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Original Article

Acute coronary syndrome in antineutrophil cytoplasmic antibody-associated vasculitis: a Korean single-centre cohort study

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Objective: This study investigated the incidence and patterns of the acute coronary syndrome (ACS) after AAV diagnosis and searched for the predictors of ACS in a single-centre cohort of Korean patients diagnosed with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV).

Methods: A total of 262 patients with AAV were included in this study. ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and unstable angina (UA) were defined as ACS in this study. Only ACS that occurred during or after AAV diagnosis was counted.

Results: The incidence of ACS in patients with AAV was 2.7% (7 patients), and the most common type of ACS was NSTEMI regardless of the affected site or the number of coronary arteries. Five patients with ACS were diagnosed with microscopic polyangiitis (MPA) and all of them had myeloperoxidase (MPO)-ANCA (or perinuclear [P]-ANCA), whereas the remaining two patients were diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA). Of the seven patients, 2 patients experienced ACS within the first year after AAV diagnosis, and 2 experienced ACS 5 years after AAV diagnosis. Among clinical variables, only the male sex was a predictor of ACS during the follow-up period in patients diagnosed with AAV.

Conclusion: The incidence of ACS was 2.7%, and the most common type of ACS was NSTEMI in Korean patients with AAV.

Keywords: Antineutrophil cytoplasmic antibody, Vasculitis, Acute coronary syndrome

INTRODUCTION

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a necrotising vasculitis that affects small to medium vessels and exhibit immunopathologic features of necrotising vasculitis with immune deposits ranging from few to none [1]. AAV is divided into three subtypes, microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic GPA (EGPA), according to clinical, laboratory, radiologic and histologic features [1-3]. Among the detailed items of cardiovascular manifestation of AAV, acute coronary syndrome (ACS) can be fatal despite its low incidence rate in AAV patients compared to other systemic manifestations, because it may leave permanent sequelae [1]. A previous study with 186 patients diagnosed with AAV reported a rate risk for ischaemic heart disease of 1.5 [4]. Another similar study with 293 patients diagnosed with GPA revealed that the risk for ischaemic heart disease increased by up to 1.9 (95% confidence interval [CI], 1.4~2.4), and acute myocardial infarction (MI) was as high as 2.5 (95% CI, 1.6~3.7) [5]. A previous study including 131

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patients with AAV demonstrated a hazard ratio (HR) for cardiovascular events of 2.23 [6]. Nevertheless, since AAV mainly affects capillaries and adjacent arterioles and venules, it primarily invades major organs with a number of capillaries such as the kidneys and lungs. Therefore, the incidence of ACS remains uncertain despite previous sporadic studies. Conversely, systemic vasculitides that could affect the coronary arteries are primarily known as Takayasu arteritis, polyarteritis nodosa, and Kawasaki disease [7]. Furthermore, among the cardiovascular manifestations based on the Birmingham vasculitis activity score (BVAS) v3, a score assigned to ischaemic cardiac pain does not surpass those of cardiomyopathy and congestive cardiac failure [8]. This may mean that the clinical implications of ACS in patients with AAV have not yet been highlighted. Therefore, this study investigated the incidence and patterns of ACS in a single-centre cohort of Korean patients diagnosed with AAV. In addition, this study searched for the predictors of ACS in patients with AAV.

MATERIALS AND METHODS

Patients

This study included a total of 262 patients diagnosed with AAV who had been enrolled in the ANCA-associated vasculitides cohort. The inclusion criteria were as described in the previous studies [9,10]: (1) patients who were been first diagnosed with MPA, GPA, and EGPA at the tertiary university hospital, from October 2000 till November 2021; (2) patients who met the 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides and the 2007 European Medicine Agency algorithm for AAV [1,2]; (3) patients who had the medical records sufficient to collect clinical, laboratory, radiologic, and immunopathologic data for the classification of AAV and the assessment of BVAS and five-factor score (FFS) [8,11]. BVAS v3 was applied to GPA patients to unify the scoring system [12]; (4) patients who had been followed up for >3 months after AAV diagnosis; (5) patients who did not have concurrent malignancies, infectious diseases, and systemic vasculitides other than AAV; (6) patients who had not received immunosuppressive drugs within 1 month before AAV diagnosis; (7) patients diagnosed with ACS which occurred at or after AAV diagnosis; (8) patients who underwent either percutaneous coronary intervention (PCI) or coronary artery bypass graft.

