Evaluation of Clinical Measures and Different Criteria for Diagnosis of Adult-onset Still's Disease in a Chinese Population

LINDI JIANG, ZHEN WANG, XIAOMIN DAI, and XUEJUAN JIN

ABSTRACT. ***Objective.*** To determine the value of clinical measures in diagnosis of adult-onset Still's disease (AOSD), and to identify the optimal set of proposed classification criteria, in a Chinese population.

Methods. A total of 70 patients with AOSD and 140 non-AOSD inpatients with fever were retrospectively identified at Zhongshan Hospital, Shanghai, from January 2003 to December 2009. Clinical measures and 4 sets of diagnostic criteria (Yamaguchi, Calabro, Cush, and Reginato) were evaluated by sensitivity, specificity, positive/negative predictive value (PPV, NPV), and positive/negative likelihood ratio (PLR, NLR) for diagnosis of AOSD.

Results. In our series, higher sensitivity included hyperpyrexia (temperature ≥ 39°C, 94.29%), arthralgia (80.0%), polymorphonuclear neutrophils (PMN) ≥ 75% (84.29%), serum ferritin ≥ 2-fold the upper normal value (90.0%), negative antinuclear antibodies (85.29%), and rheumatoid factor (84.38%); while higher specificity included transient erythema (98.57%), sore throat (85.0%), leukocytes ≥ 15,000/mm^3 (87.86%), and PMN ≥ 85% (85.0%). Rash, arthralgia, and sore throat were found to have better sensitivity and specificity (PLR 3.29–4.86). Leukocytes ≥ 10,000/mm^3, PMN ≥ 80%, and serum ferritin ≥ 5-fold the upper normal limit were set as critical points. The Reginato criteria set had the highest specificity, 99.29%. The Yamaguchi set had the highest sensitivity, 78.57%, with a better accuracy of 87.14%.

Conclusion. The Yamaguchi diagnostic criteria had better accuracy in Chinese patients. Indicators such as rash, arthralgia, sore throat, leukocytes ≥ 10,000/mm^3, PMN ≥ 80%, and serum ferritin ≥ 5-fold the upper normal limit were helpful for diagnosis of AOSD. We recommend using these indicators in combination instead of alone. (First Release Feb 1 2011; J Rheumatol 2011;38:741–6; doi:10.3899/jrheum.100766)

Key Indexing Terms:
ADULT-ONSET STILL'S DISEASE DIAGNOSIS CLASSIFICATION CRITERIA CHINESE

Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder of unknown etiology. Clinical presentation is nonspecific and heterogeneous. Symptoms commonly include high-spiking fevers, evanescent rash, and arthritis/arthralgia. Multiple organs may be involved simultaneously. Since there is no specific feature, no consensus on diagnostic criteria has been reached. The most commonly used classification criteria[1] were proposed by Yamaguchi, *et al*[2,3,4,5,6,7,8,9,10,11,12,13]. Other criteria include those of Cush, *et al*[14], Calabro, *et al*[15], and Reginato, *et al*[16]. All these criteria are based on elimination of other diseases, such as chronic infection, tumors, and other autoimmune disorders. Differential diagnosis is often based on treatment responses, and therefore may delay the establishment of the true causes. To date, few studies have examined the validity of the above-noted classification criteria[17,18,19].

Our objective was to assess the influence of the various clinical and laboratory measures suggestive for AOSD, and determine a more accurate set of classification criteria for AOSD in a Chinese population.

MATERIALS AND METHODS

Patients. We retrospectively reviewed the records of 210 adult patients treated at the Department of Internal Medicine, Zhongshan Hospital (affiliated to Fudan University), from January 2003 to December 2009. Among them, 70 cases were labeled AOSD by the attending physicians; a diagnosis other than AOSD was established for the remaining 140 cases complaining of fever during the same period. Demographic and medical information were extracted from medical records and telephone followup, and entered into the database using a standardized questionnaire. Results of routine laboratory tests, such as hemograms, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and liver enzymes, were available for all patients. The majority of cases also had data concerning antinuclear antibodies (ANA), rheumatoid factor (RF), and serum ferritin at the time of diagnosis.

