Application of the 2023 ACR/EULAR antiphospholipid syndrome classification criteria to patients fulfilling the 2006 revised Sapporo criteria

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Abstract

Objective

The American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR) developed new classification criteria for antiphospholipid syndrome (APS) in 2023. Although the new criteria yielded high specificity, further validation is needed in Asia, as the clinical characteristics of APS differ across ethnicities. We applied the 2023 ACR/EULAR criteria to Korean patients classified as having APS by the 2006 revised Sapporo criteria and assessed the concordance rate between the criteria.

Methods

For this study, 126 patients with APS were included. Clinical and laboratory data were reviewed, and the fulfilment of the 2023 ACR/EULAR criteria was assessed for each patient.

Result

Of the 126 patients classified by the 2006 revised Sapporo criteria, 107 had APS according to the 2023 ACR/EULAR criteria, accounting for a concordance rate of 84.9%. The concordance rate differed according to the index event. Patients with venous thromboembolism had the highest concordance rate (100%), followed by those with arterial thrombosis (76.4%). Patients with obstetric events had the lowest concordance rate (45.5%), attributable to the stricter obstetric criterion in the 2023 ACR/EULAR criteria than in the 2006 revised Sapporo criteria.

Conclusion

In Korean patients with APS, the concordance rate between the 2023 ACR/EULAR criteria and the 2006 revised Sapporo criteria was high. The concordance rate was considerably lower when confined to patients with obstetric APS. The 2023 ACR/EULAR criteria are stricter, particularly for obstetric events; its emphasis on specificity may result in the exclusion of patients with clinically significant obstetric APS.

Key words

antiphospholipid syndrome, 2023 ACR/EULAR criteria, 2006 revised Sapporo criteria

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Introduction

Antiphospholipid syndrome (APS) is characterised by recurrent venous or arterial thrombosis or pregnancy morbidities in the presence of persistent antiphospholipid autoantibodies (aPL) (1). For the diagnosis of APS, the Sapporo criteria, which were published in 1999 (2) and revised in 2006 (3), have been widely adopted in clinical practice over the years. Although classification criteria and diagnostic criteria are apparently different, both are often used interchangeably by many clinicians, especially for heterogeneous diseases which lack a gold standard for diagnosis such as APS (4). To be classified as having APS, the 2006 revised Sapporo criteria require ≥1 clinical feature (thrombosis or pregnancy morbidity) and ≥1 laboratory feature (positive lupus anticoagulant [LA], immunoglobulin [Ig] G/IgM anti-β2 glycoprotein I antibodies [anti-β2 GPI], or IgG/IgM anti-cardiolipin antibodies [aCL] with at least two aPL tests performed at least 12 weeks apart (3). However, the 2006 revised Sapporo criteria have been criticised owing to several limitations (5-7). First, the risk factors of thrombosis were not considered. Given that the cardiovascular risk factors are closely related to thromboembolic events in APS (8), the lack of consideration of these risk factors is an important limitation. Second, clinical manifestations such as cardiac valvulopathy and thrombocytopenia, which are relatively less common, were not included as clinical criteria, and the definition of pregnancy morbidity was somewhat general. Notably, non-criteria clinical manifestations are common and should not be overlooked, as they are also associated with damage accrual in APS (9). Finally, despite accumulating evidence on the different risks of thrombosis and pregnancy morbidity according to the aPL profile, risk stratification by the aPL profile is lacking in the 2006 revised Sapporo criteria. Given the limitations of the 2006 revised Sapporo criteria, the American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR) developed new classification criteria for APS in 2023 (the 2023 ACR/EULAR classification criteria) (10). In the new classification criteria, at least one positive aPL test within 3 years of identification of an aPL-associated clinical condition is required as an entry criterion. Then, manifestations are clustered into six clinical domains (venous thromboembolism [VTE], arterial thrombosis [AT], microvascular, obstetric, cardiac valve, and haematologic domains) and two laboratory domains (LA and IgG/IgM anti-β2 GPI or aCL) with differently weighted scores. Patients with ≥3 points from clinical domains and ≥3 points from laboratory domains can be classified as having APS (10). The new classification criteria yielded a sensitivity and specificity of 84% and 99%, respectively, in the validation cohort (10). However, in the validation cohort, most patients were white; less than 10% were Asian (10). Given that clinical characteristics of APS differ across different ethnicities (11), further validation studies on various ethnic populations are needed.