Ethical disclosure

This study was approved by the Institutional Review Board (IRB) of Yonsei University Severance Hospital (Seoul, Korea; IRB No. 4-2020-1071) and was conducted in accordance with the Declaration of Helsinki. Given the retrospective design of the study and the use of anonymised patient data, the requirement for written informed consent was waived by the IRB.

Clinical data

The variables used in this study are summarised in Table 1. The follow-up period was defined as the period from AAV diagnosis until the last visit. The follow-up period based on ACS was defined as the period from the diagnosis of AAV till the occurrence of ACS in patients with ACS and that from the diagnosis of AAV till the last visit for those without ACS. The BVAS and FFS were assessed as AAV-specific indices and erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were collected as acute-phase reactants. The number of patients that were administered medications administered during the follow-up was counted.

Acute coronary syndrome

In this study, ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and unstable angina (UA) were defined as ACS. Only the number of patients that had ACS during or after AAV diagnosis was counted.

ANCA measurement

Myeloperoxidase (MPO)-ANCA and proteinase 3 (PR3)-ANCA were measured using an immunoassay, and perinuclear (P)-ANCA or cytoplasmic (C)-ANCA were detected using an indirect immunofluorescence assay. MPO-ANCA and PR3-ANCA were first accepted as ANCA positivity; however, P-ANCA and C-ANCA were also considered when AAV was strongly suspected in the absence of MPO-ANCA and PR3-ANCA [9,10,13].

Statistical analyses

We performed all statistical analyses using the SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, NY, USA). The significant differences between the two categorical variables and the two continuous variables were compared by the chi-square and Fisher's exact tests and the Mann–Whitney U test, respectively. HRs of the variables for ACS were obtained by the

Table 1. Characteristics of patients with AAV and comparison of variables between patients with and those without ACS

Variable	All patients (n=262)	Patients without ACS (n=255)	Patients with ACS (n=7)	p-value
At the diagnosis of AAV				
Demographic data				
Age (yr)	59.0 (20.3)	59.0 (20.0)	64.0 (29.0)	0.772
Male, sex	92 (35.1%)	87 (34.1%)	5 (71.4%)	0.101
Variants of AAV				0.262
MPA	140 (53.4%)	135 (52.9%)	5 (71.4%)	
GPA	69 (26.3%)	69 (27.1%)	0 (0.0%)	
EGPA	53 (20.2%)	51 (20.0%)	2 (28.6%)	
ANCA positive				1.000
MPO-ANCA (or P-ANCA)	175 (66.8%)	170 (66.7%)	5 (71.4%)	
PR3-ANCA (or C-ANCA)	46 (17.6%)	45 (17.6%)	1 (14.3%)	
ANCA negative	51 (19.5%)	50 (19.6%)	1 (14.3%)	
Both ANCAs	10 (3.8%)	10 (3.9%)	0 (0.0%)	
AAV-specific indices				
BVAS	12.0 (11.0)	12.0 (11.0)	14.0 (5.0)	0.303
FFS	1.0 (1.75)	1.0 (2.0)	2.0 (1.0)	0.059
Co-morbidities				
HTN	106 (40.5%)	101 (39.6%)	5 (71.4%)	0.123
DM	65 (24.8%)	64 (25.1%)	1 (14.3%)	1.000
CKD	76 (29.0%)	75 (29.4%)	1 (14.3%)	0.677
Dyslipidaemia	54 (20.6%)	51 (20.0%)	3 (42.9%)	0.156
Acute-phase reactants				
ESR (mm/h)	58.0 (74.0)	57.0 (74.0)	74.0 (56.0)	0.631
CRP (mg/L)	13.2 (64.1)	13.2 (63.6)	59.5 (71.8)	0.228
During follow-up				
Follow-up period (mo)	37.0 (63.0)	36.9 (63.4)	55.1 (108.2)	0.190
ACS	7 (2.7%)	N/A	N/A	N/A
Age at ACS occurrence	63.5 (14.8)	N/A	63.5 (14.8)	N/A
Follow-up period based on ACS (mo)	35.9 (63.0)	N/A	35.9 (63.0)	N/A
Medications administered				
Glucocorticoids	247 (94.3%)	240 (94.1%)	7 (100%)	1.000
Cumulative dose (equivalent to prednisolone, mg)	5,106.5 (8,710.1)	5,099.6 (8,761.9)	7,614.8 (16,335.2)	0.190
Cyclophosphamide	145 (55.3%)	140 (54.9%)	5 (71.4%)	0.466
Rituximab	46 (17.6%)	46 (18.0%)	0 (0.0%)	0.610
Mycophenolate mofetil	42 (16.0%)	41 (16.1%)	1 (14.3%)	1.000
Azathioprine	145 (55.3%)	142 (55.7%)	3 (42.9%)	0.704
Calcineurin inhibitor	24 (9.2%)	24 (9.4%)	0 (0.0%)	1.000
Methotrexate	25 (9.5%)	24 (9.4%)	1 (14.3%)	0.509