Classification procedure. This was a retrospective analysis. The diagnosis

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of AOSD was based on the following steps: (1) The initial clinical assessment of patients presenting with clinical features (the typical symptoms and signs) of AOSD. (2) A thorough history, physical examination, and laboratory assessment for differential diagnosis; alternative diagnoses (e.g., infections, malignant tumor, and other autoimmune disorders) were fully considered by the attending physicians and eliminated based on an extensive panel of analysis such as bone marrow, imaging examinations, pathologic findings, and microbiological test results. ANA, anti-dsDNA antibody, and antineutrophil cytoplasmic antibody were routinely investigated to exclude other autoimmune diseases. (3) Assessment of prognosis: The "gold standard" diagnostic criteria were referred to for the effect of treatments, the disease courses, and complications. All patients were followed up at clinics or by telephone.

The mean followup period of patients with AOSD was 2.5 ± 1.6 years (range 1~80.4 months). Sixty-eight patients (97.1%) received glucocorticoid therapy, except for 2 patients who had good response to nonsteroidal antiinflammatory drugs. Sixty patients (83.6%) exhibited a monocyclic disease pattern, 4 (6.6%) experienced a polycyclic pattern, 3 (4.9%) exhibited a chronic course and had persistent articular symptoms in the absence of systemic features, and 3 (4.9%) died.

The control group included 140 patients with diseases other than AOSD, including infectious, neoplastic, and autoimmune diseases, established on the basis of clinical manifestations, laboratory tests, imaging examinations, pathologic findings, and microbiological test results.

Statistical analysis. Chi-square testing was performed for comparison of proportions. When small numbers of patients were compared, Fisher's exact test was used. Clinical features and laboratory tests were evaluated for sensitivity, specificity, positive/negative predictive value (PPV, NPV), and likelihood ratio of a positive/negative test result (PLR, NLR). Sensitivity and specificity were defined as the percentage of positive (sensitivity) or negative (specificity) findings of the variable from all AOSD or non-AOSD patients, according to the diagnostic gold standard. Positive and negative predictive values were defined as the percentage of the measure by correctly identified positives or negatives, respectively, from all positives or negatives. The PLR was calculated as (sensitivity/1 – specificity). The NLR was calculated as (1 – sensitivity/specificity). Receiver operating characteristic (ROC) curves of leukocytes, polymorphonuclear neutrophils (PMN), and serum ferritin were generated. A p value < 0.05 was considered statistically significant.

RESULTS

Demographics and control diagnosis. Seventy patients with AOSD (26 men, 44 women; age 36.1 ± 14.5 yrs, range 18–72 yrs, at time of diagnosis) were identified. Of the 140 control patients (75 men, 65 women; age 46.9 ± 18.5 yrs, range 16–89 yrs, at diagnosis), 69 had infectious diseases, 19 had neoplasms, and the remaining 52 had systemic autoimmune disorders other than AOSD (Table 1).

Clinical features. The most common symptoms and signs included fever (100%), hyperpyrexia (temperature ≥ 39°C, 94.29%), arthralgia (80.0%), sore throat (72.86%), lymphadenectasis (71.43%), rash (75.71%), and myalgia (41.43%). Compared with previous large series, fever (84.7%~100%), arthralgia (64.1%~100%), sore throat (38.7%~91.9%), myalgia (56.2%~83.9%), and rash (51.8%~87.1%) were reported[3,8,17,18,19].

In comparison to disease controls, the frequency of rash, arthralgia, arthroncus, sore throat, myalgia, lymphadenectasis, hepatomegaly, leukocytosis, neutrophilia, negative ANA and RF, and serum ferritin in AOSD patients was significantly higher ($p < 0.05$ for all). There were no significant differences in the frequency of cardiac effusion, pleural effusion, interstitial pneumonia, anemia, and thrombocytosis between the 2 groups.

