Original Article

DOI: 10.7860/JCDR/2018/35554.11859

Clinical Predictors of Outcome in Buerger's Disease using BVAS and DEI.Tak Scoring Systems

Internal Medicine Section

PRASANTA PADHAN[1], SUNIL AGARWAL[2],DEBASHISH DANDA[3]

ABSTRACT

Introduction: Buerger's disease is an unclassifiable vasculitis of the small and medium-sized distal arteries and superficial veins. BVAS (Birmingham Vasculitis Activity Score) is a validated disease activity index for vasculitis of different types. DEI.Tak (Disease Extent Index. Takayasu's arteritis) scoring system is a validated disease extent Index used for Takayasu arteritis.

Aim: The aim of this study was to assess outcome in patients with Buerger's disease using various clinical features, laboratory parameters, BVAS and DEI.Tak scoring system.

Materials and Methods: Case records of 136 patients diagnosed with Buerger's disease in our hospital between August 1996 and July 2006 were studied retrospectively. Various clinical features (smoking history, claudication pain, loss of pulse), laboratory parameters, treatment modalities and outcome measures were recorded in a defined proforma. BVAS and DEI.Tak scoring was done using the data from medical records documented during the patients' last visit to the hospital. Outcome of any patient requiring amputation was considered as bad outcome. Others, who could be managed by antiplatelet drugs, sympathectomy and revascularization procedures without any amputation were classified within the good outcome subset. Statistical analysis was done using Chi-square test and Non parametric Mann-Whitney test was performed to correlate outcome with all the recorded parameters including those embedded in BVAS and DEI.Tak scoring systems.

Results: Sixty eight patients were in each group, namely the good outcome and bad outcome subsets. The mean BVAS score were 10.29±1.26 and 10.88±2.57 and mean DEI.Tak score were 5.29±1.75 and 7.93±2.43 and these scores were observed to be significantly different (p=0.038, p=0.014 respectively) among the good outcome subsets and bad outcome patients with respectively. Proportion of patients with claudication pain and absent upper limb pulse were observed significantly higher in the bad outcome group.

Conclusion: Buerger's disease with higher DEI.Tak score has significantly higher risk of bad outcome. DEI.Tak score can be used as an important predictor of outcome in Buerger's disease.

Keywords: Disease activity, TAO, Vasculitis

INTRODUCTION

Buerger's disease or Thrombo Angiitis Obliterans (TAO) is a segmental occlusive inflammatory condition of vessels, characterized by thrombosis and recanalization of the affected arteries and veins [1,2]. It is a non-atherosclerotic inflammatory disease affecting small and medium sized arteries and veins, predominantly of the lower extremities; although upper extremity vessels can also be affected [3]. The disease is found worldwide, the highest incidence of TAO is found in the Middle and Far East countries [4,5] . The prevalence of the disease among all patients with peripheral arterial disease ranges between 0.5 and 5.6% in Western Europe; however, values as high as 45 to 63% have been reported from India, 16 to 66% in Korea and Japan, and 80% among the Jews of Ashkenazi ancestry living in Israel [6]. Several studies have reported an increase in the prevalence of the disease in women ranging from 11% to 23% [7]. The disease course of TAO is variable with intermittent acute exacerbations. The trophic lesions often progress during flare-ups, with either extension of lesion proximally or new limb being affected. One of the indication of severity of the disease is need for repeated amputations [8]. Therapeutic options in TAO are largely individualized and the treatment of choice is yet to be established [9].

Assessment of disease activity in TAO is challenging. Most of the patients have no systemic manifestations and vascular features progress very slowly. Clinical features do not correlate with acute phase reactants in TAO patients. In contrast to other vasculitides that affect the small- and medium-sized vessels, histology is rarely available to diagnose and assess activity in patients with TAO.

BVAS is a validated disease activity index for vasculitis of different types [10]. DEI.Tak [11] is a clinical index developed for assessment and the follow-up of Takayasu arteritis, without the requirement of any imaging techniques.

The present study was conducted to assess outcome in patients with Buerger's disease using various clinical features, laboratory parameters, BVAS and DEI.Tak scoring system.