Values are expressed as median (interquartile range) or number (%). AAV: ANCA-associated vasculitis, ACS: acute coronary syndrome, ANCA: antineutrophil cytoplasmic antibody, BVAS: Birmingham vasculitis activity score, C: cytoplasmic, CKD: chronic kidney disease, CRP: C-reactive protein, DM: diabetes mellitus, EGPA: eosinophilic granulomatosis with polyangiitis, ESR: erythrocyte sedimentation rate, FFS: five-factor score, GPA: granulomatosis with polyangiitis, HTN: hypertension, MPA: microscopic polyangiitis, MPO: myeloperoxidase, P: perinuclear, PR3: proteinase 3.

univariable and multivariable Cox hazards model analyses. The cumulative survival rates between the two groups were also compared by the Kaplan–Meier survival analysis with the log-rank test. $p<0.05$ was considered statistically significant in this study.

RESULTS

Characteristics of patients and comparison between those with and without ACS

Regarding the variables at AAV diagnosis, the median age at diagnosis was 59.0 years and 35.1% of patients were male. Of the 262 patients with AAV, 140, 69, and 53 were diagnosed with MPA, GPA, and EGPA, respectively. MPO-ANCA (or P-ANCA) and PR3-ANCA (or C-ANCA) were detected in 175 and 46 patients. A total of 106, 65, 76, and 54 patients with AAV had hypertension, diabetes mellitus (DM), chronic kidney disease (CKD), and dyslipidaemia, respectively. Regarding the variables during follow-up, the incidence of ACS in patients with AAV was 2.7%, with a median follow-up period based on ACS of 35.9 months. When comparing variables between patients with ACS and those without ACS, patients with ACS tended to have higher median BVAS and FFS than those without ACS but it was not statistically significant (Figure 1). In addition, patients with ACS showed a higher median cumulative dose of glucocorticoids than those without ACS (equivalent to prednisolone, 7,614.8 mg vs. 5,099.6 mg) but it was not significant either. There were no significant differences in the remaining variables at diagnosis and during the follow-up between the two groups (Table 1).

ACS patterns and affected coronary arteries according to ANCA type and AAV subtype

The most common type of ACS was NSTEMI (57.1%), followed by UA (28.6%) and STEMI (14.3%). Furthermore, according to the affected sites of the coronary arteries, two patients exhibited 1 vessel disease (1vd), two had 3 vessel disease (3vd), two had left main (LM) and one had 2 vessel disease (2vd) (Figure 2A and 2B). In terms of ANCA type, of the seven patients with ACS, five patients had MPO-ANCA (or P-ANCA), one had PR3-ANCA (or C-ANCA) and one had no ANCAs. Of the affected sites of the coronary arteries, patients with MPO-ANCA (or P-ANCA) showed all the affected sites, whereas patients with PR3-ANCA (or C-ANCA) exhibited LM, and patients with ANCA showed 1vd (Figure 2C and 2D). Out of the seven patients with ACS, five and two patients were classified as MPA and EGPA, respectively. None of the patients with GPA had ACS in this study. Patients with MPA exhibited all the types of ACS, whereas those with EGPA experienced UA and NSTEMI. Of the affected sites in the coronary arteries, patients with MPA similarly exhibited all the affected sites, whereas, patients with EGPA experienced 1vd and LM (Figure 2E and 2F).