In this study, we applied the 2023 ACR/EULAR criteria to Korean patients with APS who were classified according to the 2006 revised Sapporo criteria and assessed the concordance rate between the two criteria.

Methods

Patients

This study included 126 patients classified as having APS according to the 2006 revised Sapporo criteria (3) at two tertiary hospitals in South Korea. All patients were Korean. The following clinical data at the time of APS diagnosis were collected by electronic medical record review: age, sex, presence of VTE, high-risk VTE profile, AT, high-risk cardiovascular disease (CVD) profile, pregnancy morbidity (≥3 consecutive pre-foetal [<10 w] or early foetal [10 w 0 d–15 w 6 d] deaths, foetal death [16 w 0 d–33 w 6 d] in the absence of pre-eclampsia (PEC) with severe features or placental insufficiency (PI) with severe features. Additionally, PEC with severe features (<34 w 0 d) or PI with severe features (<34 w 0 d) with or without foetal death, PEC with severe features (<34 w 0 d), and PI with severe features (<34 w 0 d) with or

without foetal death, cardiac valvulopathy (valve thickening, and vegetation), and thrombocytopenia (platelet count 20–130×10^9/L) were collected from the medical review. High-risk VTE profile was defined as ≥1 major VTE risk factors (active malignancy, hospital admission, major trauma, and surgery [general/spinal/epidural anaesthesia for >30 min within 3 months prior to the event]) or ≥2 minor VTE risk factors (active systemic autoimmune disease or active inflammatory bowel disease, acute or active severe infection, central venous catheter, hormone replacement therapy or oestrogen containing oral contraceptives/ongoing *in vitro* fertilisation treatment, long distance travel, obesity, pregnancy or postpartum period, prolonged immobilisation, surgery (general/spinal/epidural anaesthesia for <30 min within 3 months prior to the event) (10). High-risk CVD profile was defined as ≥1 high CVD risk factor (arterial hypertension (systolic blood pressure ≥180 mmHg or diastolic blood pressure ≥110 mmHg), chronic kidney disease, diabetes mellitus (with organ damage or long disease duration), and hyperlipidaemia (total cholesterol ≥310 mg/dl or low-density lipoprotein-cholesterol >190 mg/dl). High-risk CVD profile was also defined as ≥3 moderate CVD risk factors (arterial hypertension [on treatment or with systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg], current tobacco smoking, diabetes mellitus [without organ damage and short disease duration], hyperlipidaemia [on treatment or with total cholesterol <310 mg/dl or low-density lipoprotein-cholesterol <190 mg/dl], and obesity) (10).

aPL profile

LA was tested using an ACL TOP 700 coagulation analyser (Instrumentation Laboratory, Milan, Italy) with an assay kit utilising diluted Russell's viper venom (HemosIL Diluted Russell's Viper Venom Time Screen/Confirm kit, Instrumentation Laboratory). The IgG/IgM aCL and anti-β2 GPI were measured using an automated fluorescence enzyme immunoassay (EliA; Phadia, Sweden). The thresholds for moderate positive and high positive were 40 units and 80 units, respectively, for IgG/IgM aCL and anti-β2 GPI.

Table I. Characteristics of the 126 patients classified as APS according to the 2006 revised Sapporo classification criteria.

Characteristics	Values
Demographic data	
Age, years	40 (24)
Female sex	62 (49.2)
Vascular thrombosis	
AT	72 (57.1)
VTE	56 (44.4)
Small-vessel thrombosis	2 (1.6)
Pregnancy morbidity	
≥1 foetal death at or beyond the 10w of gestation	6 (4.8)
≥1 premature birth before the 34w of gestation because of eclampsia, severe PEC, or PI	5 (4.0)
≥3 consecutive abortions before the 10w of gestation	5 (4.0)
aPL positivity	
LAC	96 (76.2)
IgG anti-β2 GPI	34 (27.0)
IgM anti-β2 GPI	15 (11.9)
IgG aCL	34 (27.0)
IgM aCL	8 (6.3)

Values are expressed as median (interquartile range) or number (percentage).
APS: anti-phospholipid syndrome; AT: arterial thrombosis; VTE: venous thromboembolism; PEC: pre-eclampsia; PI: placental insufficiency; aPL: anti-phospholipid autoantibodies; LAC: lupus anticoagulant; Ig: immunoglobulin; anti-β2 GPI: anti-β2 glycoprotein I antibodies; aCL: anti-cardiolipin antibodies.

