Gait characteristics in patients with ankylosing spondylitis: a systematic review

J. Soulard[1,2], J. Vaillant[1], C.-T. Agier[1], N. Vuillerme[1,3,4]

[1]University of Grenoble Alpes, AGEIS;
[2]Grenoble Alpes University Hospital;
[3]LabCom Telecom4Health, University of Grenoble Alpes & Orange Labs, Grenoble;
[4]Institut Universitaire de France, Paris, France.

Julie Soulard, MSc
Jacques Vaillant, PhD
Clara-Themis Agier
Nicolas Vuillerme, PhD

Please address correspondence to:
Julie Soulard,
Faculte de Medecine,
Université Grenoble Alpes
AGEIS
23 Avenue Maquis du Grésivaudan,
38000 Grenoble, France.
E-mail: juliesoulard.physio@gmail.com

Received on February 27, 2020; accepted in revised form on May 18, 2020.

Clin Exp Rheumatol 2021; 39: 173-186.

Key words: gait, walk, spondyloarthritis, wearable devices, clinical tests, laboratory gait assessment

This review was partly presented at the World Confederation for Physical Therapy congress in Geneva in May 2019.
This study is part of the PhD thesis of the first author J. Soulard, (Univ. Grenoble Alpes, AGEIS Lab, France, and Grenoble Alps University Hospital, Grenoble, France).

Funding: This work is supported by the French Ministry of Health and Solidarity with the "Nursing and Paramedical Hospital Research Program" year 2016 (PHRIP-16-0528) and by the French National Research Agency in the framework of the "Investissements d'avenir" program (ANR-10-AIRT-05 and ANR-15-IDEX-02).
The sponsors had no involvement in the review and approval of the manuscript for publication. This work further forms part of a broader translational and interdisciplinary research project, GaitAlps.

Competing interests: none declared.

ABSTRACT

Objective. *Ankylosing spondylitis (AS) is a chronic rheumatic disease which affects the axial skeleton and sacroiliac joints. By impacting spinal mobility and physical functions, AS could also potentially impair gait. However, while published data are rather sparse, it appears that discrepancies exist regarding AS consequences on gait characteristics, tasks and analysis techniques used to assess gait ability of patients with AS. The review questions are twofold: (1) How is gait assessed in patients with AS? and (2) What are the consequences of AS on gait?*

Methods. *Databases were systematically searched to identify studies satisfying the search criteria, using the synonyms of ankylosing spondylitis and gait. Two reviewers extracted from the articles study characteristics, methods and main results in relation to gait.*

Results. *192 titles were extracted from databases and 21 studies were included in the review. 16 studies (76%) used clinical gait measurements and 5 (23%) used laboratory gait measurements. Only 7 involved a healthy control group. Studies used various protocols, instructions and parameters when assessing gait. Gait of patients with AS was associated with decreased stride length, pelvic movements and lower limbs angles in the sagittal plane, and increased hip abduction and external rotation compared to healthy controls.*

Conclusion. *Only few studies have assessed gait characteristics in patients with AS and published data evidence that kinematic parameters of gait is altered, but no consensus exists regarding gait analysis methods for patients with AS. Guidelines are provided to improve the design and methodology for future studies on gait and AS.*

Introduction

In Europe, ankylosing spondylitis (AS) affects 1.30 to 1.56 million people, with a prevalence of 23.8 persons per 10,000 (1). AS belongs to a category of chronic inflammatory diseases called "spondyloarthritis" (SpA), with common clinical and pathophysiological features (2). AS causes inflammatory back pain, with spinal mobility impairment, adverse consequences on physical functions (1), that can significantly worsen the quality of life of patients with AS (3, 4). Gait is widely accepted as being a defining factor in the quality of life (5-8).

In patients with AS, gait may be affected in relation with back pain, spinal mobility impairment, altered posture, or feet abnormalities (9-11). Besides, patients with AS have intensified transmissibility of vibrations (12), and thus tend to avoid shocks when walking, leading to a more cautious gait (13) with reduced ground reaction force (12). With thorax and pelvis stiffness, pelvis-shoulder coordination can be altered (14) while it appeared to be decisive to maintain stability and reduce the energetic cost of locomotion (15). Another point for altered gait in patients with AS is the decrease of lower limb passive ranges of motion that can be associated to reduced ranges of motion during gait, notably in the sagittal plane (13, 14, 16, 17). However, only few studies have focussed on gait in patients with AS. In addition, the wide variety of protocols, types of equipment and outcomes raised in the scientific literature (18-20) makes the comparison between studies rather difficult.