Age at the time of ACS and time-sequence between AAV and ACS according to the AAV subtype

All patients with EGPA experienced ACS before the age of 40 years. Conversely, three patients with MPA presented with ACS at an age between 60 and 70 years, and two suffered from ACS after 70 years of age. Out of the seven patients with ACS, three patients experienced ACS at the time of AAV diagnosis. Two patients experienced ACS within the first year after AAV diagnosis, and two experienced ACS 5 years after AAV diagnosis. The time gap between AAV diagnosis and ACS occurrence did not seem to be associated with the AAV subtype.

Overall detailed clinical data of 7 patients with ACS

All seven patients presented with chest pain and dyspnoea

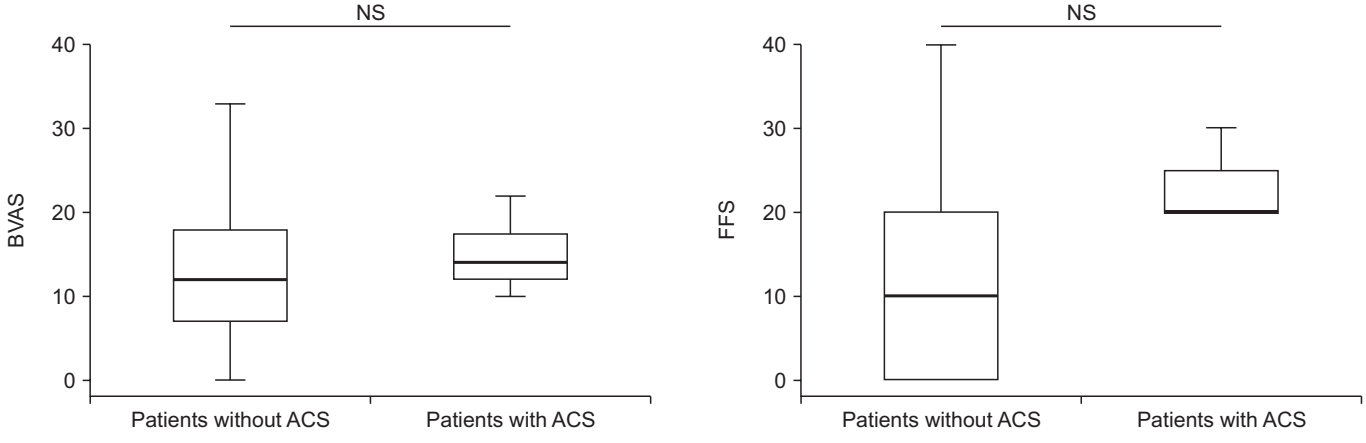

Figure 1. Comparison of BVAS and FFS between patients with ACS and those without ACS. ACS: acute coronary syndrome, BVAS: Birmingham vasculitis activity score, FFS: five-factor score, NS: not significant.