Diagnostic efficacy of clinical and laboratory measures. Clinical features that were sensitive for establishing diagnosis of AOSD (≥ 80%) included hyperpyrexia (≥ 39°C, 94.29%) and arthralgia (80.0%) (Table 2). Clinical features with ≥ 80% specificity included transient erythema (98.57%) and sore throat (85.0%). The highest PPV was for transient erythema (92.59%). The top 4 highest NPV were hyperpyrexia (≥ 39°C, 92.86%), arthralgia (88.33%), rash, (86.72%) and sore throat (86.23%). Laboratory tests with ≥ 80% sensitivity included PMN ≥ 75% (84.29%), serum ferritin ≥ 2-fold the upper normal limit (90.0%), negative ANA (85.29%), and RF (84.38%). Laboratory tests with ≥ 80% specificity included leukocytes ≥ 15,000/mm^3 (87.86%) and PMN ≥ 85% (85.0%). The measures with higher PPV were leukocytes ≥ 15,000/mm^3 (67.92%) and serum ferritin ≥ 5-fold the upper normal limit (70.69%). The 3 laboratory tests with the highest NPV were leukocytes ≥ 10,000/mm^3 (86.49%), PMN ≥ 75% (88.30%), and serum ferritin ≥ 4-fold the upper normal limit (86.96%). The PLR was > 2.5 for hyperpyrexia (≥ 40°C, 2.52), transient erythema (24.97), arthralgia (3.29), rash (3.65), sore throat (4.86), leukocytes ≥ 10,000/mm^3 (2.50), PMN ≥ 80% (2.72), and serum ferritin ≥ 5-fold the upper normal limit (3.04). The highest PLR was for transient erythema, 24.97. The NLR was low for hyperpyrexia (≥ 39°C, 0.15), arthralgia (0.26), PMN ≥ 75% (0.26), and serum ferritin ≥ 2-fold the upper normal limit (0.20).

Serial tests revealed increased specificity and PLR when 1 out of the following 6 measures was combined with hyperpyrexia (≥ 39°C): rash, sore throat, arthralgia, leukocytes ≥

Table 1. Control group diagnoses.

Category of Control Disease	Diagnosis
Infectious diseases (n = 69)	Septicemia (5); pneumonia (16); encephalitis or meningitis (6); infectious endocarditis (5); viral infections (13); tuberculosis (18); others (6)*
Neoplasms (n = 19)	Hematological malignancies (18); multiple myeloma (1)
Systemic autoimmune diseases (n = 52)	Systemic lupus erythematosus (11); systemic vasculitis (10); polymyositis or dermatomyositis (9); others (14)**

* Cholecystitis (2), liver abscess (2), pelvic inflammatory disease (1), and maxillofacial cellulitis (1). ** Rheumatoid arthritis (3), Behçet's disease (1), panniculitis (4), Sjögren's Syndrome (1), undifferentiated connective tissue disease (2), sarcoidosis (1), necrotic lymphadenitis (2).

Table 2. Analysis of variables on diagnosis of AOSD in our series.