Ethics approval

This study was approved by the Institutional Review Board (IRB) of Severance Hospital (IRB no.: 4-2024-0628) and conformed with the Declaration of Helsinki. Owing to the retrospective nature of the study, the requirement for informed consent was waived.

Application of the 2023 ACR/EULAR criteria

Based on the clinical and laboratory data reviewed, clinical domains (six domains) and laboratory domains (two domains) were each scored according to the 2023 ACR/EULAR criteria (10). The proportion of patients fulfilling the 2023 ACR/EULAR criteria (clinical domains score ≥3 and laboratory domains score ≥3) was evaluated. The characteristics of patients who did not fulfil the 2023 ACR/EULAR criteria were summarised in detail.

Statistical analyses

Continuous variables and categorical variables were expressed as median (interquartile range) and number (%), respectively. The distributions of clinical domains score and laboratory domains score were visualised using histograms. All analyses were performed using SPSS software v. 28.0 (IBM Corporation, Armonk, NY, USA).

Results

Patients' characteristics

The characteristics of the 126 patients classified as having APS according to the 2006 revised Sapporo criteria are shown in Table I. The median age of the patients was 40 (24) years, and 49.2% were female. AT, VTE, and small-vessel thrombosis were present in 72 (57.1%), 56 (44.4%), and 2 (1.6%) patients, respectively. Furthermore, ≥1 foetal death at or beyond the 10th week of gestation, ≥1 premature birth before the 34th week of gestation because of eclampsia, severe PEC, or PI, and ≥3 consecutive abortions before the 10th week of gestation occurred in 6 (4.8%), 5 (4.0%), and 5 (4.0%) patients, respectively. LA, IgG anti-β2 GPI, IgM anti-β2 GPI, IgG aCL, and IgM aCL were positive in 96 (76.2%), 34 (27.0%), 15 (11.9%), 34 (27.0%), and 8 (6.3%) patients, respectively.

Application of the 2023 ACR/EULAR criteria

The scores of each domain of the 2023 ACR/EULAR criteria are summarised in Table II. The median values

Table II. Fulfilment of each criterion of the 2023 ACR/EULAR APS classification criteria.

Domains	Score	Values
Clinical domains		
Domain 1. Macrovascular (VTE)		
VTE with a high-risk VTE profile	1	7 (5.6)
VTE without a high-risk VTE profile	3	49 (38.9)
Domain 2. Macrovascular (AT)		
AT with a high-risk CVD profile	2	17 (13.5)
AT without a high-risk CVD profile	4	55 (43.7)
Domain 3. Microvascular		
Suspected	2	2 (1.6)
Established	5	0 (0.0)
Domain 4. Obstetric		
≥3 Consecutive pre-foetal (<10w) and/or early foetal (10w 0d-15w 6d) deaths	1	6 (4.8)
Foetal death (16w 0d-33w 6d) in the absence of PEC with severe features or PI with severe features	1	4 (3.2)
PEC with severe features (<34w 0d) or PI with severe features (<34w 0d) with/without foetal death	3	4 (3.2)
PEC with severe features (<34w 0d) and PI with severe features (<34w 0d) with/without foetal death	4	2 (1.6)
Domain 5. Cardiac valve		
Thickening	2	56 (44.4)
Vegetation	4	5 (4.0)
Domain 6. Haematology		
Thrombocytopenia	2	20 (15.9)
Laboratory domains		
Domain 7. aPL test by coagulation-based functional assay		
Positive LAC (single-one time)	1	14 (11.1)
Positive LAC (persistent)	5	96 (76.2)
Domain 8. aPL test by solid phase assay		
Moderate or high positive (IgM) (aCL and/or anti-β2 GPI)	1	12 (9.5)
Moderate positive (IgG) (aCL and/or anti-β2 GPI)	4	20 (15.9)
High positive (IgG) (aCL or anti-β2 GPI))	5	18 (14.3)
High positive (IgG) (aCL and anti-β2 GPI)	7	8 (6.3)
Fulfilment of 2023 ACR/EULAR APS classification criteria	-	107 (84.9)

