Association of blood pressure and hypertension with radiographic damage among the patients with ankyloing spondylitis

Chun-Hsiung Chen, MD, MSc\(^{a,b,*}\), Hung-An Chen, MD\(^c\), Hsien-Tzung Liao, MD, PhD\(^d\), Chung-Tei Chou, MD\(^d\), Chen-Hung Chen, MD, PhD\(^{a,b}\)

1. Introduction

Spondyloarthritis (SpA) is classified as axial SpA, affecting the spine, pelvis and thoracic cage, or peripheral SpA, affecting the extremities. SpA is characterized by inflammatory back pain, sacroilitis and peripheral arthritis.\(^{[1]}\) Axial SpA is divided to radiographic SpA with radiographic sacroilitis, and non-radiographic SpA without radiographic sacroilitis, or sacroilitis on Magnetic Resonance Imaging, or positive HLA-B27 with clinical features. Peripheral manifestations of SpA include arthritis, enthesitis and dactylitis. Patients with SpA can have some extra-articular manifestations, including acute anterior uveitis, bowel inflammation and psoriasis. Ankylosing spondylitis (AS) is the prototype of axial SpA. The most common symptom of AS is chronic back pain and rest stiffness. Chronic inflammation in AS patients can cause syndesmophyte formation and lead to spinal ankylosis, resulting in limitation of spinal mobility.\(^{[2]}\)

The study was supported by grants from Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation (TCHR-TPE-107-23), Taiwan.

The authors have no conflicts of interest to disclose.

Abbreviations: AS = ankylosing spondylitis, AUC = Area under the curve, BASFI = Bath Ankylosing Spondylitis Functional Index, BASMI = Bath Ankylosing Spondylitis Metrology Index, BASRI = Bath Ankylosing Spondylitis Radiology Index, BMI = body mass index, CRP = C-reactive protein, DM = diabetes mellitus, DMARDs = disease-modifying antirheumatic drugs, m-SASSS = modified Stoke Ankylosing Spondylitis Spinal Score, NSAIDs = non-steroidal anti-inflammatory drugs, OR = odds ratios, ROC = receiver operating characteristic, SpA = Spondyloarthritis, WC = waist circumference, WHtR = waist-to-height ratio.

Keywords: ankylosing spondylitis, blood pressure, hypertension, radiographic damage, TNF-α blocker

Abstract

To investigate the association of blood pressure and hypertension with disease severity among the patients with ankyloing spondylitis (AS). There were 167 AS patients enrolled in the cross-sectional study. Blood pressure was measured and the presence of hypertension was recorded. Patient's disease severity, including disease activity, functional ability, patient's global assessments, physical mobility and radiographic damage were evaluated. ESR and CRP levels were tested. We recorded patient's medication use of NSAIDs, DMARDs and TNF-α blockers. Smoking, exercise habit, diabetes mellitus, hypercholesterolemia and obesity indices were assessed. Multivariate linear regression showed that systolic blood pressure was associated with TNF-α blocker [standard coefficient (β) = 0.194, P = .007], DMARDs (β = 0.142, P = .046), age (β = 0.211, P = .003), male gender (β = 0.242, P = .001) and body mass index (BMI) (β = 0.245, P = .001). Diastolic blood pressure was associated with cervical rotation (β = −0.174, P = .037), lateral lumbar flexion (β = −0.178, P = .019), m-SASSS (β = 0.198, P = .038) and BMI (β = 0.248, P = .003). Notably, multivariate logistic regression showed that hypertension was associated with m-SASSS (OR = 1.033, P = .003), age (OR = 1.098, P = .0010) and BMI (OR = 1.210, P = .003). Using ROC cure analyses, age, BASMI, BASRI-Total, m-SASSS, waist circumference, BMI and waist-to-height ratio were useful in predicting hypertension, and m-SASSS is the best (AUC = 0.784, P < .001). Advanced radiographic damage is an independent risk factor of hypertension in AS, and m-SASSS is the most useful disease severity parameter in predicting the presence of hypertension. Advanced radiographic damage, poor cervical rotation, lateral lumbar flexion, older age, male gender, TNF-α blocker, DMARDs use and obesity are associated with increased blood pressure.

\( P = .001 \)

\( P = .003 \)

\( P = .007 \)

\( P = .003 \)

\( P = .003 \)

\( P = .001 \)

\( P = .001 \)

\( P = .003 \)

\( P = .003 \)

\( P = .003 \)

\( P = .003 \)

\( P = .003 \)

\( P = .003 \)
Radiographic damage in the cervical spines, lumbar spine, hip joint and sacroiliac joints were assessed by the Bath Ankylosing Spondylitis Radiology Index (BASRI), modified Stoke Ankylosing Spondylitis Spinal Score (m-SASSS) and modified New York criteria. Radiographs with anteroposterior and lateral view of cervical and lumbar spine, pelvis and hip were taken in these AS patients. The total BASRI score ranged from 2 to 16, and the m-SASSS score ranged from 0 to 72.