MATERIALS AND METHODS

It was a hospital based retrospective study. Duration of the study was the interval between August 1996 and July 2006. One hundred and thirty six TAO patients fulfilling the diagnostic criteria of Olin for TAO who were attending outpatient and inpatient services of Christian Medical College Hospital, Vellore were considered [12]. Case records of patients diagnosed with Buerger's disease in our hospital were studied; various clinical and laboratory parameters, treatment modalities as well as outcome features were recorded in the defined proforma. As the DEI.Tak form has been available only since 2006, these were filled retrospectively from hospital records for patients who were on routine follow-up until 2006. BVAS scoring was also done for all patients. The study was approved by the institutional research and ethics committee of Christian Medical College Hospital, Vellore.

Patients with signs and symptoms of TAO such as smoking history, age of onset less than 50 years and infrapopliteal arterial occlusion were included in the study. Those who had systemic hypertension, diabetes mellitus, systemic sclerosis, Raynaud's disease and age of onset greater than 50 years were excluded from the study.

Disease Activity Assessment: Patient details such as demography, disease duration, smoking history, physical findings,

routine laboratory tests such as complete blood counts, ESR, liver function tests, renal function tests, fasting blood sugar, lipid profile, routine urine analysis, Chest X-ray PA view and C-reactive protein results were recorded. BVAS and DEI.Tak scoring were done using the medical record data of the patients' last visits to the hospital. BVAS, a well validated composite scoring system, is used in routine rheumatology practice for monitoring of several systemic vasculitic diseases [10]. As Buerger's disease is a vasculitic condition, use of BVAS was attempted to assess this disorder. DEI.Tak has been developed as a derivative from BVAS for disease assessment in Takayasu's arteritis and there is good correlation between the 2 scoring systems in Takayasu's arteritis [13].

All the patients were classified into two broad subsets based on their clinical outcome. Any patient who underwent any amputation was labeled into the bad outcome group. All the rest who could be managed conservatively by antiplatelet drugs, sympathectomy and revascularization procedures without requiring any amputation were classified within the good outcome subset.

STATISTICAL ANALYSIS

Statistical analysis was done using statistical software SPSS version 13 (SPPS Corp, Chicago, IL, USA). Chi-square and Non parametric Mann-Whitney test were done to correlate outcome with all the parameters recorded including those in BVAS and DEI.Tak scoring.

RESULTS

Between July 1996 and August 2006, one hundred thirty six patients were diagnosed to have Buerger's disease in our centre. Various demographic parameters are shown in [Table/Fig-1]. All the patients were males. The mean age was 40 years with average disease duration of 4.9 years. All of them were smokers with mean smoking pack years of 14. The mean ankle brachial pressure index on right side was 0.56±0.226 and on the left side, it was 0.62±0.26. All of them had gangrene in either of the lower limbs with loss of pulse. None had gangrene in upper limb.

The patients were further classified into two subset based on their clinical outcome. The comparisons between the groups based on their various clinical parameters and laboratory parameters are shown in [Table/Fig-2]. Claudication pain was seen in 55(46.2%) with in good outcome subset and 64(53.8%) in bad outcome subset. Absent upper limb pulses were seen in 4 (17.4%) and 19 (82.6%), Leucocytosis in 8 (32%) and 17 (68%), Thrombocytosis in 5(31.3%) and 11(68.8%), respectively. The mean BVAS score were 10.29±1.26 and 10.88±2.57 and mean DEI.Tak score were 5.29±1.75 and 7.93±2.43, respectively in the 2 subsets. The absent upper limb pulse and DEI.Tak scores were significantly associated with the bad outcome group.

Parameter	Good outcome (N=68) Mean±SD	Bad outcome(N=68) Mean±SD	p-value
Age in years	41.2±10.8	38.9±8.3	0.214
Duration in years	4.6±3.98	5.2±3.85	0.031
Smoking in Pack years	13.56±6.59	15.41±8.23	1.500

[Table/Fig-1]: Subset wise demography of patients with Buerger's disease.