Values are expressed as median (interquartile range) or number (percentage).
ACR: American College of Rheumatology; EULAR: European Alliance of Associations for Rheumatology; APS: anti-phospholipid syndrome; VTE: venous thromboembolism; AT: arterial thrombosis; CVD: cardiovascular disease; PEC: pre-eclampsia; PI: placental insufficiency; aPL: anti-phospholipid autoantibodies; LAC: lupus anticoagulant; Ig: immunoglobulin; anti-β2 GPI: anti-β2 glycoprotein I antibodies; aCL: anti-cardiolipin antibodies.

of clinical domains score and laboratory domains score were 4 (3) and 5 (1), respectively. The distributions of the clinical domains score and laboratory domains score are shown in Figure 1. Clinical domain score ≥3 was met in 116 (92.1%) patients, and laboratory domain score ≥3 was met in 117 (92.9%) patients. The 2023 ACR/EULAR criteria were fulfilled in 107 patients, accounting for a concordance rate of 84.9% with the 2006 revised Sapporo criteria.

Characteristics of the patients not classifiable with APS

The characteristics of the 19 patients who did not fulfil the 2023 ACR/EULAR criteria are reported in Table III. Of the 19 patients, 10 patients (no. 1-10) did not fulfil clinical domains score ≥3, whereas nine patients (patients no. 11–19) did not fulfil laboratory domains score ≥3. Of the 10 patients with clinical domains score <3, five patients (no. 1–5) had obstetric events, accounting for 31.3% of the total 16 patients who had obstetric events as an index event; five patients (no. 6–10) had AT events, accounting for 6.9% of the total 72 patients who had AT events as an index event; and no patient had VTE events. Of the nine patients who did not fulfil laboratory domains score ≥3, six patients (no. 11–16) had moderate or high positive IgM aCL or anti-β2 GPI with negative LA, and three patients (no. 17–19) had moderate or high positive IgM aCL or anti-β2 GPI with single positive LA.

Considering that the proportion of patients who do not fulfil clinical domains score ≥3 differs according to the index events, we next investigated the concordance rate between the two criteria according to the index events. The concordance rate between the two criteria was 100% in patients whose index events were VTE events (with or without other events). The concordance rate in patients who had AT events only was 76.4%. Patients who had obstetric events only had the lowest concordance rate (45.5%) (Table IV). The concordance rate was 100% in patients who had more than one event.

Discussion

In this study, we applied the 2023 ACR/EULAR criteria for APS to Korean patients with APS classified based on the 2006 revised Sapporo criteria. We found that the concordance rate between the two criteria was 84.9%. The concordance rate differed according to the index event, with patients with VTE events having the highest concordance rate (100%) and those with obstetric events having the lowest concordance rate (45.5%). To our knowledge, this is the first study to apply the new criteria to Korean patients with APS. Our data suggest that most Korean patients classified as having APS according to the 2006 revised Sapporo criteria can still be enrolled in research according to the new criteria, except for the patients with obstetric APS.

Validation studies from China have reported sensitivity and specificity of the 2006 revised Sapporo criteria and the 2023 ACR/EULAR criteria, respectively (12, 13) (Table V). The reported sensitivity and specificity of the 2006 revised Sapporo criteria from the two studies exhibited high heterogeneity, with an I^2 of 97.0% and 65.1%, respectively, indicating a low level of agreement between the studies. In contrast, the reported sensitivity and specificity of the 2023 ACR/EULAR criteria from the two studies demonstrated low heterogeneity, with an I^2 of 0.0% and 0.0%, respectively, suggesting a high level of agreement between the studies.