2.4. Medication use

The patient’s medication use for Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) or Disease-Modifying Antirheumatic Drugs (DMARDs) was recorded. The patients were asked the following question. Do you use NSAIDs during past 3 months: yes almost daily use, occasionally, or no. Patients were subgroup as regular NSAIDs user (yes) and non regular NSAIDs user (occasionally and no). Patients were subgroup as NSAIDs user (yes or occasionally) and non NSAIDs user (no).

Do you use DMARDs (Sulfasalazine or Methotrexate) during past 3 months: yes almost daily use, occasionally, or no. Patients were subgroup as regular DMARDs user (yes) and non regular DMARDs user (occasionally or no). Patients were subgroup as NSAIDs user (yes or occasionally) and non DMARDs user (no).

The patients who were under Tumor Necrosis Factor-α (TNF-α) blocker use were recorded as TNF-α blocker user.

2.5. Life style

The patient’s smoking habits were recorded as current smoker, past smoker and nonsmoker. Current and past smoker were grouped as ever smoker.

The patient’s exercise habit was recorded. The patients were asked the following questions. Do you have regular exercise during the past 3 months (more than 30 minutes each time of exercise): yes more than 2 times per week, occasionally, or no. The patients were grouped as regular exercise (yes), and non regular exercise (occasionally or no).

2.6. Obesity indices

Patient’s obesity indices, including body mass index (BMI), waist circumference (WC) and waist-to-height ratio (WHtR) were estimated. The patient’s body weight and height were measured. BMI was determined as the weight divided by the square of the height [weight (kg)/height (m)2]. WC was measured in the halfway between the lowest rib border and the iliac crest at the end of patient’s normal exhalation. WHtR was the WC divided by the height [WC (cm)/height (cm)]. BMI is an index for patient’s total obesity. WC and WHtR are indices for patient’s central obesity.

2.7. Statistical analysis

We used the SPSS statistical package (SPSS for Windows, Chinese Version 10.0.7C, SPSS Inc., 2000) to carry out the statistical analyses. Continuous variables were described as mean ± standard deviation (SD). Categorical variables were described as ratio (percentages). Univariate linear regression analyses were used to assess correlation of systolic and diastolic blood pressure with independent variables. The results were expressed as regression coefficient [95% confidence intervals (CI)] and standard coefficient (β). Independent variables with a P value < .1 in univariate linear regression analyses were further tested in multivariate linear regression analyses. Univariate logistic regression analyses were used to calculate the odds ratios (OR) (95% CI) for prediction of hypertension. Independent variables with a P value < .1 in univariate logistic
3. Results

3.1. Clinical features

The characteristic features of the 167 AS patients are shown in Table 1. The mean (SD) age were 47.029 (12.720) years, and disease duration were 18.619 (11.595) years in the 167 patients. The male to female ratio was 135:32. There were 20.9% (35/167) patients had hypertension, 6.5% (11/167) patients had DM, and 5.9% (10/167) patients had hypercholesterolemia. There were 10.7% (18/167) patients under TNF-α blocker use, including Etanercept or Adalimumab. The TNF-α blocker use duration were mean (SD), 53.222 (30.907) months.

3.2. Univariate linear regression analyses of clinical factors correlated with systolic and diastolic blood pressure among the 167 AS patients

Univariate linear regression analyses of clinical factors associated with systolic and diastolic blood pressure are shown in Table 2. In the univariate linear regression analyses, systolic blood pressure positively correlated with male gender (standard coefficient ($\beta$) = 0.294, $P < .001$) and CRP ($\beta$ = 0.180, $P = .020$). Systolic blood pressure positively correlated with BASRI-Total ($\beta$ = 0.159, $P = .047$) and m-SASSS ($\beta$ = 0.263, $P = .001$). Systolic blood pressure positively correlated TNF-α blocker ($\beta$ = 0.207, $P = .007$) and DMARDs use ($\beta$ = 0.178, $P = .022$). Systolic blood pressure positively correlated with WC ($\beta$ = 0.329, $P < .001$), BMI ($\beta$ = 0.311, $P < .001$) and WHR ($\beta$ = 0.341, $P < .001$). These results suggesting that male gender, active inflammation, advanced radiographic damage, TNF-α blocker, DMARDs use and obesity were significantly associated with increased systolic blood pressure in the AS patients.

In the univariate linear regression analyses, diastolic blood pressure positively correlated with male gender ($\beta$ = 0.295, $P < .001$). Diastolic blood pressure significantly correlated with BASMI ($\beta$ = 0.205, $P = .011$), tragus-to-wall distance ($\beta$ = 0.154, $P = .048$), cervical rotation ($\beta$ = -0.212, $P = .008$), lateral lumber flexion ($\beta$ = -0.201, $P = .009$), chest expansion ($\beta$ = -0.200, $P = .010$) and occiput-to-wall distance ($\beta$ = 0.202, $P = .009$). Diastolic blood pressure positively correlated with BASRI-Total ($\beta$ = 0.204, $P = .001$) and m-SASSS ($\beta$ = 0.224, $P = .005$). Diastolic blood pressure positively correlated with ever smoker ($\beta$ = 0.166, $P = .034$). Diastolic blood pressure positively correlated with WC ($\beta$ = 0.303, $P < .001$), BMI ($\beta$ = 0.304, $P < .001$) and WHR ($\beta$ = 0.294, $P < .001$). These results suggested that male gender, poor physical mobility, particular cervical, lumbar spine and chest expansion, advanced radiographic damage, ever smoker and obesity were significantly associated with increased diastolic blood pressure in the AS patients. Male gender, advanced radiographic damage and obesity were significantly associated with both systolic and diastolic blood pressure.