Variables	AOSD Group*, n = 70	Control Group*, n = 140	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	PLR (95% CI)	NLR (95% CI)
Fever								
≥ 39° C	66/70	88/140	94.29 (86.01–98.42)	37.14 (29.13–45.71)	42.86 (34.92–51.07)	92.86 (82.71–98.02)	1.50 (1.30–1.73)	0.15 (0.06–0.41)
≥ 40° C	39/70	31/140	55.71 (43.34–67.59)	77.86 (70.07–84.43)	55.71 (43.34–67.59)	77.86 (70.07–84.43)	2.52 (1.73–3.66)	0.57 (0.43–0.75)
Rash	53/70	29/140	75.71 (63.99–85.17)	79.29 (71.62–85.67)	64.63 (53.30–74.88)	86.72 (79.59–92.07)	3.65 (2.58–5.19)	0.31 (0.20–0.47)
Transient erythema	25/70	2/140	35.71 (24.61–48.07)	98.57 (94.93–99.83)	92.59 (75.71–99.09)	75.41 (68.51–81.46)	24.97 (6.10–102.54)	0.65 (0.55–0.78)
Arthralgia	56/70	34/140	80.00 (68.73–88.61)	75.71 (67.75–82.56)	62.22 (51.38–72.23)	88.33 (81.20–93.47)	3.29 (2.40–4.51)	0.26 (0.16–0.43)
Myalgia	29/70	29/140	41.43 (29.77–53.83)	79.29 (71.62–85.67)	50.00 (36.58–63.42)	73.03 (65.24–79.90)	2.00 (1.30–3.07)	0.74 (0.60–0.92)
Sore throat	51/70	21/140	72.86 (60.90–82.80)	85.00 (77.99–90.47)	70.83 (58.93–80.95)	86.23 (79.34–91.50)	4.86 (3.19–7.39)	0.32 (0.22–0.47)
Leukocytes								
≥ 10,000/mm^3	55/70	44/140	78.57 (67.13–87.48)	68.57 (60.19–76.15)	55.56 (45.22–65.55)	86.49 (78.69–92.23)	2.50 (1.90–3.29)	0.31 (0.20–0.50)
≥ 15,000/mm^3	36/70	17/140	51.43 (39.17–63.56)	87.86 (81.27–92.76)	67.92 (53.68–80.08)	78.34 (71.07–84.51)	4.24 (2.57–6.99)	0.55 (0.43–0.71)
PMN								
≥ 75%	59/70	57/140	84.29 (76.62–91.89)	59.29 (50.67–67.50)	50.86 (41.42–60.26)	88.30 (80.03–94.01)	2.07 (1.66–2.59)	0.26 (0.15–0.46)
≥ 80%	49/70	36/140	70.00 (57.87–80.38)	74.29 (66.22–81.29)	57.65 (46.45–68.30)	83.20 (75.47–89.29)	2.72 (1.98–3.75)	0.40 (0.28–0.59)
≥ 85%	30/70	21/140	42.86 (31.09–55.25)	85.00 (77.99–90.47)	58.82 (44.17–72.42)	74.84 (67.36–81.38)	2.86 (1.77–4.61)	0.67 (0.54–0.83)
Serum ferritin†								
≥ 2N	45/50	31/63	90.00 (79.18–96.67)	50.79 (37.89–63.62)	59.21 (47.33–70.35)	86.49 (71.23–95.46)	1.83 (1.40–2.39)	0.20 (0.08–0.47)
≥ 4N	44/50	23/63	88.00 (75.69–95.47)	63.49 (50.40–75.27)	65.67 (53.06–76.85)	86.96 (73.74–95.06)	2.41 (1.71–3.39)	0.19 (0.09–0.41)
≥ 5N	41/50	17/63	82.00 (68.56–91.42)	73.02 (60.35–83.43)	70.69 (57.27–81.91)	83.64 (71.20–92.23)	3.04 (1.98–4.66)	0.25 (0.13–0.45)
Negative ANA	58/68	84/120	85.29 (74.61–92.27)	30.00 (21.98–39.04)	40.85 (32.68–49.40)	78.26 (63.64–89.05)	1.22 (1.05–1.42)	0.49 (0.26–0.92)
Negative RF	54/64	70/101	84.38 (73.14–92.24)	30.69 (21.90–40.66)	43.55 (34.67–52.74)	75.61 (59.70–87.64)	1.22 (1.03–1.44)	0.51 (0.27–0.97)

* Positive cases/detection cases. † Normal values 400.0 ng/ml for men, 150.0 ng/ml for women. ≥ 2N: higher than 2-fold the upper normal limit. PPV: positive predictive value; NPV: negative predictive value; PLR: likelihood ratio of positive test result; NLR: liklihood ratio of negative test result; PMN: polymorphonuclear neutrophils; ANA: anti-nuclear antibodies; RF: rheumatoid factor.

10,000/mm^3, and PMN ≥ 80% (76.43%~95.71% vs 37.14%~85.0% for single items; PLR 3.21~12.99 vs 1.50~4.86). The combination of rash with the following items had PLR > 6: leukocytes ≥ 10,000/mm^3 (PLR 8.66), arthralgia (PLR 11.20), sore throat (PLR 7.80), and PMN ≥ 80% (PLR 6.17). A majority of the combination of 3 items yielded a PLR > 10: 28.97 for rash or sore throat or leukocytes ≥ 10,000/mm^3; 24.03 for hyperpyrexia (≥ 39°C) or arthralgia or sore throat; and 20.03 for sore throat or arthralgia or leukocytes ≥ 10,000/mm^3.

A comparison of our results with those from the Fautrel[18] and Yamaguchi[1] criteria is shown in Table 3.

