



## Treatment by Using the Endoscopic Thoracic Sympathectomy and the Autologous Bone Marrow Monocytes Transplantation for Raynaud's Disease

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### Abstract

**Objective:** To assay analyze effects of the Endoscopic Thoracic Sympathectomy (ETS), the Autologous Bone Marrow Monocytes Transplantation (ABMMT) and the combination of these procedures ultimate for the patients with Raynaud's phenomenon disease.

**Background:** There are some studies to treat Raynaud's Phenomenon (RP) wABMMT have been already used for upper extremities ischemia, such as Thromboangiitis Obliterans (TAO or Buerger's disease). However, long-term results of these treatments are not so high. Therefore, studies for good long-term results must be performed.

**Patients and Methods:** Sixty patients diagnosed Raynaud's phenomenon at the thoracic surgery department of Pyongyang medical college, Kim Il Sung University was included is prospective. Patients are divided into three groups. We had used ETS, ABMMT and the combination of both treatments according to the groups. Results from every group were estimated.

**Results:** The effect of patients treated with the combination of both approaches is better than those treated with either of two methods (group 1; 70.0%, group 2; 45.0%, group 3; 25.0%; p<0.05).

**Conclusion:** Long-term results of treatment for Reynaud's disease can be increased with the combination of ETS and ABMMT.

**Keywords:** Autologous bone marrow monocyte; Thoracic sympathectomy; Raynaud's phenomenon

### Introduction

Maurice Raynaud (1834 year to 1881 year) first described in 1862 the disease as episodic, acral vasospasm characterized by pallor, cyanosis, suffusion, and a sense of fullness or tautness, which may be painful [1,2]. Another author defined the phenomenon as In 1930, after observing that even when reflex vasodilation is produced by warming the body, vasospasm could still be induced by putting the hands in cold water, and conversely, that vasospasm could not be produced by body cooling if the hands were kept warm, Sir Thomas Lewis concluded that Raynaud's phenomenon was due to a "local fault" rather than a defect in the central nervous system. While the underlying pathophysiology of the disease is not really understood until now, it is triggered by cold, damp weather and emotional stress [3,4]. RP most often affects the hands and the RP was reported. Idiopathic (RP) associated with connective tissue diseases (RP) [5,6]. Overall, Raynaud Phenomenon is a transient and peripheral vasoconstrictive response to cold temperatures or emotional stress. Raynaud phenomenon can be categorized as either primary or secondary.

Psychological press leads patients with Raynaud's phenomenon a passive life. The importance of treatments for patients with Raynaud's phenomenon is to achieve an improvement of blood flows to affected digital, and smoking or by (vasodilatory agents) treatment ultimate [7,8].

The therapeutic goal is to achieve palliation through conservative methods such as protection from cold, reduction of emotional stress, and quitting smoking in addition to medical treatment [6].

The Endoscopic Thoracic Sympathectomy (ETS) procedure is being used increasingly in recent

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years to eliminate the circulation disorder and pain in the upper extremities in Raynaud's disease cases where frequent and severe attacks, tissue damages such as dystrophic changes occur in the extremities despite correct and adequate medical treatment [6]. ETS reduces the peripheral vascular resistance, hence increasing the blood flow in the peripheral vascular system [9].

ETS is being used for ischemic diseases of upper extremities such as Raynaud's phenomenon [6]. Although the long term efficacy of ETS was moderate, due to its low invasiveness ETS is a valuable option in the management of upper limb ischemia [1,10].

Autologous Bone Marrow Monocytes Transplantation (ABMMT) is also being accepted for patients with ischemic disease, such as Buerger's disease, due to the improvement of blood flow to ischemic tissue [11-14]. However, the aim we suggested that the good effects can be gained by the combination of two therapies.

Although the therapeutic effect to ischemic tissues of the sympathectomy is different with one of ABMMT, both ETS and ABMMT are effective for the management of patients with ischemic disease like thromboangiitis obliterans or Raynaud's phenomenon [1,3,4,6,15]. Therefore, both procedures are introduced to achieve good long-term results by the improvement of blood flow to ischemic tissues. Results suggest that the combination of the both therapies improves the therapeutic effects in not only short-term but also long-term.