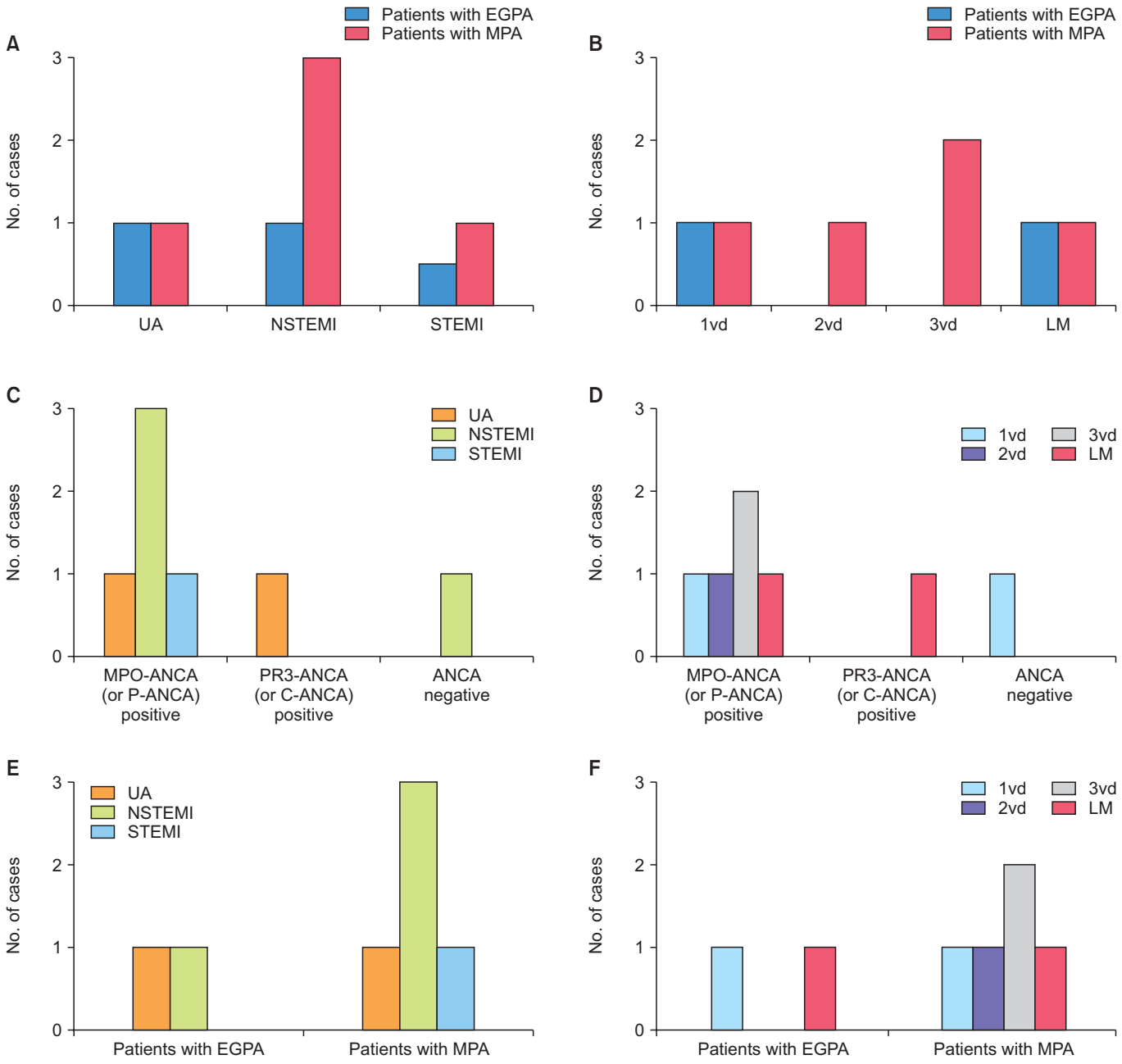

Figure 2. ACS patterns and affected coronary arteries. (A, B) Type of ACS and affected coronary arteries according to ANCA subtype. (C, D) ANCA type according to ACS patterns and affected coronary arteries. (E, F) AAV subtype according to ACS patterns and affected coronary arteries. ACS: acute coronary syndrome, ANCA: antineutrophil cytoplasmic antibody, C: cytoplasmic, EGPA: eosinophilic granulomatosis with polyangiitis, LM: left main, MPA: microscopic polyangiitis, MPO: myeloperoxidase, NSTEMI: non-ST-segment elevation myocardial infarction, P: perinuclear, PR3: proteinase 3, STEMI: ST-segment elevation myocardial infarction, UA: unstable angina, vd: vessel disease.

as the first ACS-related manifestation. The most common comorbidity before PCI was hypertension (5 patients), followed by dyslipidaemia (3 patients). One patient had cerebrovascular disease and another patient had both DM and CKD. Of the seven patients, two experienced ACS recurrence, and the time gap between the first and second episodes of ACS ranged from 16 to 29 months. Two patients with EGPA and ACS exhibited eosinophilic myocarditis at the time of EGPA diagnosis, suggestive of EGPA involvement. In addition, the affected site of the coronary arteries for those with RCA was the same, regardless of LM (Table 2).

Table 2. Characteristics of AAV patients with ACS

Patient number	AAV subtype	Sex/age at diagnosis	ANCA type	Comorbidities	The gap-time from AAV to ACS (mo)	Type of ACS	Affected site of the coronary arteries	ACS recurrence	Others
1	EGPA	F/25	PR3-ANCA (C-ANCA) positive	HTN Dyslipidemia Old CVA	70.4	UA	LM RCA	Yes	Myocardial involvement at diagnosis
2	EGPA	M/38	ANCA negative	Epilepsy	0	NSTEMI	RCA	No	Myocardial involvement at diagnosis
3	MPA	M/62	MPO-ANCA (P-ANCA) positive	HTN Dyslipidemia	8.7	UA	LAD	No	
4	MPA	M/67	MPO-ANCA (P-ANCA) positive	DM CKD	0.7	NSTEMI	LAD	Yes	
5	MPA	F/64	MPO-ANCA (P-ANCA) positive	HTN	78.8	STEMI	LAD RCA	No	
6	MPA	M/67	MPO-ANCA (P-ANCA) positive	HTN Dyslipidemia	0	NSTEMI	RCA	No	
7	MPA	M/82	MPO-ANCA (P-ANCA) positive	HTN	0	NSTEMI	LAD LCX RCA	No	

