Will the HALP score help to assess the activity and predict the prognosis of antineutrophil cytoplasmic antibody-associated vasculitis?

Sirs,

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is defined as a group of small-vessel vasculitides based on the Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides (1, 2). AAV is classified as granulomatosis with polyangiitis (GPA), eosinophilic GPA (EGPA) and microscopic polyangiitis (MPA) (1), or myeloperoxidase (MPO)-ANCA vasculitis, proteinase 3 (PR3)-ANCA vasculitis and ANCA negative vasculitis (3). HALP score, a systemic indicator, was recently introduced and it is derived from the following formula: HALP score = haemoglobin (g/L) x serum albumin (g/L) x lymphocyte count (/L) / platelet count (/L) (4). So far, there have been several studies to demonstrate that the HALP score could predict the prognosis of various types of cancer (5-7). However, no study has reported a clinical implication of the HALP score in AAV patients. Hence, in this study, we investigated whether the HALP score at diagnosis could reflect the cross-sectional activity and predict the prognosis of AAV during follow-up.

We retrospectively reviewed the medical records of 212 immunosuppressive drug-naïve patients with AAV who met the inclusion criteria as described in our previous study (8, 9). This study was approved by the Institutional Review Board of Severance Hospital (4-2017-0673), who waived the need for patient written informed consent, as this was a retrospective study. AAV activity was represented by Birmingham vasculitis activity score (BVAS) version 3 (10) and all-cause mortality, relapse and end-stage renal disease (ESRD) were defined as the poor prognosis of AAV. The follow-up period was determined as described in our previous study (8, 9). The linear regression analyses were used for assessing the association between the HALP score and BVAS at diagnosis and the Cox hazards model analyses were used for evaluating the predictive value of the HALP score at diagnosis for the poor prognosis.

At diagnosis, 116 patients were classified as MPA, 54 as GPA and 42 as EGPA. The median age was 59.0 years old and 32.1% of patients were men. In the multivariable linear regression analysis, HALP score (standardised β = -0.319) was significantly associated with BVAS at diagnosis along with PR3-ANCA (or C-ANCA) (standardised β= -0.135) and blood urea nitrogen (standardised β=0.309) (Table I). However, HALP score was not associated with the poor prognosis in patients with AAV or its variants during the mean follow-up duration of 32.2 months (Table II).

There is a well-established indicator to assess the activity of AAV such as BVAS (10). Nevertheless, we seek an additional indicator that could reflect the activity of AAV with reasons as follows: BVAS consists of organ-oriented indices, but not the cross-sectional laboratory results such as ESR, CRP and four variables of HALP. Therefore, BVAS cannot reflect the degree of inflammation as well as the dynamic changes in the activity of AAV. In addition, BVAS includes irreversible systemic complications of AAV such as end-stage renal disease, and thus it may give arise to con-

Table I. Linear regression analysis of variables for BVAS at diagnosis.

Variables	Univariable			Multivariable		
At diagnosis	Correlation Coefficient (R=beta)	95% confidence interval	*p*-value	Standardised Correlation Coefficient beta	95% confidence interval	*p*-value
Demographic data						
Age (year old)	0.115	-0.010, 0.119	0.095			
Male gender (n, (%))	-0.077	-3.147, 0.865	0.264			
BMI	-0.028	-0.384, 0.254	0.688			
ANCA (N, (%))						
MPO-ANCA (or P-ANCA) positivity	0.197	0.934, 4.822	0.004	-0.029	-2.527, 1.675	0.690
PR3-ANCA (or C-ANCA) positivity	-0.159	-5.342, -0.457	0.020	-0.135	-4.870, -0.034	0.047
Both ANCAs positivity	-0.047	-6.246, 3.060	0.500			
ANCA negativity	-0.104	-4.082, 0.524	0.129			
Laboratory results						
White blood cell count (/mm^3)	0.164	0.000, 0.000	0.017	0.051	0.000, 0.001	0.529
Lymphocyte count (/mm^3)	-0.189	-0.003, -0.001	0.006	0.105	-0.001, 0.003	0.364
Haemoglobin (g/dL)	-0.411	-1.616, 0.867	<0.001	-0.125	-0.943, 0.185	0.187
Platelet (x1,000/mm^3)	0.173	0.002, 0.015	0.012	-0.037	-0.011, 0.008	0.712
Prothrombin time (INR)	0.208	4.132, 19.446	0.003	0.062	-5.800, 12.793	0.459
Fasting glucose (mg/dL)	0.120	-0.002, 0.041	0.081			
Blood urea nitrogen (mg/dL)	0.344	0.066, 0.144	<0.001	0.309	0.034, 0.155	0.002
Creatinine (mg/dL)	0.221	0.311, 1.249	0.001	-0.11	-1.001, 0.293	0.282
Total cholesterol (mg/dL)	-0.248	-0.055, -0.017	<0.001	-0.077	-0.033, 0.010	0.306
Total protein (g/dL)	-0.011	-0.203, 0.172	0.869			
Serum albumin (g/dL)	-0.357	-4.390, -2.083	<0.001	0.016	-1.780, 2.074	0.889
Alkaline phosphatase (IU/L)	0.075	-0.005, 0.019	0.275			
Aspartate aminotransferase (IU/L)	0.065	-0.022, 0.063	0.348			
Alanine aminotransferase (IU/L)	-0.041	-0.038, 0.020	0.552			
Total bilirubin (mg/dL)	0.087	-0.270, 1.242	0.207			
ESR (mm/hr)	0.273	0.025, 0.072	<0.001	0.012	-0.030, 0.034	0.889
CRP (mg/L)	0.246	0.014, 0.045	<0.001	0.000	-0.022, 0.022	0.997
HALP score	-0.393	-0.187, -0.097	<0.001	-0.319	-0.233, -0.004	0.043