3.3. Multivariate linear regression analyses of clinical factors correlated with systolic and diastolic blood pressure among the 167 AS patients

Independent variables with a $P$ value < .1 in the univariate linear regression analyses were further tested in the multivariate linear regression analyses to assess their correlation with systolic and diastolic blood pressure (Table 3). In the multivariate linear regression analyses, systolic blood pressure positively correlated with TNF-α blocker use ($\beta$ = 0.194, $P = .007$), after adjusted by age ($\beta$ = 0.211, $P = .003$), gender ($\beta$ = 0.242, $P = .001$), DM ($\beta$ = -0.024, $P = .745$), hypercholesterolemia ($\beta$ = -0.053, $P = .460$) and BMI ($\beta$ = 0.245, $P = .001$). Systolic blood pressure positively correlated with DMARDs use ($\beta$ = 0.142, $P = .046$), after adjusted by age, gender, DM, hypercholesterolemia and BMI. These results suggested that TNF-α blocker and DMARDs use were independently associated with increased systolic blood pressure in the AS patients. Older age, male gender and obesity were also independently associated with increased systolic blood pressure.

In the multivariate linear regression analyses, diastolic blood pressure significantly correlated with cervical rotation ($\beta$ = -0.174, $P = .037$) and lateral lumber flexion ($\beta$ = -0.178, $P = .019$), after adjusted by age, gender, DM, hypercholesterolemia and BMI. Diastolic blood pressure positively correlated with m-SASSS ($\beta$ = 0.198, $P = .038$), after adjusted by age ($\beta$ = -0.119, $P = .177$), gender ($\beta$ = 0.155, $P = .053$), DM ($\beta$ = -0.106, $P = .185$), hypercholesterolemia ($\beta$ = 0.008, $P = .918$) and BMI ($\beta$ = 0.248, $P = .003$). These results suggested

### Table 1

| Characteristic | Total AS patients (n = 167) |
|---------------|-----------------------------|
| Age (yr) (n = 167) | 47.029 (12.720) |
| Male gender (n = 167), male/female | 135/32 (80.8%) |
| Onset age (yr) (n = 159) | 28.506 (11.884) |
| Disease duration (yr) (n = 159) | 18.619 (11.595) |
| HLA-B27 (+/-) (n = 164) | 145/19 (88.4%) |
| ESR (mm/h) (n = 165) | 13.472 (14.578) |
| CRP (mg/dL) (n = 166) | 0.706 (1.085) |
| BASDAI (n = 163) | 2.861 (1.724) |
| ASDAS-ESR (n = 161) | 1.968 (0.861) |
| ASDAS-CRP (n = 162) | 2.035 (0.964) |
| BASFI (n = 165) | 1.139 (1.477) |
| BAS-G (n = 167) | 3.465 (2.701) |
| BASMI (n = 153) | 2.841 (1.363) |
| Tragus-to-wall distance (cm) (n = 166) | 13.356 (5.988) |
| Modified schober index (cm) (n = 166) | 4.674 (2.288) |
| Intermalleolar distance (cm) (n = 167) | 113.368 (23.078) |
| Cervical rotation (degree) (n = 156) | 67.868 (28.262) |
| Lateral lumber flexion (cm) (n = 167) | 12.409 (8.651) |
| Fingertip-to-floor distance (cm) (n = 167) | 17.538 (14.323) |
| Chest expansion (cm) (n = 167) | 3.209 (2.108) |
| Occiput-to-wall distance (cm) (n = 167) | 5.026 (6.047) |
| BASRI-total (n = 156) | 9.198 (2.580) |
| m-SASSS (n = 156) | 28.730 (17.055) |
| Uveitis (n = 167) | 47/120 (28.1%) |
| TNF-α blocker use (n = 167) | 18/149 (10.7%) |
| Regular NSAIDs use (n = 166) | 63/103 (37.9%) |
| Regular DMARDs use (n = 166) | 13/29 (22.5%) |
| Regular exercise (n = 167) | 68/99 (40.7%) |
| Ever smoker (n = 164) | 40/124 (24.3%) |
| Hypertension (n = 167) | 30/132 (20.9%) |
| Diabetes mellitus (n = 167) | 11/156 (6.5%) |
| Hypercholesterolemia (n = 167) | 10/157 (5.9%) |
| Waist circumference (WG) (cm) (n = 165) | 90.818 (12.154) |
| Body mass index (BMI) (kg/m²) (n = 166) | 25.345 (4.501) |
| Waist to Height Ratio (WHR) (n = 163) | 0.543 (0.073) |

Values are shown as mean (standard deviation) or ratio (yes/no/percentage).