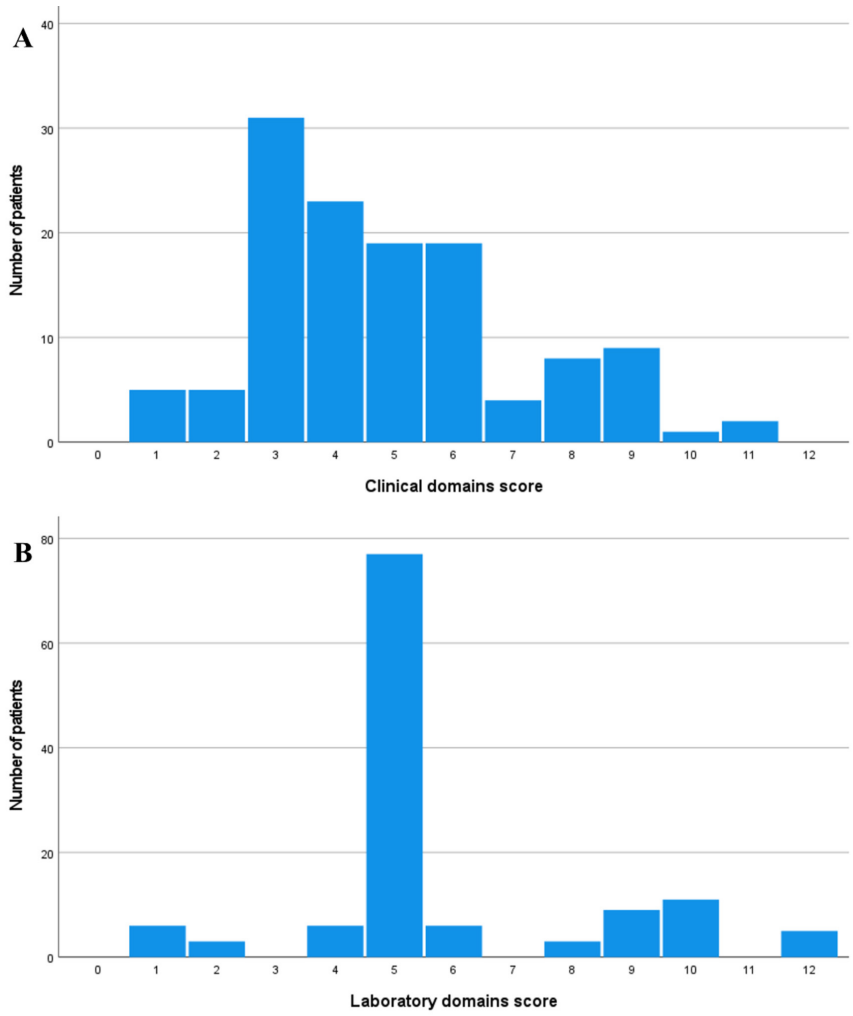

Fig. 1. Distributions of the (**A**) clinical domains score and (**B**) laboratory domains score.

Thus, given the higher level of agreement across studies, the 2023 ACR/EULAR criteria may be more advantageous than the 2006 revised Sapporo criteria in selecting a more homogeneous study population. In addition, the specificity was higher (98% *vs.* 90–95%) and the sensitivity was lower (82% *vs.* 85–98%) for the 2023 ACR/EULAR criteria compared to the 2006 revised Sapporo criteria (12, 13). This agrees with the data from the validation cohort for developing the 2023 ACR/EULAR criteria (10). Given that classification criteria are intended to include homogenous populations for research, high specificity is desirable, even at the expense of sensitivity (4). In this regard, the 2023 ACR/EULAR criteria represent a significant improvement for classifying patients with APS. Our study expands on previous reports by analysing the concordance rate between the 2006 revised Sapporo criteria and the 2023 ACR/EULAR criteria, which had not been previously reported. We found that the overall concordance rate between the two criteria was 84.9%. However, this rate varied depending on the index event, with a notably lower concordance observed in patients with obstetric events. This finding likely reflects the substantial modifications made to the obstetric domain in the 2023 ACR/EULAR criteria compared to the 2006 revised Sapporo criteria.