Comparison of different classification criteria sets. Among the 4 classification criteria sets, the Reginato criteria had the highest specificity, 99.29%, with accuracy of 83.33%. The Yamaguchi criteria set had the highest sensitivity, 78.57%, with better accuracy: 87.14%. A comparison of our criteria series with those of Fautrel[18] and Yamaguchi[1] is shown in Table 4.

DISCUSSION

Fever is a prominent feature of AOSD (incidence 95.7%–100%) and frequently presents as hyperpyrexia (≥ 39°C)[2,3,4,5,6,7,8]. In our study, hyperpyrexia (≥ 39°C) was noted in 66 patients with AOSD (94.29%) and displayed a NPV of 92.86% with a NLR of 0.15, indicating that a diagnosis of AOSD is unlikely in patients without hyperpyrexia. However, fever is also the common symptom for tumors and

Table 3. Comparison of sensitivity and specificity in measures between our series and previous series in patients with adult-onset Still's disease (AOSD) and non-AOSD.

Measure	Our Series, n = 70/140*	Fautrel[18] n = 72/130*	Yamguchi[1] n = 90/267*
Fever ≥ 39° C			
Sensitivity, %	94.29	84.7	76
Specificity, %	37.14	63.8	76
Arthralgia			
Sensitivity, %	80.00	88.9	90
Specificity, %	75.71	57.7	48
Sore throat			
Sensitivity, %	72.86	52.8	70
Specificity, %	85.00	95.4	83
Typical rash			
Sensitivity, %	35.71	33.5	87
Specificity, %	98.57	96.2	99
Myalgia			
Sensitivity, %	41.43		56
Specificity, %	79.29		64
Leukocytes ≥ 10,000/mm^3			
Sensitivity, %	78.57	88.9	89
Specificity, %	68.57	62.3	58
PMN ≥ 80%			
Sensitivity, %	70.00	69.4	83
Specificity, %	74.29	83.1	66
Negative ANA			
Sensitivity, %	85.29	91.7	93
Specificity, %	30.00	19.2	18
Negative RF			
Sensitivity, %	84.38	98.6	94
Specificity, %	30.69	11.5	27

* AOSD/non-AOSD. PMN: polymorphonuclear cells; ANA antinuclear antibodies; RF: rheumatoid factor.

infections. A previous study[20] reported only slight fever in elderly patients with AOSD. Caution must be exercised to exclude AOSD if the patient has unexplained fever. Therefore patients with fever were selected as the control group in our series.

In our series, rash, arthralgia, and sore throat[1,16,18,21] were more sensitive (> 70%) and specific (> 70%), with a PLR of 3.29–4.86, suggesting that these 3 features are helpful for establishing a diagnosis of AOSD. The NLR of the 3 features was lower (0.26–0.32), indicating their value in ruling out AOSD based on the absence of these features. Actually, articular involvement is included in all major AOSD criteria sets[1,14,15,16]. Rash is listed in the major criteria in most criteria sets[1,15,16]. Transient erythema had a specificity of 98.57% and a PLR of 24.97 in our series. Its sensitivity, however, was lower (35.71%), and therefore it cannot be used alone in a criteria set. Sore throat has been adopted only by the Yamaguchi and Reginato criteria as a minor item. We noted a higher PLR for sore throat than for any other clinical or laboratory measure except for transient erythema in our series. As a prominent symptom of AOSD, sore throat is also the common symptom in thyroid and upper respiratory tract disorders. Careful inquiry and physical examination are essential in order to establish a diagnosis of AOSD.

Leukocytosis and/or neutrophilia were added to all criteria sets, but the cutoff value was inconsistent. Better sensitivity (> 70%) and specificity (> 70%) with a PLR of 2.7 and NLR of 0.40 were observed when the cutoff value of leukocytes (PLR 2.5; NLR 0.31) was set as not less than 10,000/mm^3 and PMN was 80% in the study (ROC of leukocytes and PMN are shown in Figure 1A and Figure 1B, respectively)[1,16]. Serum ferritin is an acute-phase reactant. A significant increase in serum ferritin has been proposed as an item of diagnosis or activity marker[4,5,6,7,8,10,11,12,13]. In our series, multiple cutoff values were used for serum ferritin, including > 2, > 4, and > 5-fold the upper normal limit. Among these cutoff values, an increase > 5-fold had the highest specificity at 73.02% (compared to 50.79% for > 2-fold) and a PLR of 3.04 (compared to 1.83 for > 2-fold); the sensitivity did not change significantly (the ROC for

Table 4. Evaluation of various sets of criteria for AOSD in our series compared to previous series.