AAV: ANCA-associated vasculitis, ACS: acute coronary syndrome, ANCA: antineutrophil cytoplasmic antibody, C: cytoplasmic, CKD: chronic kidney disease, CVA: cerebrovascular accident, DM: diabetes mellitus, EGPA: eosinophilic granulomatosis with polyangiitis, F: female, HTN: hypertension, LAD: left anterior descending artery, LCX: left circumflex coronary artery, LM: left main, M: male, MPA: microscopic polyangiitis, MPO: myeloperoxidase, NSTEMI: non-ST-segment elevation myocardial infarction, P: perinuclear, PR3: proteinase 3, RCA: right coronary artery, STEMI: ST-segment elevation myocardial infarction, UA: unstable angina.

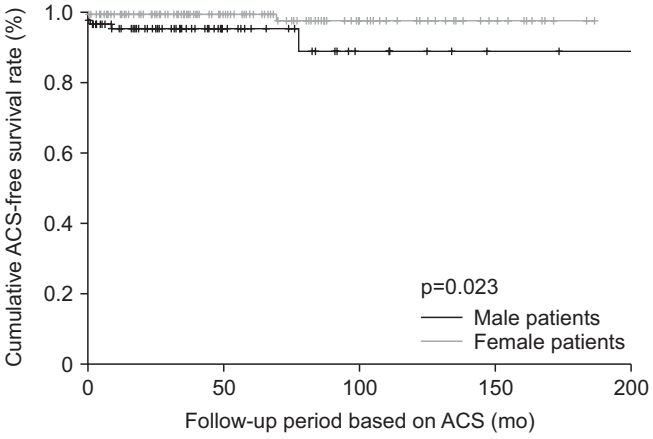

Figure 3. Comparison of cumulative ACS-free survival rates. ACS: acute coronary syndrome.

Cox hazards model analysis

In the univariate Cox analysis, among the variables at the time of AAV diagnosis, AAV-specific indices were not associated with ACS occurrence during follow-up. Among the conventional risks for ACS [14], only the male sex was significantly associated with ACS occurrence during the follow-up (HR, 5.506; 95% CI, 1.058~28.667). As only one variable was found to be associated with ACS occurrence, a multivariate Cox analysis could not be conducted (Supplementary Table 1).

Comparison of cumulative ACS-free survival rates

Among the conventional and AAV-related risk factors for ACS, male patients with AAV exhibited a significantly lower cumulative ACS-free survival rate than female patients (p=0.023) (Figure 3).

DISCUSSION

This study investigated the incidence and patterns of ACS and searched for independent predictors of ACS occurrence during the follow-up period of AAV in a single-centre cohort of Korean patients with AAV. Several findings were obtained in this study. First, the incidence of ACS in patients with AAV was 2.7%, and the most common type of ACS was NSTEMI. However, the affected sites of the coronary arteries were evenly distributed. Second, five patients with ACS were diagnosed with MPA and all of them had MPO-ANCA (or P-ANCA), whereas the remaining two patients were diagnosed with EGPA. But, the type of ACS

and the affected sites of the coronary arteries were not significantly associated with the AAV subtype or ANCA type. Third, of the seven patients, 2 patients experienced ACS within the first year after AAV diagnosis, and 2 experienced ACS 5 years after AAV diagnosis. Fourth, only the male sex was a predictor of ACS during the follow-up period in patients diagnosed with AAV.