AS = ankylosing spondylitis, ASDAS-ESR = Ankylosing Spondylitis Disease Activity Score with ESR, ASDAS-CRP = Ankylosing Spondylitis Disease Activity Score with CRP, ASDAS-SRI = Ankylosing Spondylitis Disease Activity Index, BASFI = Bath Ankylosing Spondylitis Functional Index, BAS-G = Bath Ankylosing Spondylitis Patient Global Score, BASMI = Bath Ankylosing Spondylitis Metrology Index, BASRI = Bath Ankylosing Spondylitis Radiology Index, m-SASSS = modified Stoke Ankylosing Spondylitis Spinal Score.
that poor cervical rotation, lateral lumbar flexion and advanced radiographic damage were independently associated with increased diastolic blood pressure in the AS patients. Obesity was independently associated with increased diastolic blood pressure.

Systolic blood pressure showed the trend to have association with CRP levels after multivariate adjustment ($\beta = 0.125$, $P = 0.090$). Diastolic blood pressure showed the trend to have association with BASMI ($\beta = 0.163$, $P = 0.055$), chest expansion ($\beta = 0.139$, $P = 0.068$), BASI-Total ($\beta = 0.164$, $P = 0.058$) and DMARDs use ($\beta = 0.121$, $P = 0.097$), after multivariate adjustment.

3.4. Univariate logistic regression analyses of clinical factors for hypertension among the 167 AS patients

Univariate logistic regression analyses of clinical factors for hypertension are shown in Table 4. In univariate logistic regression analyses, hypertension was associated with BASFI [OR = 1.300 (1.035–1.623), $P = 0.024$], BASMI [OR = 1.341 (1.096–1.641), $P = 0.004$], tragus-to-wall distance [OR = 1.065 (1.002–1.132), $P = 0.041$], intermalleolar distance [OR = 0.792 (0.955–0.989), $P = 0.001$], cervical rotation [OR = 0.986 (0.973–0.999), $P = 0.031$], lateral lumbar flexion [OR = 0.919 (0.866–0.975), $P = 0.005$], chest expansion [OR = 0.782 (0.614–0.996), $P = 0.046$], and occiput-to-wall distance [OR = 1.079 (1.017–1.145), $P = 0.012$]. These results suggested that the prevalence of hypertension was increased in the AS patients with older age, longer disease duration, poor functional ability and physical mobility.

Hypertension was associated with BASI-Total [OR = 1.219 (1.051–1.413), $P = 0.009$] and m-SASSS [OR = 1.053 (1.030–1.077), $P < 0.001$]. The presence of hypertension was increased in the AS patients with advanced radiographic damage.

Hypertension was associated with DM [OR = 5.235 (1.500–18.405), $P = 0.009$], hypercholesterolemia [OR = 4.233 (1.152–15.562), $P = 0.030$], WC [OR = 1.059 (1.024–1.095), $P = 0.001$], BMI [OR = 1.185 (1.080–1.301), $P < 0.001$], and WHR [OR = 142,906.709 (390.072–52,355,269.7), $P < 0.001$].
presence of hypertension was increased in the AS patients with DM, Hypercholesterolemia and obesity.

3.5. Multivariate logistic regression analyses of clinical factors for hypertension among the 167 AS patients

Independent variables with a $P$ value < .1 in the multivariate logistic regression analyses were further tested in the multivariate logistic regression analyses to assess their association with hypertension (Table 5). Most importantly, in multivariate logistic regression analyses, hypertension was associated with m-SASSS [OR = 1.033 (1.003–1.063), $P = .033$], adjusted by age [OR = 1.098 (1.039–1.160), $P = .001$], gender [OR = 0.447 (0.111–1.801), $P = .258$], DM [OR = 1.849 (0.427–8.007), $P = .411$], hypercholesterolemia [OR = 5.020 (0.970–25.967), $P = .054$], and BMI [OR = 1.210 (1.096–1.370), $P = .003$]. The above results suggested that advanced radiographic damage with m-SASSS scoring was independently associated with the presence of hypertension among the AS patients. Older age and obesity were also independently associated with hypertension in AS.

3.6. ROC curve analysis to evaluate clinical variables in predicting the AS patients with hypertension

Continuous variables that showed significant associations with hypertension in univariate logistic regression analyses were further assessed by ROC curve analyses, including age, disease duration, BASFI, BASMI, BASRI-Total, m-SASSS, WC, BMI, and WtHR (Table 6). We used ROC curve analyses to evaluate the clinical variables in predicting the AS patients with hypertension. The variables which showed significant in predicting the presence of hypertension among the AS patients were age [Area under the curve (AUC) = 0.756, $P < .001$], BASMI (AUC = 0.699, $P = .001$), BASRI-total (AUC = 0.687, $P = .003$), m-SASSS (AUC = 0.784, $P < .001$), WC (AUC = 0.699, $P = .001$), BMI (AUC = 0.622, $P = .010$), and WtHR (AUC = 0.731, $P < .001$). Older age, poor physical mobility, advanced radiographic damage and obesity were useful in predicting the patients with hypertension. The m-SASSS demonstrated the highest AUC value in predicting the presence of hypertension among the patients with AS.