Criteria	AOSD, n	Controls, n	Sensitivity, %	Specificity, %	PPV, %	NPV, %	PLR	NLR	Accuracy, %
Our series	70	140							
Reginato	36*	1†	51.43	99.29	97.30	80.35	72.44	0.49	83.33
Yamaguchi	55*	12†	78.57	91.43	82.09	89.51	9.17	0.23	87.14
Cush	43*	3†	61.43	97.86	93.48	83.54	28.71	0.39	85.71
Calabro	48*	7†	68.57	95.00	87.27	85.81	13.71	0.33	86.19
Fautrel[18]	72	130							
Yamaguchi	57*	8†	79.2	93.8	87.7	89.1			88.6
Yamaguchi[1]	53	164							
Reginato			51.2	99.2					87.9
Yamagucci	51*	13†	96.2	92.1					93.1
Cush			80	96.9					92.8
Calabro			60.9	98.1					88.7

* Number of positive patients by the evaluating criteria in the AOSD group. † Number of positive patients by the evaluating criteria in the control group. PPV: positive predictive value; NPV: negative predictive value; PLR: positive likelihood ratio; NLR: negative likelihood ratio.

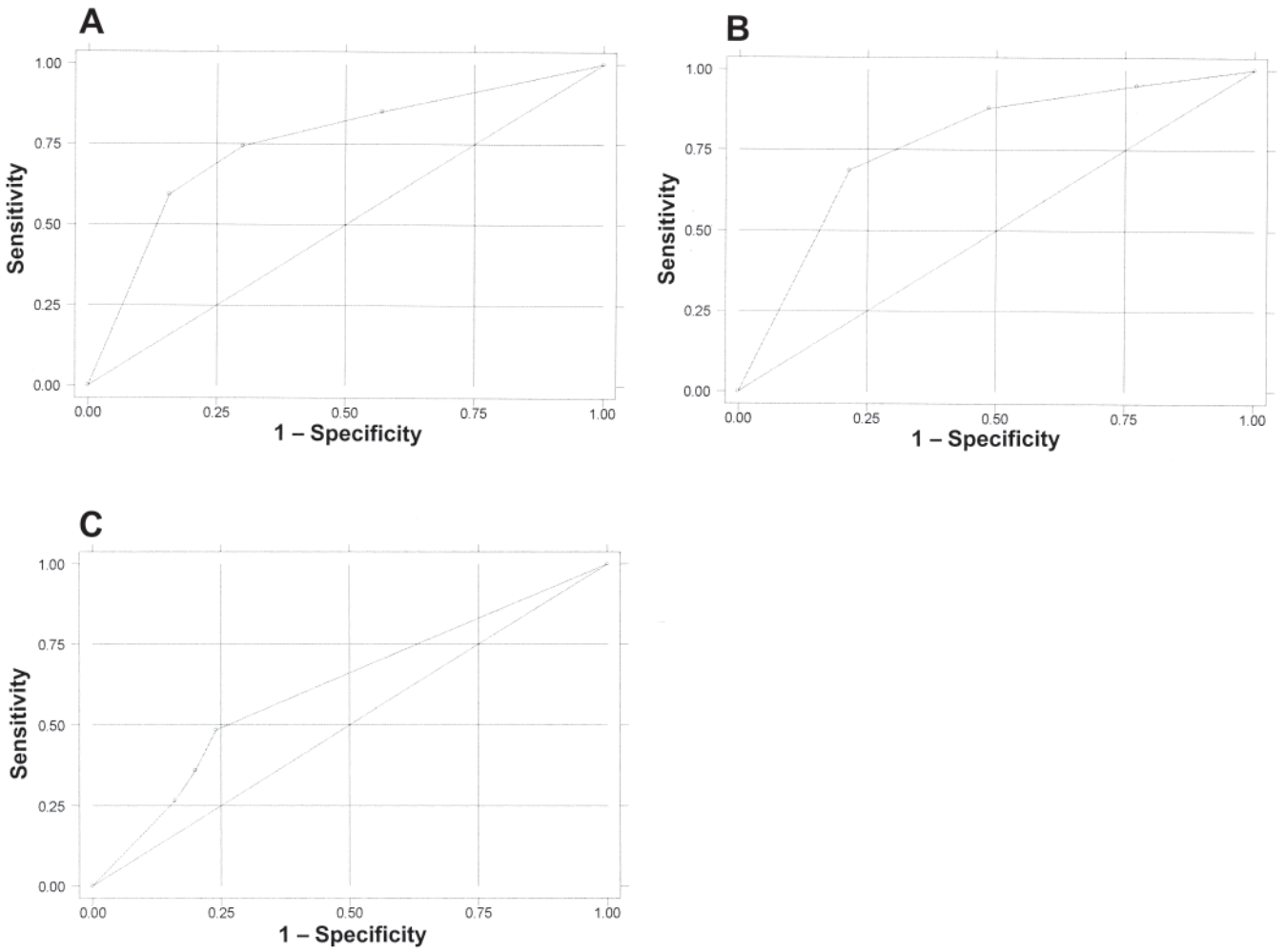

Figure 1. Receiver operating characteristic (ROC) curves for leukocytes (A), PMN (B), and serum ferritin (C). Area under the curve: A, 0.7546; B, 0.7698; C, 0.6147.

serum ferritin is shown in Figure 1C). We therefore recommend using serum ferritin ≥ 5-fold the upper normal limit as the critical point for diagnosis of AOSD[12]. Negative ANA and RF have high sensitivity (84.38%, 94.29%, respectively) but low specificity (30.0%, 37.14%, respectively), indicating these 2 measures are prone to misdiagnosis if used singly. Thus these 2 measures became one of the items in various criteria sets for differentiation of other autoimmune diseases[1,14,15,16].

Our study also validated that the diagnostic possibility of AOSD could increase greatly when findings of hyperpyrexia were combined with 2 or 3 of sore throat, arthralgia, rash, PMN ≥ 80%, and leukocytes ≥ 10,000/mm^3.