In this study, the incidence of ACS in patients with AAV was 2.7%, which was significantly higher than in the general Korean adult population, ranging from 0.5% to 0.6% [15]. Moreover, the prevalence per 1,000 individuals after adjusting the incidence by the follow-up duration based on the occurrence of ACS in patients with AAV was calculated as 8.2, which was also significantly higher than that reported in the general population of South Korea ranging from 4.5 to 6.4 from 2004 to 2009 [15]. These results could be explained by the hypothesis of the chronic inflammatory burden of AAV. Various forms of inflammation exist in the pathogenesis of AAV, ranging from rapidly elevated inflammation, such as cytokine storms, to inflammation maintained continuously by complement 5a [16,17]. Furthermore, chronic inflammation has been known to increase the risk of residual inflammation, which in turn dysregulates pro-atherogenic and anti-atherogenic immunomodulatory effects, resulting in an increased risk of ACS in the general population [18]. This hypothesis can be verified by previous studies on the occurrence of ACS in patients with rheumatoid arthritis. The incidence of MI in Korean patients with rheumatoid arthritis was reported as 0.8%~1.4%, of which the odds ratio was elevated compared to that in the general population [19,20]; and the high incidence of ACS in patients with rheumatoid arthritis was primarily explained by the enhanced production of circulating pro-inflammatory cytokines, contributing to the acceleration of ACS development [21].

In this study, five of seven patients exhibited ACS occurrence within the first year after AAV diagnosis. The remaining two patients experienced ACS more than 70 months after AAV diagnosis. Given the time gap from AAV diagnosis to ACS occurrence, it could be reasonably assumed that different mechanisms might be involved in the occurrence of ACS between the two groups. In other words, ACS occurring within the first year of AAV diagnosis is directly or indirectly affected by AAV itself, but ACS occurring after 70 months may be accompanied by additional risk factors of ACS such as ageing and drug-related or AAV-related complications. Therefore, this study included all patients with ACS due to the small sample size; however, we suggest that future studies should divide the patients according to the time of ACS occurrence and investigate the clinical patterns.

A previous study using data from the Korea Acute Myocardial Infarction Registry from 2006 to 2013 reported the mean age of onset of STEMI and NSTEMI was in the mid-sixties [21]. In this study, there were 2 patients with EGPA who had ACS before 40 years of age. Two assumptions were made. First, there may be a link between age at AAV diagnosis and ACS occurrence during the follow-up. In this study, patients with EGPA were younger than those with MPA and GPA (53.0, 61.9, and 53.0 yr, respectively). Therefore, although there was no statistical significance, this pattern of age at AAV diagnosis might have influenced the age of onset of ACS in patients with AAV. Second, there may be a link between the myocardial involvement of AAV and ACS occurrence during the follow-up, regardless of the age of AAV diagnosis. To date, there have been a few reports of concurrent myocarditis and ACS in patients with AAV [22-24]. Therefore, although clear evidence cannot be proposed, a close association between myocarditis and ACS in AAV patients, particularly those with EGPA, should be considered when the first classification of AAV is made.

On the other hand, based on the items of BVAS, cardiovascular manifestation includes loss of pulses, valvular heart disease, pericarditis, ischemic cardiac pain, cardiomyopathy, and congestive heart failure [8]. In this study, patients with cardiovascular manifestations at diagnosis exhibited a lower ACS-free cumulative rate than those without cardiovascular manifestations (Supplementary Figure 1). Myocarditis, which is locally initiated by AAV involvement, can influence endothelial dysfunction in the coronary arteries and subsequently accelerate atherosclerosis [25,26]. In particular, a previous study reported that the enhanced expression of proinflammatory cytokines and pattern recognition receptors, such as Toll-like receptor 4, were identified in endomyocardial tissues obtained from patients with myocarditis due to necrotising vasculitis compared to those due to other causes [27]. Another study demonstrated that anti-heart autoantibodies, including anti-heat shock protein 60 and anti-endothelial cell antibodies, were produced during AAV-related myocarditis and in turn, accelerated atherosclerosis, resulting in a high incidence of ACS [28-31]. Therefore, in addition to MPA patients with MPO-ANCA, more attention should be paid to AAV patients with myocarditis or cardiovascular manifestations

at diagnosis.

In terms of AAV subtype, it has been reported that heart involvement of AAV was observed more frequently in MPA (10%~20%) and EGPA (up to 49%) patients than in GPA (5%~15%) patients [32]. In the present study, five of the 140 MPA patients (3.8%), and 2 of the 53 EGPA patients (3.8%) had suffered from ACS, whereas none of the 69 GPA patients had ever experienced ACS during follow-up. Among AAV subtypes and ANCA types, it was impossible to draw a significant hypothesis on the protective role of C-ANCA or GPA in ACS occurrence, due to the small number of patients in this study. However, given that this study exhibited a similar pattern as previous studies [32], it could be speculated that the predisposing potential of ACS in GPA patients might be less than that in MPA or EGPA patients.