Compared to the 2006 revised Sapporo criteria, significant changes have been made in the obstetric domain. Abortion has been widely used as a criterion for classifying APS for a long time (2, 3); however, the direct link between aPL and recurrent miscarriage, whether it occurs early or late in pregnancy, is a topic of ongoing debate (14-16). Assessing other potential causes of pregnancy loss remains complex and challenging. Conversely, there is a clearer association between aPL and conditions like PI, PEC, or eclampsia, which exhibit stronger specificity in the context of APS (17). Accordingly, in the new criteria, cases of abortion without PEC or PI are assigned a score of one point and cannot independently meet the clinical domain of the new criteria (10). Attributable to this more stringent criterion, we observed that a substantial proportion (6 of 11 patients, 54.5%) of patients with obstetric APS according to the 2006 revised Sapporo criteria were not classifiable as APS according to the new criteria. The more stringent criterion improves specificity; however, it also poses a challenge in clinical research, as it excludes severe pathological pregnancy events with aPL positivity but lacking PEC or PI. The applicability of the new criteria in patients with obstetric APS needs further validation. Before additional validation data accumulate, the 2006 revised Sapporo criteria could be used complementarily to the 2023 ACR/EULAR criteria for patients who only have obstetric events.

Another important change in the new criteria is the integration of VTE and CVD risk factors in the VTE domain and AT domain, respectively (10). Stratification of the macrovascular events by traditional risk factors contributes to a more specific classifying process (12). In our study, 29.4% (5 of 17) of patients with AT with a high-risk CVD profile were not classifiable as having APS according to the new criteria, whereas only 10.9% (6 of 55) of patients with AT without a high-risk CVD profile were not classifiable as having APS. This difference between individuals with and without high-risk profiles reflects the importance of considering traditional risk factors of macrovascular events when diagnosing APS.

This study has some limitations. First, this was a retrospective study. As the data collection was done based on a retrospective electronic medical record review, the presence of some rare manifestations, such as livedo racemose, and adrenal haemorrhage, could be

Table III. Characteristics of the 19 patients not classified as APS according to the 2023 ACR/EULAR APS classification criteria.

Patients (age/sex)	Characteristics	Clinical domains	Laboratory domains
n. 1 (38/F)	Foetal death (29w) in the absence of PEC with severe features or PI with severe features, persistently positive LAC	1	5
n. 2 (38/F)	Early foetal (10w) death, persistently positive LAC, high positive IgG anti-β2 GPI (97.0 U/mL)	1	10
n. 3 (37/F)	≥3 Consecutive pre-foetal (<10w), persistently positive LAC, high positive IgG aCL (841.0 GPL) and IgG anti-β2GPI (4756.7 U/mL)	1	12
n. 4 (42/F)	Foetal death (30w) in the absence of PEC with severe features or PI with severe features, moderate positive IgG aCL (49.0 GPL)	1	4
n. 5 (41/F)	Foetal death (31w) in the absence of PEC with severe features or PI with severe features, single positive LAC, moderate positive IgG aCL (57.4 GPL)	1	5
n. 6 (45/M)	AT with high-risk CVD profile, persistently positive LAC, moderate positive IgG anti-β2 GPI (76.0 U/mL)	2	9
n. 7 (34/M)	AT with high-risk CVD profile, persistently positive LAC	2	5
n. 8 (44/M)	AT with high-risk CVD profile, high positive IgG anti-β2 GPI (88.0 U/mL)	2	5
n. 9 (39/M)	AT with high-risk CVD profile, single positive LAC, moderate positive IgG aCL (47.1 GPL)	2	5
n. 10 (48/M)	AT with high-risk CVD profile, moderate positive IgG aCL (42.0 GPL)	2	4
n. 11 (66/F)	≥3 Consecutive pre-foetal (<10w), mitral valve thickening, high positive IgM anti-β2 GPI (101.6 U/mL)	3	1
n. 12 (26/F)	AT without high-risk CVD profile, high positive IgM aCL (92.5 MPL)	4	1
n. 13 (48/M)	AT without high-risk CVD profile, moderate positive IgM anti-β2GPI (59.0 U/mL)	4	1
n. 14 (42/M)	AT without high-risk CVD profile, moderate positive IgM anti-β2 GPI (40.0 U/mL)	4	1
n. 15 (66/M)	AT without high-risk CVD profile, mitral valve/tricuspid valve thickening, moderate positive IgM anti-β2 GPI (49.0 U/mL)	6	1
n. 16 (68/M)	AT without high-risk CVD profile, mitral valve thickening, moderate positive IgM anti-β2 GPI (65.2 U/mL)	6	1
n. 17 (88/F)	AT with high-risk CVD profile, mitral valve thickening, single positive LAC, high positive IgM aCL (170.0 MPL)	4	2
n. 18 (47/M)	AT with high-risk CVD profile, mitral valve/tricuspid valve thickening, single positive LAC, moderate positive IgM anti-β2 GPI (51.0 U/mL)	4	2
n. 19 (30/F)	AT without high-risk CVD profile, mitral valve thickening, single positive LAC, moderate positive IgM aCL (43.0 MPL)	6	2