This systematic review aims to compile published studies that have assessed gait in patients with AS to better understand AS consequences on gait. More precisely, the review questions are as follows: (1) How is gait assessed

in patients with AS? and (2) What are the consequences of AS on gait?

Materials and methods

The protocol of this systematic review has been registered in PROSPERO (CRD42018102540) and published in JMIR Res. Protoc (21).

When conducting our systematic review, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines provided by Moher *et al*. (22).

Inclusion criteria

Studies had to fulfil the following inclusion criteria:

- Original research published in English in a peer-reviewed scientific journal, with an observational or experimental study designs;
- Including participants older than 18 years old, with a diagnosis of ankylosing spondylitis;
- Reporting clinical and/or laboratory gait measurements.

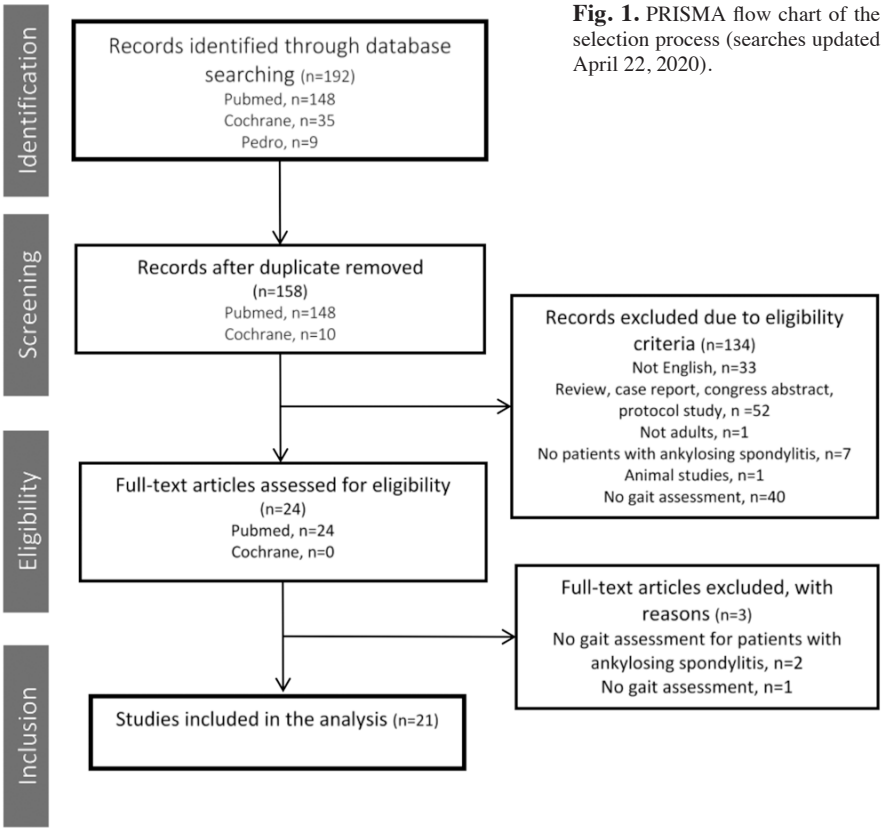

Fig. 1. PRISMA flow chart of the selection process (searches updated April 22, 2020).

Exclusion criteria

Studies were excluded if they fulfilled the following exclusion criteria:

- Case reports, abstracts, editorials, conference abstracts, letters to the editor, reviews and meta-analysis;
- Gait outcomes not reported adequately (without mean and SD or median associated with interquartile range or first and third quartile), or if the extraction of mean and SD of gait outcomes from the results section was impossible.

Data sources and search strategy

Searches were first conducted with no date restrictions, on June 5, 2018 in three electronic databases (PubMed, Cochrane, Physiotherapy Evidence Database) (21) and were updated on April 22, 2020.

The search terms were the combinations of the Medical Subject Headings terms (1) of the population, ankylosing spondylitis (23, 24). and (2) of the outcome, gait (25). The search strategy included a combination of these terms found in the abstract or the title of the selected articles: ("gait" OR "walk" OR "walking" OR "locomotor" OR "locomotion") AND ("ankylosing spondylitis" OR "spondyloarthritis"). More details on search strategy can be found in the supplementary materials (Suppl. file).