## Patients and Methods

### Patients

The 60 patients diagnosed Raynaud's disease is prospective at the thoracic surgery department of Pyongyang medical college, Kim II Sung University from 1<sup>st</sup> January, 2014 to 30<sup>th</sup> December 2016 were included (male: 26, female: 34, the range of patient's age: 20 years to 59 years). The severity of patients was different, from the simple Raynaud's attack to the necrosis. Patients were divided into three groups. There was no significant difference in the clinical symptoms between the groups. From January 2014 to December 2014, all patients were operated by ETS. ABMMT was performed from January 2015 to October 2015. The combination of both treatments was started at October 2015.

### Methods

Patients with RP were divided into three groups according to the sort of therapies; ETS; group 1, ABMMT; group 2, the combination of both procedures; group 3.

### Endoscopic thoracic sympathectomy

Under the general anesthesia, we made a port on the 3<sup>rd</sup> intercostals space of the anterior axillary line for an insertion of the thoracoscope and other one on the 2<sup>nd</sup> intercostals space of the middle clavicular Medio clavicular line for an insertion of the hook. We resected the thoracic sympathetic ganglions No. 2, 3 and their branches with the electronic cauterization and then measured the temperature of fingertip to confirm the resection of thoracic sympathetic ganglions.

### Collection of the bone marrow

We collected the bone marrow (amount about 200 mL) on 10 spots of the bilateral ilium with the fine needle aspiration under the local anesthesia in group 2. In group 3, the collection of the bone marrow was performed continuously after ETS. Collected bone marrow of patients was immediately sent to the laboratory for the

**Table 1:** The temperature of the fingertip skin immediately postoperative : p<0.05.

Group	The temperature for fingertip skin (Mean ± SD)	
	Pre-operative temperature	Post-operative temperature
Group 1 (n=20)	25.2 ± 3.5	32.3 ± 1.6*
Group 2 (n=20)	24.7 ± 3.8	31.6 ± 1.7*
Group 3 (n=20)	24.8 ± 3.8	32.0 ± 1.5*

**Table 2:** Short-term results (3 months postoperative): Changes in signs.

Group	Symptoms	Signs			
		Attack (n)	Paleness (n)	Pain (n)	Cold (n)
Group 1 (n=20)	Preoperative	20	16	13	20
	Post-operative	2	4	2	3
Group 2 (n=20)	Preoperative	20	15	11	20
	Post-operative	3	4	2	3
Group 3 (n=20)	Preoperative	20	15	12	20
	Post-operative	1	2	-	1

separation of monocytes.

### Separation of monocytes

The collected medullary blood was centrifuged in 2000 rpm, filtered and washed with PBM and Physiological saline solution. Following the separation of monocytes, the condition of monocytes was confirmed with the microscope before transplantation.

### The transplantation of bone marrow monocytes

The separated monocytes have been transplanted in the flexor, extensor and interosseous muscles of the affected forearm, palms and fingers. Residual blood was transfused intravenously.

### The estimation of patients

Skin temperature of fingertips and skin condition, such as Raynaud's attack, skin color, healing of the skin ulcer, and the pain of fingers were studied. We took the results 3 months following the treatments as a post operatively for the short-term result, and the results from 4 months to 12 months (median 8 months) as a long-term result.

### Statistical analysis

Here collected prospectively in a excel databank and student t-test was used to take a statistical analysis.

## Results

### Results in the short-term

Immediately after operation, the fingertip temperature increased significantly in all groups (p<0.05) (Table 1). Within the first three months, we saw a relief of severe symptoms up to full recovery in almost all patients independent of treatment setting. However, the temperature of the fingertip skin was increased significantly after than before the treatment in all groups.

### Changes in signs and findings

This table shows obvious improvements of signs in all groups, but significant difference was not confirmed statistical in the long-term follow-up, number of patients with RP attacks were decreased statistically in group 3 compared to the other groups (group 1; 70.0%, group 2; 45.0%, group 3; 25.0%; p<0.05) (Table 2-4). There was no statistical difference in the overall satisfaction with the treatment

**Table 3:** Short-term effects (3 months postoperative): Changes in findings p and necrosis. All findings were improved in all groups after the surgical treatment. Results in the long-term follow-up (4 months to 12 months, median: 8 months).