4. Discussion

4.1. Radiographic damage associated with blood pressure and hypertension

Our study showed that 20.9% patients with AS had hypertension. Hypertension was the most prevalent comorbidity among the patients with AS, compatible with previous studies. Radiographic damage, particular the m-SASSS positively correlated with diastolic blood pressure in multivariate linear regression analysis. Only the m-SASSS was associated with the presence of hypertension in multivariate logistic regression analysis. These results in our study indicate that radiographic damage is an independent risk factor associated with increased blood pressure and the presence of hypertension in AS. The AS patients with advanced radiographic damage have increased the risk of hypertension, and possibly have more incidences of cardiovascular morbidity and mortality.

4.2. Male gender and older age associated with blood pressure and hypertension

In our study, male gender positively correlated with increased systolic blood pressure in multivariate linear regression analyses. Yao-Min et al showed that male AS patients had an increased risk for all cardiovascular diseases as compared to the general population. Male AS patient may have increased blood pressure and higher incidence of cardiovascular diseases. Older age increased the risk of hypertension in multivariate logistic regression analysis. Older age was associated with carotid intima-media thickness and atherosclerotic plaques in chronic arthritis patients. Older AS patients have increased risk for all cardiovascular diseases compared to the general population. Older age was associated with the presence of hypertension in the patients with AS.
### Table 4

Univariate logistic regression analyses of clinical factors for hypertension among the 167 AS patients.

| Clinical factors | Hypertension | Odds ratio (OR) (95% CI) | P value |
|------------------|--------------|--------------------------|---------|
| Age (yr) (n = 167) |              | 1.093 (1.050–1.137)      | <.001* |
| Male gender (n = 167) |          | 1.185 (0.446–3.153)     | .733    |
| Onset age (y/o) (n = 169) |      | 1.029 (0.996–1.060)     | .084    |
| Disease duration (yr) (n = 159) |   | 1.055 (1.020–1.091)     | .002*   |
| ESR (mm/h) (n = 165) |              | 1.023 (0.999–1.047)     | .061    |
| CRP (mg/dL) (n = 166) |              | 1.018 (0.726–1.427)     | .917    |
| BASDAI (n = 163) |              | 0.905 (0.712–1.125)     | .342    |
| ASDAS-ESR (n = 161) |              | 1.154 (0.748–1.783)     | .517    |
| ASDAS-CRP (n = 162) |              | 0.926 (0.622–1.378)     | .926    |
| BASFI (n = 163) |              | 1.300 (1.035–1.623)     | .024*   |
| BAS-G (n = 167) |              | 1.027 (0.896–1.176)     | .700    |
| BASMI (n = 153) |              | 1.341 (1.096–1.641)     | .004*   |
| Tragus-to-wall distance (cm) (n = 166) | | 1.065 (1.002–1.132) | .041* |
| Modified Schober index (cm) (n = 166) | | 0.902 (0.755–1.079) | .259 |
| Intermalleolar distance (cm) (n = 167) | | 0.972 (0.955–0.989) | .001* |
| Cervical rotation (degree) (n = 156) | | 0.996 (0.973–0.999) | .031* |
| Lateral lumbar flexion (cm) (n = 167) | | 0.919 (0.886–0.953) | .005* |
| Finger-tip-to-floor distance (cm) (n = 167) | | 1.018 (1.009–1.044) | .175 |
| Chest expansion (cm) (n = 167) | | 0.782 (0.614–0.966) | .046* |
| Occiput-to-wall distance (cm) (n = 167) | | 1.073 (1.017–1.145) | .012* |
| BASRI-total (n = 156) | | 1.219 (1.051–1.413) | .009* |
| m-SASSS (n = 156) | | 1.053 (1.030–1.077) | <.001* |
| Uretis (n = 167) | | 1.446 (0.651–3.211) | .645 |
| TNF-α-blocker use (n = 167) | | 2.069 (0.716–5.975) | .179 |
| Regular NSAIDs use (n = 166) | | 0.520 (0.225–1.202) | .126 |
| NSADs use (n = 166) | | 0.381 (0.245–1.542) | .300 |
| Regular DMARDs use (n = 166) | | 0.743 (0.348–1.586) | .443 |
| DMARDs use (n = 166) | | 1.444 (0.624–3.345) | .391 |
| Regular exercise (n = 166) | | 2.011 (0.947–4.270) | .069 |
| Current smoker (n = 164) | | 0.292 (0.231–1.588) | .308 |
| Ever smoker (n = 164) | | 0.793 (0.366–1.719) | .556 |
| Diabetes mellitus (n = 167) | | 5.255 (1.500–18.405) | .009* |
| Hypercholesterolemia (n = 167) | | 4.233 (1.152–15.562) | .030* |
| Waist circumference (WC) (cm) (n = 165) | | 1.059 (1.024–1.095) | .001* |
| Body mass index (BMI) (kg/m²) (n = 166) | | 1.185 (1.080–1.301) | <.001* |
| Waist to Height Ratio (WtHR) (n = 164) | | 142,906.709 (390.072–52,355,269.7) | <.001* |

Listwise deletion for missing data.