In addition, it has been reported that among EGPA patients, ANCA-negative EGPA patients exhibited heart involvement of AAV more frequently than ANCA-positive EGPA patients, and furthermore, on cardiac magnetic resonance (CMR), overt heart diseases are found in EGPA patients with ANCA positivity more commonly than those without [33]. Conversely, in this study, one ANCA-positive and one ANCA-negative EGPA patient had ACS, and thus, it could not tell the association between ANCA positivity and ACS occurrence in EGPA. This discrepancy might be due to two facts: heart involvement of AAV included several heart diseases in addition to ACS [8], and the common heart disease detected on CMR is myocarditis which is related to the ANCA-negative vasculitis phase of EGPA [34].

According to the previous study investigating the current status of acute MI in the Korean population, the proportion of STEMI gradually decreased from 64.3% in 2005 to 48.4% in 2018, whereas that of NSTEMI persistently increased from 35.7% in 2005 to 51.6% in 2018 [35]. Similarly, in this study, the overall proportion of NSTEMI was higher than that of STEMI (57.1% vs. 14.3%, respectively). However, since the present study included patients who had been diagnosed with MPA, GPA, and EGPA from 2000 till 2021, it might be difficult to directly compare the proportions of ACS type between the general population and AAV patients in this study. It was not easy to compare the proportion of UA and ACS comorbidities between the general population and AAV patients in this study for the same reason.

The primary merit of this study is that it is the first to report the incidence and clinical patterns of ACS in Korean AAV patients. A recent study in France reported increased ischaemic stroke, ACS, and mortality in patients with MPA and GPA [36]. However, given the real clinical settings in which the classification of MPA, GPA and EGPA is confusing, the inclusion of patients with EGPA may be another merit of this study. In addition, given the ethnic and geographical differences, it is noteworthy that this study provides valuable information on AAV involvement in the coronary arteries of Korean patients.

This study has several limitations. The primary limitation of this study was that the sample size was not large enough to sufficiently represent all Korean patients with AAV, and the study was retrospectively conducted. Owing to the small number of patients with ACS, the subgroup analysis on the effects of the traditional risks for ACS such as hypertension, DM, CKD, and dyslipidaemia on ACS occurrence in AAV patients could not be performed [37], and in particular, the baseline high-sensitive CRP levels, which are associated with ACS more closely than CRP levels, could not be collected owing to the retrospective study design [38]. However, because the same three rheumatologists participated in the classification and reclassification of AAV at the beginning of the cohort of AAV patients, and established a consensus by validating the classification, it is believed that the little inter-observer variation might overcome this limitation. In addition, smoking history, one of the most important conventional risk factors for ACS, could not be included because the pack-year of smoking had not been exactly evaluated in all the patients at the initial diagnosis of AAV, although a majority of the patients did not smoke. Therefore, this study has an advantage as a pilot study and a future prospective study with a large number of AAV patients. More detailed and clearer clinical data including conventional risk factors for ACS will provide more reliable information on the incidence and clinical patterns of ACS in Korean patients with AAV.

CONCLUSION

In the present study, the incidence of ACS was 2.7%, and the most common type of ACS was NSTEMI regardless of the affected site or the number of coronary arteries in patients with AAV. In addition, MPA patients with MPO-ANCA (or P-ANCA) and EGPA patients with myocardial involvement might have exhibited a tendency to be vulnerable to the occurrence of ACS at or after AAV diagnosis. Therefore, we suggest that more attention should be paid to these patients with AAV.

SUPPLEMENTARY DATA

Supplementary data can be found with this article online at https://doi.org/10.4078/jrd.2023.0002.

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None.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

J.S.K., Y.B.P., and S.W.L. conceived the work. J.S.K. and S.W.L. performed data curation. J.S.K., Y.B.P., and S.W.L. performed formal analysis. Y.B.P. and S.W.L. performed funding acquisitions. J.S.K. and S.W.L. wrote the original draft. Y.B.P. and S.W.L. reviewed and edited the manuscript.

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