BVAS: Birmingham vasculitis activity score; AAV: antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody; BMI: body mass index; MPO: myeloperoxidase; P: perinuclear; PR3: proteinase 3; C: cytoplasmic; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; HALP: haemoglobin (g/L) x albumin (g/L) x lymphocyte count (/L)/platelet count (/L); FFS: five-factor score.

FFS was not included in the linear regression analysis due to the collinearity with BVAS. Clinical manifestations were excluded in the multivariable linear regression analysis because they are the items of BVAS and FFS.

There was no significant collinearity among HALP, haemoglobin, serum albumin, lymphocyte count and platelet count.

Table II. Cox hazards model analysis of the HALP score at diagnosis for the poor prognosis of AAV during follow-up.

Variables	Univariable analysis		
At diagnosis	Hazard ratio	95% confidence interval	*p*-value
In 212 patients with AAV			
HALP score for all-cause mortality	0.976	0.947, 1006	0.114
HALP score for relapse	0.991	0.977, 1.005	0.202
HALP score for ESRD	0.985	0.965, 1.005	0.148
In 170 patients with MPA and GPA			
HALP score for all-cause mortality	0.977	0.949, 1.007	0.129
HALP score for relapse	0.989	0.975, 1.005	0.173
HALP score for ESRD	0.979	0.956, 1.002	0.074
In 116 patients with MPA			
HALP score for all-cause mortality	0.973	0.934, 1.013	0.185
HALP score for relapse	0.986	0.966, 1.007	0.195
HALP score for ESRD	0.973	0.944, 1.002	0.064
In 54 patients with GPA			
HALP score for all-cause mortality	0.986	0.944, 1.031	0.543
HALP score for relapse	0.992	0.971, 1.014	0.485
HALP score for ESRD	0.996	0.958, 1.035	0.823
In 42 patients with EGPA			
HALP score for all-cause mortality	N/A	N/A	N/A
HALP score for relapse	1.011	0.966, 1.057	0.638
HALP score for ESRD	1.107	0.986, 1.244	0.085

HALP: haemoglobin (g/L) x albumin (g/L) x lymphocyte count (/L)/platelet count (/L); AAV: antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; EGPA: eosinophilic granulomatosis with polyangiitis; N/A: not applicable.

fusion between the cross-sectional and the cumulative activity of AAV. Based on this point, we expect that the HALP score may precisely reflect the degree of inflammation at the time of the laboratory test and furthermore reflect the dynamic changes in the activity of AAV, better than BVAS.

We first demonstrated that the HALP score at diagnosis was an efficient indicator to reflect the cross-sectional activity. However, this study also has several limitations. Due to a retrospective study design, we could not provide the serial HALP scores. Also, the small number of subjects required a validation study with the larger number of patients. In conclusion, the HALP score at diagnosis could reflect the cross-sectional activity, but it could not predict the prognosis in AAV patients.

Key messages

- HALP score at diagnosis could reflect the cross-sectional activity of AAV.
- HALP score at diagnosis could not predict all-cause mortality, relapse and end-stage renal disease during the follow-up of AAV.

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