mm, or even 10 mm, and can also be calcified, then the calcified fibrous scars would tightly wrap around and oppress the heart and large vessels. Under a long term oppression, the myocardium would suffer from ischemia and become pale and the myocardial fiber degeneration would thicken the myocardium<sup>13</sup>. Based on the pathogenesis of tuberculous pericarditis as well as its occurrence and development process, our conclusion was as follows: diagnosis shall be made as soon as possible. The duration of subjects enrolled in our study were all less than one month. After being confirmed with tuberculous pericarditis, the therapy of standardized anti tuberculosis program+paracentesis pericardii+glucocorticoid could achieve an ideal effect. Limitations of our study: the number of sample was relatively small; there was a lack of a large number of relevant observation data on studying whether the effective patients would have constrictive pericarditis and at what time window would they form cardiac calcification. And also, there was lacking in relevant clinical guidance and more data support on whether surgical intervention was needed or not. So, a large sample size and long-term follow-up observation were still needed.

#### Conflicts of interest

The authors declare no conflicts of interest.

#### References

- 1) DE ROSA G, PARDEO M, STABILE A, RIGANTE D. Rheumatic heart disease in children: from clinical assessment to therapeutical management. *Eur Rev Med Pharmacol Sci* 2006; 10: 107-110.
- 2) JAUME SS, AXEL SM, JORDI SS. Diagnosis and management of pericardial effusion. *World J Cardiol* 2011; 3: 135-143.
- 3) SHENJIE T, WEN G. *Clinical phthisiology*. Beijing: People's Medical Publishing House, 2011; pp. 419-428.
- 4) KHANDAKER MH, ESPINOSA RE, NISHIMURA RA, SINAK LJ, HAYES SN, MELDUNI RM, OH JK. Melduni. *Pericardial disease: diagnosis and management*. *Mayo Clin Proc* 2010; 85: 572-593.
- 5) LI P, LIU XY. Clinical analysis of 128 children with pericardial effusion in Chongqing and Sichuan areas. *J Clin Cardiol* 2013; 29: 221-223.
- 6) VINSONNEAU U, BRONDEX A, PALEIRON N, CASTELLANT P, CORNILY JC, ARLES F, QUINIOU G. A pericardial effusion-Acute tuberculous pericarditis. *Rev Med Interne* 2010; 31: 451-452.
- 7) XIAOHUA Y, JUN Y, MINGYING P, LURONG H, LEI S. Clinical curative effect of indwelling central venous catheters combined with urokinase intrapericardial lavage on treatment of acute tuberculous pericarditis. *Prog Mod Biomed* 2011; 11: 926-928.
- 8) MORI T, SAKATANI M, YAMAGISHI F, TAKASHIMA T, KAWABE Y, NAGAO K, SHIGETO E, HARADA N, MITARAI S, OKADA M, SUZUKI K, INOUE Y, TSUYUGUCHI K, SASAKI Y, MAZUREK GH, TSUYUGUCHI I. Specific detection of tuberculosis infection: an interferon gamma based assay using new antigens. *Am J Resp Crit Care* 2004; 170: 59-64.
- 9) FIORANI CM, TIBERI R. Tuberculosis today: evolution of a disease (Editorial). *Eur Rev Med Pharmacol Sci* 1998; 2: 3-9.
- 10) IMAZIO M, BRUCATO A, MAYOSI BM, DEROSA FG, LESTUZZI C, MACOR A, TRINCHERO R, SPODICK DH, ADLER Y. Medical therapy of pericardial diseases Part II: noninfectious pericarditis, pericardial effusion and constrictive pericarditis. *J Cardiovasc Med* 2010; 11: 785-794.
- 11) VIJAYA K S, KUMAR DM, BAGGA M, SASI KM, GAUTHAMAN K. A systematic review of different type of tuberculosis. *Eur Rev Med Pharmacol Sci* 2010; 14: 831-843.
- 12) WIYSONGE CS, NTSEKHE M, GUMEDZE F. Contemporary use of adjunctive corticosteroids in tuberculous pericarditis. *Int J Cardiol* 2008; 124: 388-390.
- 13) SHENJIE T, WEN G. *Clinical tuberculosis*. People's Medical Publishing House, 2011; pp. 419-428.