Parameter	Good outcome	Bad outcome	Total number	p-value
Claudication {n (%)} Present/Yes Absent/Yes	 55(46.2%) 13(19.1%)	 64(53.8%) 4 (23.5%)	 119 17	0.036
Upper limb pulses {n (%)} Absent Present	 4(17.4%) 70 (61.9%)	 19(82.6%) 43(38.1%)	 23 113	0.001
Leucocytosis {n (%)} Present Absent	 8(32%) 59 (53.1%)	 17(68%) 52 (46.8%)	 25 111	0.056
Thrombocytosis {n (%)} Present Absent	 5(31.3%) 67 (55.8%)	 11(68.8%) 53 (44.2%)	 16 120	0.064
BVAS score (Mean±SD)	10.29±1.26	10.88±2.57	136	0.038
DEI.Tak score (Mean±SD)	5.29±1.75	7.93±2.43	136	0.014

[Table/Fig-2]: Comparison of clinical/laboratory features and scorings between good and bad outcome subsets.

DISCUSSION

Present study found smoking as the universal risk factor for the development of lower limb gangrene as well as pulse loss in all patients with Buerger's disease. This is keeping with the vast majority of publications reporting current or past smoking as prerequisite for the diagnosis of this condition. Non-smokers comprise less than 5% of patients with Buerger's disease [13]. Cold, frostbite, trauma to the extremities and abuse of sympathomimetic drugs may be the triggering factors amongst the nonsmokers. None of our cases had such a history. Distal lower limb involvement as the disease pattern in Buerger's disease is a major differentiating point as opposed to involvement of upper limbs in atherosclerotic peripheral vascular disease [8]. However, a significant number of patients with bad outcome amongst our patients had upper limb pulse loss as compared to those who had good outcome. There was no difference in terms of disease duration and pack years of smoking between these two groups in present study.

In this study, the major objective was to assess the patient with Buerger's disease by the two scoring systems for vasculitic disorders namely BVAS (originally used for ANCA associated vasculitides) and DEI.Tak (usually used to assess disease extent in Takayasu's arteritis). Both these scores acted well, as tools to evaluate disease outcome in our cohort of Buerger's disease, as patients with bad outcome and high disease activity had higher scores.

BVAS is like mother of all assessment scores in vasculitic disorders and it is very comprehensive. In this study, DEI.Tak appears to be an ideal disease assessment score for Burger's disease too, as the later is another pulseless disease with vasculitic etiology similar to Takayasu arteritis. In fact, DEI.Tak is a better tool to assess peripheral pulse loss, which is also an important finding in Buerger's disease as in Takayasu's arteritis. Although DEI.Tak scoring system is derived from BVAS, pulse loss is given higher weightage in it [11]. Pulse loss being a major clinical manifestation in Buerger's disease, therefore, warrants the use of DEI.Tak as disease assessment tool for this illness. Also, we found significantly higher DEI.Tak score in patients with bad outcome as compared to the subset with good outcome. Patients with higher DEI.Tak score had higher risk of amputation due to more severe disease.

Based on present study findings, DEI.Tak can be used as novel instruments to assess and monitor the disease during follow up, as there is no other reliable clinical or laboratory disease activity marker for this disease till date.

As the distribution of vascular lesions in Buerger's disease is not uniform, it may be important to combine clinical assessment of the patient with the Colour Duplex Ultrasound (CDU) findings, in future studies. However, recent finding of Platelet Microparticle (PMP) levels as a potential biomarker for this disease is encouraging [14,15].

Fazeli B et al., attempted to find a disease-specific activity score for TAO using risk of limb loss associated with each clinical sign or symptom and Complete Blood Count (CBC) data. They noted leucocytosis, anaemia and thrombocytosis in the CBC of TAO patients, in particular those who underwent below knee amputation [16]. However these haematological findings are non specific and can be attributed to many other conditions such as coexisting nutritional anaemia and infections in TAO patients. Hence CBC

findings cannot be utilized for scoring of TAO patients in routine clinical practice.

LIMITATION

The present study is based on the retrospective analysis of a small scale single center data and hence a multicentric prospective study with larger sample size will be more useful to further validate the current findings.