Among the 4 criteria sets included in our study, the Reginato criteria displayed the highest specificity, 99.29%; whereas the Yamaguchi criteria had the highest sensitivity, 78.57%, and better accuracy: 87.14%. The results from the Yamaguchi set are similar to the conclusions of Fautrel, *et al*[18], and the results from the Reginato or Calabro sets are similar to Yamaguchi[1]. The sensitivities of various sets of AOSD criteria are lower than that of the study of Masson, *et al*[17] (Reginato: 55.25%; Yamaguchi: 93.5%; Cush and Calabro: 80.6%).

The sensitivity and specificity of many AOSD disease features, including hyperpyrexia, arthralgia, and negative ANA and RF, in our series differed significantly in comparison with previous reports. For example, the specificity of fever in our study was lower than previously reported. Different control groups may have contributed to the observed differences. Our controls complaining of fever were different from those of the Fautrel study completing ferritin and glycosylated ferritin testing[18], and were also different from the Yamaguchi study including rheumatic disease, infectious disease, and fever of unknown origin[1]. Moreover, the control group in our study included more disorders that are difficult to differentiate from AOSD (Table 1), and this may have contributed to different sensitivity and specificity.

It is noteworthy that the frequency of myalgia (41.43%) was lower in our series compared with that in other reports (56.2%–83.9%). Consistent with our findings, one study conducted in Chinese people reported a low frequency of myalgia (27.9%)[10], thus indicating an ethnic difference.

In summary, the Yamaguchi diagnostic criteria[1] were found to have better accuracy in our series. Our results also indicate that rash, arthralgia, sore throat, leukocytes ≥ 10,000/mm^3, PMN ≥ 80%, and serum ferritin ≥ 5-fold the upper normal limit are helpful for diagnosis of AOSD. We recommend using these features in combination instead of alone.