APS: anti-phospholipid syndrome; ACR: American College of Rheumatology; EULAR: European Alliance of Associations for Rheumatology; AT: arterial thrombosis; CVD: cardiovascular disease; PEC: pre-eclampsia; PI: placental insufficiency; LAC: lupus anticoagulant; Ig: immunoglobulin; anti-β2 GPI: anti-β2 glycoprotein I antibodies; aCL: anti-cardiolipin antibodies.

Table IV. Fulfilment of 2023 ACR/EULAR APS classification criteria according to the index event.

	Fulfilment of 2023 ACR/EULAR criteria
VTE only (n=42)	42 (100.0)
AT only (n=55)	42 (76.4)
Obstetric event only (n=11)	5 (45.5)
VTE + AT (n=13)	13 (100.0)
VTE + Obstetric (n=1)	1 (100.0)
AT + Obstetric (n=4)	4 (100.0)

Values are expressed as number (percentage).
ACR: American College of Rheumatology; EULAR: European Alliance of Associations for Rheumatology; APS: anti-phospholipid syndrome; VTE: venous thromboembolism; AT: arterial thrombosis.

Table V. Summary of sensitivity, specificity, and heterogeneity across studies.

	Sensitivity (95% CI)	Specificity (95% CI)	Concordance rate between the two criteria
Yang, *et al*. (12), 2006 criteria	0.98 (0.96-0.99)	0.90 (0.87-0.92)	N/A
Zhao, *et al*. (13), 2006 criteria	0.853 (0.814-0.886)	0.950 (0.893-0.981)	
I^2	97.0%	65.1%	
Yang, *et al*. (12), 2023 criteria	0.82 (0.78-0.85)	0.98 (0.97-0.99)	
Zhao, *et al*. (13), 2023 criteria	0.818 (0.777-0.854)	0.983 (0.941-0.998)	
I^2	0.0%	0.0%	
Present study	N/A	N/A	84.9%

CI: confidence interval; N/A: not applicable.

underestimated. Second, the IgG/IgM aCL and anti-β2 GPI were measured using automated laboratory systems, not enzyme-linked immunosorbent assays (ELISAs). The cut-off values for moderate (40–79) and high (≥80) IgG/IgM aCL and anti-β2 GPI in the 2023 ACR/EULAR criteria are based on ELISAs, not automated laboratory systems (10). The thresholds for moderate and high IgG/IgM aCL and anti-β2 GPI measured by automated platforms are not provided in the 2023 ACR/EULAR criteria, and the Steering Committee suggested the need for further studies to evaluate the thresholds for moderate and high IgG/IgM aCL and anti-β2 GPI measured by automated platforms (10). As the thresholds for moderate and high IgG/IgM aCL and anti-β2 GPI measured by automated platforms are currently unclear, we adopted the thresholds from ELISAs. We acknowledge the use of thresholds from ELISAs in our data as a limitation of our study. Nonetheless, it is unlikely that the thresholds would have affected

the concordance rate. For patients no. 11–19 (those who had laboratory domains score <3) in Table III, even if the threshold changes and moderate positive becomes high-positive or *vice versa*, the laboratory domains scores remain unchanged, and all patients remain as laboratory domains score <3 and are not classifiable as having APS. However, we do not claim that using these thresholds is correct when the IgG/IgM aCL and anti-β2 GPI are measured using automated laboratory systems. Further studies assessing the appropriate thresholds are warranted.

In conclusion, 107 of the 126 patients classified as APS according to the 2006 revised Sapporo criteria were classifiable as APS according to the 2023 ACR/EULAR criteria, accounting for a concordance rate of 84.9%. The concordance rate was considerably lower in patients with obstetric APS (45.5%). The 2023 ACR/EULAR criteria represent a significant step forward in the classification of APS (10); however, our findings suggest that the 2023 ACR/EULAR criteria's emphasis on specificity may inadvertently lead to the exclusion of patients with clinically significant APS manifestations, particularly those with obstetric events only.

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