Group	Symptoms	Findings	
		Ulcer (n)	Necrosis (n)
Group 1 (n=20)	Preoperative	4	3
	Post-operative	1	-
Group 2 (n=20)	Preoperative	4	2
	Post-operative	1	-
Group 3 (n=20)	Preoperative	3	3
	Post-operative	-	-

**Table 4:** The existence of Raynaud's attack in long term and the satisfaction at surgical treatments. Follow-up (median 8 months; range 4 months to 12 months) \*: p<0.05; RP: Raynaud's phenomenon.

Group	Patients	Patients
	RP attack (%)	Satisfaction at therapies (%)
Group 1 (n=20)	14 (70.0)	10 (50.0)
Group 2 (n=20)	9 (45.0)	13 (65.0)
Group 3 (n=20)	5 (25.0)*	17 (85.0)

between the groups.

## Discussion

Although most patients with RP can be successfully managed by medical therapies, endoscopic thoracic sympathectomy has a role in cases of treatment resistant severe RP [10]. Patients with secondary RP benefit more than those with primary RP from surgical therapy [10]. Landry et al. published a detailed algorithm for treatment for patients suffering from RP [7]. Especially in patients with severe symptoms, such as digital ulcers or necrosis, endoscopic thoracic sympathectomy showed to prevent amputation due to ischemia and improve the quality of life for the patients [5,8,10,16,17]. Albeit the reported initial and short-term results are promising, the rate of recurrence of symptoms in the long-term follow-up is relatively high [6,8]. It was described may treat intractable ulcer or pain [11-14]. Since we have good clinical experience with both procedures for many years we started to combine the two procedures, ABMMT and ETS with the goal to improve the long-term results. In our opinion, there is no report of this procedure in the literature until now.

It may still reduce the severity of symptoms and may maximize tissue preservation or prevent amputation in cases of digital ulceration [1]. ETS produced a high rate of initial relief, but had the high rate of recurrence in patients with Raynaud's phenomenon [8]. The long term efficacy of ETS in some study was moderate (53%) [1].

In our series, we had neither adverse effects nor intraoperative complications. Similar to other reports, independent of the treatment arm, most patients in our trial had a clear benefit in the short term follow up [8]. We found not only an improvement of the clinical symptoms such as pain, cold, paleness and attack but also a tissue regeneration in those who had ulcer and necrosis [18]. The same applies for patients with ischemic digits due to connective tissue inflammation disease treated by ABMMT [12,19]. In contrast to the beneficial short term results, the effect of the ETS seems to decrease in the long term follow-up. Karapolat et al., [8] reported in their study about recurrent symptoms in 66.6% of patients. Moreover, all of these patients expressed that their operation was unnecessary [8]. In

a summary of 18 trials, 58% of patients with primary RP and 89% of patients with secondary RP had a benefit in the long-term follow-up [10]. Compared to the results of the literature, we could demonstrate a significant reduction of the numbers of RP attacks in patients with combined treatment. In our study, 15 patients of group 3 treated with both ETS and ABMMT had not any RP attack in long-term follow-up (75.0%). Up until now, ABMMT for RP was not described in the literature. Our results in patients treated with ABMMT with absence of RP attacks in 55% in the long-term follow-up were quite favorable. However, the most beneficial treatment was the combination of the two procedures. Typical complications associated with ETS are pneumothorax, haemothorax, pyothorax, compensatory sweating or neurologic disorders (Horner syndrome) [10]. Particularly the compensatory sweating impairs the quality of life in long-term after ETS with an incidence ranging between 3% and 98% [20]. In our study, we didn't see this complication possibly due to limitation of ETS at the T3 level.

Our study has some clear limitations. Although with 60 patients the present study is the largest one in the literature, the comparison of the treatment groups is difficult due to absence of randomization. Another problem of the study was the lack of objective confirmation of the beneficial effects. The follow-up period with a median of only 8 months is relatively short because it was reported that the recurrent symptoms usually begin already 6 months after sympathectomy [10]. Finally an evaluation of the quality of life before and after treatment would be helpful to interpret the effects on the patients.

## Conclusion

Our study demonstrated that in selected cases, ETS alone is associated with adequate long-term results. In addition, we showed clearly that the combination of ETS and ABMMT significantly improved the outcome of these patients. In the future, randomized trials are necessary to find out the best surgical option for the patients with RP.