REFERENCES

1. Yamaguchi M, Otha A, Tsunematsu T, Kasukawa R, Mizushima Y, Kashiwagi H, et al. Preliminary criteria for classification of adult Still's disease. J Rheumatol 1992;19:424-30.
2. Louthrenoo W, Aramsareewong T, Sukitawut W. Adult onset Still's disease: Clinical features and outcome in 16 Thai patients. J Clin Rheumatol 2001;7:301-30.
3. Pay S, Turkcapar N, Kalyoncu M, Simsek I, Beyan E, Ertenli I, et al. A multicenter study of patients with adult-onset Still's disease compared with systemic juvenile idiopathic arthritis. Clin Rheumatol 2006;25:639-44.
4. Efthimiou P, Paik PK, Bielory L. Diagnosis and management of adult onset Still's disease. Ann Rheum Dis 2006;65:564-72.
5. Singh S, Samant R, Joshi VR. Adult onset Still's disease: a study of 14 cases. Clin Rheumatol 2008;27:35-9.
6. Mehrpoor G, Owlia MB, Soleimani H, Ayatollahi J. Adult-onset Still's disease: a report of 28 cases and review of the literature. Mod Rheumatol 2008;18:480-5.
7. Uppal SS, Pande IRA, Kumar A, Kailash S, Sekharan NG, Adya CM. Adult onset Still's disease in northern India: Comparison with juvenile onset Still's disease. Br J Rheumatol 1995;34:429-34.
8. Pouchot J, Sampalis JS, Beaudet F, Carette S, Decary F, Salusinsky-Sternbach M, et al. Adult Still's disease; manifestations, disease course, and outcome in 62 patients. Medicine (Baltimore) 1991;70:118-36.
9. Uppal SS, Al-Mutairi M, Hayat S, Abraham M, Malaviya A. Ten years of clinical experience with adult onset Still's disease: is the outcome improving? Clin Rheumatol 2007;26:1055-60.
10. Zeng T, Zou YQ, Wu MF, Yang CD. Clinical features and prognosis of adult-onset Still's disease: 61 cases from China. J Rheumatol 2009;36:1026-31.
11. Akritidis N, Papadopoulos A, Pappas G. Long-term follow-up of patients with adult-onset Still's disease. Scand J Rheumatol 2006;35:395-7.
12. Evensen KJ, Swaak TJG, Nossent JC. Increased ferritin response in adult Still's disease: specificity and relationship to outcome. Scand J Rheumatol 2007;36:107-10.
13. Evensen KJ, Nossent HC. Epidemiology and outcome of adult-onset Still's disease in Northern Norway. Scand J Rheumatol 2006;35:48-51.
14. Cush JJ, Medsger TA, Christy WC, Herbert DC, Cooperstein LA. Adult onset Still's disease: clinical course and outcome. Arthritis Rheum 1987;30:186-95.
15. Calabro JJ, Londino AV. Adult onset Still's disease. J Rheumatol 1986;13:827-8.
16. Reginato AJ, Schumacher HR, Baker DG, O'Connor CR, Ferreiros J. Adult onset Still's disease: Experience with 23 patients and literature review with emphasis on organ failure. Semin Arthritis Rheum 1987;17:39-57.
17. Masson C, Le Loet X, Liote F, Dubost JJ, Boissier MC, Perroux-Goumy L, et al. Comparative study of 6 types of criteria in adult Still's disease. J Rheumatol 1996;23:495-7.
18. Fautrel B, Zing E, Golmard JL, Le Moel G, Bissery A, Rioux C, et al. Proposal for a new set of classification criteria for adult-onset Still disease. Medicine (Baltimore) 2002;81:194-200.
19. Ohta A, Yamaguchi M, Tsunematsu T, Kasukawa R, Mizushima H, Kashiwagi H, et al. Adult Still's disease: A multicenter survey of Japanese patients. J Rheumatol 1990;17:1058-63.
20. Cagatay Y, Gul A, Cagatay A, Kamali S, Karadeniz A, Inanc M, et al. Adult-onset Still's disease. Int J Clin Pract 2009;63:1050-5.
21. Nguyen KH, Weisman MH. Severe sore throat as a presenting symptom of adult onset Still's disease: a case series and review of the literature. J Rheumatol 1997;24:592-7.