CONCLUSION

DEI.Tak scoring can be utilized for assessment of disease activity in patients with TAO in clinical practice. Outcome of this disease can be predicted based on this score.

REFERENCES

[1] Buerger L. Thrombo-angitis obliterans; a study of the vascular lesions leading to presenile spontaneous gangrene. Am J Med. 1952;13(5):526-32.
[2] Lloyd S. The circulatory disturbances of the extremities, including gangrene, vasomotor and trophic disorders. Ann Surg. 1926;83(1):157.
[3] Olin JW, Young JR, Graor RA, Ruschhaupt WF, Bartholomew JR. The changing clinical spectrum of thromboangiitis obliterans (Buerger's disease). Circulation. 1990;82(5 Suppl):43-48.
[4] Lie JT. Thromboangiitis obliterans (Buerger's disease) revisited. Pathol Annu. 1988;23 Pt 2:257-91.
[5] Lie JT. The rise and fall and resurgence of thromboangiitis obliterans (Buerger's disease). Acta Pathol Jpn. 1989;39(3):153-58.
[6] Matsushita M, Nishikimi N, Sakurai T, Nimura Y. Decrease in prevalence of Buerger's disease in Japan. Surgery. 1998;124(3):498-502.
[7] Gallagher KA, Tracci MC, Scovell SD. Vascular arteritides in women. J Vasc Surg. 2013;57(4 Suppl):27S-36S.
[8] Puéchal X, Fiessinger J-N. Thromboangiitis obliterans or Buerger's disease: challenges for the rheumatologist. Rheumatology. 2007;46(2):192-99.
[9] Paraskevas KI. Treatment-of-choice for Buerger's disease (thromboangiitis obliterans): still an unresolved issue. Clin Rheumatol. 2008;27(4):547.
[10] Luqmani RA, Bacon PA, Moots RJ, Janssen BA, Pall A, Emery P, et al. Birmingham Vasculitis Activity Score (BVAS) in systemic necrotizing vasculitis. QJM Mon J Assoc Physicians. 1994;87(11):671-78.
[11] Sivakumar MR, Misra R, Bacon P. The Indian perspective of Takayasu arteritis and development of a disease extent index (DEI.Tak) to assess Takayasu arteritis. Rheumatology. 2005;44:36-37.
[12] Olin JW. Thromboangiitis Obliterans (Buerger's Disease). N Engl J Med. 2000;343(12):864-69.
[13] Misra R, Danda D, Rajappa SM, Ghosh A, Gupta R, Mahendranath KM, et al. Development and initial validation of the Indian Takayasu Clinical Activity Score (ITAS2010). Rheumatol Oxf Engl. 2013;52(10):1795-801.
[14] Darnige L, Helley D, Fischer A, Emmerich J, Smadja D, Fiessinger J. Platelet microparticle levels: a biomarker of thromboangiitis obliterans (Buerger's disease) exacerbation. J Cell Mol Med. 2010;14(1-2):449-51.
[15] Busch K. Buerger's disease (thromboangiitis obliterans): clinical features and assessment by colour duplex ultrasound. Australas J Ultrasound Med. 2011;14(4):18-22.
[16] Fazeli B, Ravari H. A disease-specific activity score for Thromboangiitis obliterans. Vascular. 2014;22(5):336-40.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Rheumatology, Kalinga Institute of Medical Sciences, KIIT University, Bhubaneswar, Odisha, India.
2. Professor and Head, Department of Vascular Surgery, Christian Medical College, Vellore, Tamil Nadu, India.
3. Professor and Head, Department of Clinical Immunology and Rheumatology, Christian Medical College, Vellore, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Debashish Danda,
Professor and Head, Department of Clinical Immunology and Rheumatology,
Christian Medical College, Vellore-632004, Tamil Nadu, India.
E-mail: debashishdandacmc@hotmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: There is no funding involved in this retrospective study.

Date of Submission: **Jan 14, 2018**
Date of Peer Review: **Mar 31, 2018**
Date of Acceptance: **May 18, 2018**
Date of Publishing: **Aug 01, 2018**