## References

1. Raynaud M, editor. De l' asphyxia locale et de la gangrene symetrique de extremities. Paris: Rignoux; 1862.
2. Bakst R, Merola JF, Franks AG Jr, Sanchez M. Raynaud's phenomenon: pathogenesis and management. *J Am Acad Dermatol.* 2008;59(4):633-53.
3. Lewis T. Experiments relating to the peripheral mechanism involved in spasmodic arrest of the circulation of the fingers. A variety of Raynaud's disease. *Heart.* 1929;15:7-101.
4. Stringer T, Femia AN. Raynaud's phenomenon: Current concepts. *Clin Dermatol.* 2018;36(4):498-507.
5. Wigley FM, Axford JS, Curtis MR. Clinical manifestations and diagnosis of the Raynaud phenomenon. *Uptodate.* 2018;9.
6. Musa R, Qurie A. Raynaud Disease (Raynaud Phenomenon, Raynaud Syndrome). In: *StatPearls [Internet].* Treasure Island (FL): StatPearls Publishing; 2018.
7. Landry GJ. Current medical and surgical management of Raynaud's syndrome. *J Vasc Surg.* 2013;57(6):1710-6.
8. Karapolat S, Turkyilmaz A, Tekinbas C. Effects of Endoscopic Thoracic Sympathectomy on Raynaud's Disease. *J Laparoendosc Adv Surg Tech A.* 2018;28(6):726-9.
9. Rajesh YS, Pratap CP, Woodyer AB. Thoracoscopic sympathectomy for palmar hyperhidrosis and Raynaud's phenomenon of the upper limb and excessive facial blushing: A five year experience. *Postgrad Med J.*

- 2002;78(925):682-4.
10. Coveliers HM, Hoexum F, Nederhoed JH, Wisselink W, Rauwerda JA. Thoracic sympathectomy for digital ischemia: a summary of evidence. *J Vasc Surg.* 2011;54(1):273-7.
  11. Heo SH, Park YS, Kang ES, Park KB, Do YS, Kang KS, et al. Early results of clinical application of autologous whole bone marrow stem cell transplantation for critical limb ischemia with buerger's disease. 2016;6:19690.
  12. Guo J, Guo L, Cui S, Tong Z, Dardik A, Gu Y. Autologous bone marrow-derived mononuclear cell therapy in Chinese patients with critical limb ischemia due to thromboangiitis obliterans: 10-year results. *Stem Cell Res Ther.* 2018;9(1):43.
  13. Saito S, Nishikawa K, Obata H, Goto F. Autologous bone marrow transplantation and hyperbaric oxygen therapy for patients with thromboangiitis obliterans. *Angiology.* 2007;58(4):429-34.
  14. Wan J, Yang Y, Ma ZH, Sun Y, Liu YQ, Li GJ, et al. Autologous peripheral blood stem cell transplantation to treat thromboangiitis obliterans: preliminary results. *Eur Rev Med Pharmacol Sci.* 2016;20(3):509-13.
  15. Coveliers H, Hoexum F, Rauwerda JA, Wisselink W. Endoscopic thoracic sympathectomy for upper limb ischemia. A 16 year follow-up in a single center. *Surgeon.* 2016;14(5):265-9.
  16. Hoexum F, Coveliers HM, Lu JJ, Jongkind V, Yeung KK, Wisselink W. Thoracic sympathectomy for upper extremity ischemia. *Minerva Cardioangiol.* 2016;64(6):676-85.
  17. Matsumoto Y, Ueyama T, Endo M, Sasaki H, Kasashima F, Abe Y, et al. Endoscopic thoracic sympathectomy for Raynaud's phenomenon. *J Vasc Surg.* 2002;36(1):57-61.
  18. Karapolat S, Turkyilmaz A, Tekinbas C. Effects of Endoscopic Thoracic Sympathectomy on Raynaud's Disease. *J Laparoendosc Adv Surg Tech A.* 2018;28(6):726-9.
  19. Kamata Y, Takahashi Y, Iwamoto M, Matsui K, Murakami Y, Muroi K et al. Local implantation of autologous mononuclear cells from bone marrow and peripheral blood for treatment of ischemic digits in patients with connective tissue diseases. *Rheumatology (Oxford).* 2007;46(5):882-4.
  20. Cerfolio RJ, De Campos JR, Bryant AS, Connery CP, Miller DL, DeCamp MM, et al. The Society of Thoracic Surgeons expert consensus for the surgical treatment of hyperhidrosis. *Ann Thorac Surg.* 2011;91(5):1642-8.