AS = ankylosing spondylitis, ASDAS-CRP = Ankylosing Spondylitis Disease Activity Score with CRP, ASDAS-ESR = Ankylosing Spondylitis Disease Activity Score with ESR, BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, BASFI = Bath Ankylosing Spondylitis Functional Index, BAS-G = Bath Ankylosing Spondylitis Patient Global Score, BASMI = Bath Ankylosing Spondylitis Metrology Index, BASRI = Bath Ankylosing Spondylitis Radiology Index, m-SASSS = modified Stoke Ankylosing Spondylitis Spinal Score.

* Statistical significances.

### Table 5

Multivariate logistic regression analyses of clinical factors for hypertension among the 167 AS patients.

| Clinical factors | Hypertension | Odds ratio (OR) (95% CI) | P value |
|------------------|--------------|--------------------------|---------|
| ESR (mm/h) (n = 164) |              | 1.016 (0.983–1.050)      | .346    |
| BASFI (n = 164) |              | 1.053 (0.787–1.407)      | .730    |
| BASMI (n = 152) |              | 1.068 (0.834–1.367)      | .602    |
| Tragus-to-wall distance (cm) (n = 165) | | 1.010 (0.936–1.091) | .796 |
| Intermalleolar distance (cm) (n = 166) | | 0.999 (0.968–1.015) | .453 |
| Cervical rotation (degree) (n = 155) | | 0.999 (0.984–1.015) | .936 |
| Lateral lumbar flexion (cm) (n = 166) | | 0.994 (0.877–1.016) | .122 |
| Chest expansion (cm) (n = 166) | | 0.864 (0.656–1.136) | .295 |
| Occiput-to-wall distance (cm) (n = 166) | | 1.034 (0.961–1.112) | .376 |
| BASRI-total (n = 156) | | 1.059 (0.871–1.288) | .564 |
| m-SASSS (n = 156) | | 1.033 (1.003–1.065) | .033* |
| Regular exercise (n = 166) | | 2.055 (0.706–5.516) | .153 |

Variables were adjusted by age, gender, diabetes mellitus, hypercholesterolemia, body mass index.

AS = ankylosing spondylitis, BASFI = Bath Ankylosing Spondylitis Functional Index, BASMI = Bath Ankylosing Spondylitis Metrology Index, BASRI = Bath Ankylosing Spondylitis Radiology Index, m-SASSS = modified Stoke Ankylosing Spondylitis Spinal Score.

*Statistical significances.

Listwise deletion for missing data.
4.3. CRP associated with blood pressure

CRP levels positively correlated with systolic blood pressure in univariate linear regression analysis, and showed the trend after multivariate adjustment. Active systemic inflammation may be associated with increased systolic blood pressure among the AS patients. Patients with higher CRP levels were associated with the increased risk of hypertension.[22,23] In the AS patients, there was a positive association between ASDAS-CRP and carotid intima-media thickness.[24] The carotid intima-media thickness had been shown as a predictor of developing hypertension.[25] Higher inflammation may cause increased arterial stiffness and lead to the presence of hypertension in the AS patients.

4.4. m-SASSS associated with blood pressure and hypertension

BASRI-Total and m-SASSS positively correlated with systolic/diastolic blood pressure in univariate linear regression analyses. Only the m-SASSS significantly correlated with diastolic blood pressure after multivariate linear regression adjustment. Importantly, there was an increased risk of developing hypertension for the AS patients with higher m-SASSS in multivariate logistic regression. Advanced radiographic damage with m-SASSS scoring could be associated with the presence of hypertension among the patients with AS. Notably, radiographic damage was independently associated with increase in diastolic blood pressure and the presence of hypertension in our study. The presence of syndesmophytes was independently associated with an accelerated atherosclerosis in patients with SpA.[26] Increased carotid intima-media thickness has a positive association with higher blood pressure.[27,28] Radiographic damage, including the syndesmophytes formation and ankyloosing of spine, may possibly have strong relation to vascular intima-media thickness in patients with AS. The BASRI-Total score did not show significant association with elevated blood pressure and the presence of hypertension, after multivariate linear/logistic regression adjustment. The BASRI-Total score contains only cervical and lumbar spine. Increased blood pressure and the presence of hypertension may predominate related to the spinal radiographic damage in AS.

4.5. Physical mobility associated with blood pressure

Cervical rotation and lateral lumbar flexion were positively correlated with diastolic blood pressure in multivariate linear regression adjustment. Poor physical mobility, particular cervical rotation and lateral lumbar mobility may be associated with increased blood pressure in the AS patients. Active inflammation and advanced radiographic damage could lead to patient’s poor physical mobility. The association of blood pressure with physical mobility may be due to higher inflammation and advanced radiographic damage in these AS patients.

4.6. TNF-α blocker and DMARDs associated with blood pressure

TNF-α blocker and DMARDs use had associations with increased systolic blood pressure among the AS patients in multivariate linear regression analyses. Sizheng Steven et al.[29] showed that comorbidities were associated with disease activity in axial SpA. The patients with DMARDs may possibly have higher inflammation and associated with increased systolic blood pressure. In a meta-analysis study, TNF-α blocker was associated with increased risk of developing hypertension in rheumatoid arthritis.[30] TNF-α blocker use may possibly also induce elevated systolic blood pressure among the AS patients, but the pathological mechanisms needs further investigation. A further larger prospective cohort is required to assess the association between TNF-α blocker use and the elevation of blood pressure.

4.7. Obesity, DM and hypercholesterolemia associated with hypertension

WC, BMI, and WtHR were positively correlated with systolic/diastolic blood pressure in multivariate linear regression analyses. Obesity was significantly associated with the presence of hypertension in multivariate logistic analyses. Our study suggested that obesity could be associated with increased systolic/diastolic blood pressure and presence of hypertension among the patients with AS. DM and hypercholesterolemia were associated with the presence of hypertension in univariate logistic regression analyses. The presence of DM is frequently associated with developing hypertension.[31] Hypertension is commonly observed in patients with hypercholesterolemia, due to the accelerated atherosclerosis. The association between obesity and hypertension has been well demonstrated in most racial groups.[32,33] Presence of DM and hypercholesterolemia have associations with hypertension among the patients with AS.

4.8. Age, BASMI, BASRI-total, m-SASSS, WC, BMI, and WtHR in predicting hypertension

In the ROC curve analyses, age, BASMI, BASRI-Total, m-SASSS, WC, BMI and WtHR were significant parameters in predicting the
presence of hypertension among the patients with AS. Older age, poor physical mobility, advanced radiographic damage and obesity could predict the presence of hypertension. Advanced radiographic damage with m-SASSS scoring was the most useful disease severity parameter to predict the presence of hypertension in AS.

This study has some limitations. The patients with DM, hypertension and hypercholesterolemia but without the medications use were not classified as having these comorbidities. The associations of blood pressure and hypertension with radiographic damage could not be established on such a small cross sectional cohort. A larger-scale study to assess the associations of blood pressure and hypertension with longitudinal radiographic change is needed in the AS patients.

5. Conclusion
Advanced radiographic damage with m-SASSS is an independent risk of increased blood pressure and presence of hypertension among the patients with AS. Older age, male gender, poor cervical rotation, lateral lumbar flexion, TNF-α blocker and DMARDs use are independently associated with increased blood pressure. Obesity increases the risk of elevated blood pressure and presence of hypertension in AS. Older age, poor physical mobility, advanced radiographic damage and obesity are useful indices in predicting the AS patients with hypertension, and m-SASSS is the best.

Acknowledgments
We thank Chi-Wei Chen, Sin-Huei Wu and Chun-Wei Chen for obtaining questionnaires and performing physical examination.

Author contributions
Conceptualization: Chun-Hsiung Chen, Hung-An Chen.
Data curation: Chun-Hsiung Chen, Chen-Hung Chen.
Formal analysis: Chun-Hsiung Chen.
Funding acquisition: Chun-Hsiung Chen.
Investigation: Chun-Hsiung Chen, Chen-Hung Chen, Chung-Tei Chou.
Methodology: Chun-Hsiung Chen, Hsien-Tzung Liao, Chung-Tei Chou.
Writing – original draft: Chun-Hsiung Chen.
Writing – review & editing: Chen-Hung Chen, Hung-An Chen, Hsien-Tzung Liao, Chung-Tei Chou.

References
[1] Taurog JD, Chhabra A, Colbert RA. Ankylosing Spondylitis and Axial Spondyloarthritides. N Engl J Med. 2016;374:2563–74.
[2] Chen CH, Chen HA, Liu CH, et al. Association of obesity with inflammation, disease severity and cardiovascular risk factors among patients with ankylosing spondylitis. Int J Rheum Dis 2020. 2020;23:1165–73.
[3] Michal Vinker S, Omer G, Shmuel T, et al. Ischemic heart disease and ankylosing spondylitis-assessing the role of inflammation. Clin Rheumatol. 2018;37:1035–8.
[4] Mike JP, van der Horst-Bruinsma IE, Dijkmans BA, et al. Cardiovascular risk profile of patients with spondylarthropathies, particularly ankylosing spondylitis and psoriatic arthritis. Semin Arthritis Rheum. 2004;34:585–92.
[5] Nisha NH, Michael Paterson J, Ping L, et al. Patients with ankylosing spondylitis have increased cardiovascular and cerebrovascular mortality: a population-based study. Ann Intern Med. 2015;163:408–16.
[6] Dong Hyun L, Jin Choi Y, In-Bo H, et al. Association of ischemic stroke among patients with ankylosing spondylitis: a nationwide population-based study. Ann Rheum Dis. 2010;69:1165–8.
[7] Zhao SS, Radner H, Stefan S, et al. Comorbidity burden in axial spondyloarthropathy: a cluster analysis. Rheumatology (Oxford). 2019;58:1746–54.
[8] Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis: A proposal for modification of the New York criteria. Arthritis Rheum. 1984;27:361–8.
[9] Garrett S, Jenkinson T, Kennedy LG, et al. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol. 1994;21:2286–91.
[10] Lukas C, Landewé R, Sieper J, et al. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. Ann Rheum Dis. 2009;68:18–24.
[11] van der Heijde D, Lie E, Kvisen TK, et al. ASDAS, a highly discriminatory ASAS-endorsed disease activity score in patients with ankylosing spondylitis. Ann Rheum Dis. 2009;68:1811–8.
[12] Calin A, Garrett S, Whiteclock H, et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. J Rheumatol. 1994;21:2281–5.
[13] Jones SD, Steiner A, Garrett SL, et al. The bath ankylosing spondylitis patient global score (BAS-G). Br J Rheumatol. 1996;35:66–71.
[14] Jenkinson TR, Mallorie PA, Whitelock HC, et al. Defining spinal mobility in ankylosing spondylitis (AS). The Bath AS Metrology Index. J Rheumatol. 1994;21:1694–8.
[15] Calin A, Mackay K, Santos H, et al. A new dimension to outcome: application of the Bath Ankylosing Spondylitis Radiology Index. J Rheumatol. 1999;26:988–92.
[16] Creemers MC, Fransen MJ, van’t Hof MA, et al. Assessment of outcome in ankylosing spondylitis: an extended radiographic scoring system. Ann Rheum Dis. 2005;64:127–9.
[17] D’Albensi A, Giolto A, Tagetti A, et al. Traditional cardiovascular risk factors or inflammation: Which factors accelerate atheroclerosis in arthritis patients? Int J Cardiol. 2017;236:488–92.
[18] Ahmad J, Kazem R, Bautista LE, et al. Inflammation markers and risk of developing hypertension: a meta-analysis of cohort studies. Heart 2019;105:686–92.
[19] Yassu K, Kiyoshi M, Yuki M, et al. C-reactive protein and incident hypertension in a worksite population of Japanese men. J Clin Hypertens (Greenwich). 2019;21:524–32.
[20] Erding H, Iker S, Tasicer K, et al. Assessment of subclinical atherosclerotic cardiovascular disease in patients with ankylosing spondylitis. Anatoj Cardiol. 2018;22:185–91.
[21] Hiroiuki T, Tomonori S, Shunsuke M, et al. Carotid intima-media thickness is a novel predictor of new onset of hypertension in normotensive subjects. Medicine (Baltim). 2017;96:e7710.
[22] Alessandro G, Andrea D, Giovanni C, et al. Factors associated with accelerated subclinical atherosclerosis in patients with spondyloarthrititis without overt cardiovascular disease. Clin Rheumatol. 2017;36:2487–95.
[23] Xiao XZ, Jinbo L, Hongwei Z, et al. The effect of cardiovascular risk factors on the carotid intima-media thickness in an old-aged cohort with hypertension: a longitudinal evolution with 4-year follow-up of a random clinical trial. Clin Exp Hypertens. 2019;41:49–57.
[24] Sun ML, Chang Kim H, Sang Lee H, et al. Association between blood pressure and carotid intima-media thickness. J Pediatr. 2009;154:667–71.
[25] Zhao SS, Robertson S, Reich T, et al. Prevalence and impact of comorbidities in axial spondyloarthritides: systematic review and meta-analysis. Rheumatology (Oxford). 2020;59 (Suppl4):i47–57.
[26] Qngweizi Z, Dongsheng H, Zhang Y, et al. Association between anti-TNF therapy for rheumatoid arthritis and hypertension: a meta-analysis of randomized controlled trials, Medicine (Baltim). 2015;94:e731.
[27] Mohammad-Reza M, Sudhakar S, Mehrtash H. Independent association between type 2 diabetes mellitus and hypertension over a period of 10 years in a large inpatient population. Clin Exp Hypertens. 2010;32:198–201.
[28] Branslava I, Marijana T. Hypercholesterolemia and hypertension: two sides of the same coin. Am J Cardiovasc Drugs. 2015;15:403–14.
[29] Vasilitos K, Stella S, Sofia P, et al. Mechanisms of obesity-induced hyper tension. Hypertens Res. 2010;33:386–93.
[30] Redon J. Hypertension in obesity. Nutr Metab Cardiovasc Dis. 2001;11:344–53.

9. Yao-Min H, Wei-Pin C, Cheng-Chung Wei J, et al. Midlife ankylosing spondylitis increases the risk of cardiovascular diseases in males 5 years later: a national population-based study. Medicine (Baltim). 2016;95:e3596.
10. Jiunn-Horng K, Yi-Hua C, Heng-Ching L. Comorbidity profiles among patients with ankylosing spondylitis: a nationwide population-based study. Ann Rheum Dis. 2010;69:1165–8.
11. Zhao SS, Radner H, Stefan S, et al. Comorbidity burden in axial spondyloarthropathy: a cluster analysis. Rheumatology (Oxford). 2019;58:1746–54.
12. Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis: A proposal for modification of the New York criteria. Arthritis Rheum. 1984;27:361–8.
13. Garrett S, Jenkinson T, Kennedy LG, et al. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol. 1994;21:2286–91.
14. Lukas C, Landewé R, Sieper J, et al. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. Ann Rheum Dis. 2009;68:18–24.
15. van der Heijde D, Lie E, Kvisen TK, et al. ASDAS, a highly discriminatory ASAS-endorsed disease activity score in patients with ankylosing spondylitis. Ann Rheum Dis. 2009;68:1811–8.