Study selection

The study selection was conducted by two independent reviewers (JS and CA), who screened the titles, abstracts and keywords identified by the search strategy and applied the inclusion and exclusion criteria. After this initial selection, full-length texts were subjected to the same procedure. In case of disagreement and if subsequent discussions between the two reviewers were inconclusive, a third reviewer was contacted (JV). In line with the PRISMA guidelines (22), the number of citations reviewed at each stage of the review were summarised in a flow chart (Fig. 1).

Risk of bias in individual studies

As our aim was not to evaluate the effect of an intervention, we did not use a risk of bias assessment. As mentioned above, our aim was to document the effect of AS on gait, specifically focusing on published studies that have reported clinical or laboratory gait measures in patients with AS.

Data extraction

Furthermore, the following 4 data sets were extracted from the retrieved articles (26) by two independent reviewers (JS and CA):

- Study characteristics: first author, title, year of publication, journal's name, country, study design;
- Sample description: Age, disease duration, body mass index, Bath Ankylosing Spondylitis Functional Index, Bath Ankylosing Spondylitis Activity Index;
- Methods*:* task requirement, instrumentation and data acquisition methodology, parameters assessed;
- Main results obtained from gait assessment: clinical measurements of gait (*e.g*. distance covered in the 6MWT…) and laboratory measurements of gait, (*e.g*. spatio-temporal parameters and kinematic parameters) were extracted. For experimental studies, only data from pre-test (before intervention) were extracted.

Means and SDs or medians associated

Table I. Characteristics of included studies (n=21).

Study	Year	Main objective	Intervention	AS characteristics (with gait measurements)	HC characteristics (if included)	Length of follow-up
Barkham *et al.* (28)	2010	To determine whether etanercept improves work instability as measured by the ankylosing spondylitis work instability scale	Yes (2 groups: etanercept *vs.* placebo), randomised	n=32, 32M (out of 40) Age = 40.1±9.9 (for 40) AS duration = 15.5		12 weeks
Basakci Calik *et al.* (37)	2018	To investigate the effects of inspiratory muscle training (IMT) on respiratory muscles and functional exercise capacity, as well as on the specific outcomes of the disease in AS patients	Yes (2 groups: IMT + conventional exercise *vs.* conventional exercise program only), randomised	n=32, 14M Age = 37.4±10.2 AS duration = 7.9		12 weeks
Basakci Calik *et al.* (38)	2020	To investigate the effect of the addition of aerobic training to spinal mobility exercises on disease specific outcomes and functional exercise capacity, aerobic capacity and respiratory muscle strength of AS patients	Yes (2 groups: aerobic exercise +supervised spinal mobility exercises vs supervised spinal mobility exercises only), randomised	n=31, 12M Age = 44.7±11.5 AS duration = NR		6 months
Brambila-Tapia *et al.* (39)	2013	To evaluate the association between pulmonary function and clinical variables in AS, and to compare the pulmonary function of patients with AS with that of controls	No	n=61, 45M Age = 39 AS duration = NR	n=74, 48M Age = 38	once
Çınar *et al.* (27)	2016	To assess the impact of postural deformities caused by ankylosing spondylitis on balance problems	No	n=29, 25M Age = 44.3±8.8 AS duration = 9.0	n=21, 16M Age = 36.8±9.7	once
Coksevim *et al.* (40)	2018	To investigate the effects of combination therapy with global postural reeducation exercise (GPR) and anti-TNF treatments on clinical parameters in patients with active AS	Yes, (3 groups: anti-TNF therapy + GPR program *vs.* anti-TNF + conventional exercise therapy *vs.* control), not randomised	n=60, 42M Age = 33.5±10.9 AS duration = 6.6		3 months
Del Din *et al.* (16)	2011	Aim at evaluating AS subjects gait alterations	No	n=12, 8M Age = 49.4±10.5 AS duration = 9.2	n=12, 8M Age = 55.75 ±3.2	once
Durmus *et al.* (29)	2009	To evaluate the impact of two different home based daily exercise programs on pulmonary functions in patients with AS	Yes (3 groups: exercises based on the treatment of shortened muscle chains, conventional exercise, routine treatment), not randomised	n=51, 43M Age = 38.7±8.7 AS duration = 12.2		12 weeks
Er *et al.* (41)	2017	Investigate the effects of kinesiophobia in AS on pulmonary functions tests and functional performance	No	n=31, 19M Age = 47.4±14.0 AS duration = 21.3		once
Halvorsen *et al.* (42)	2012	To compare physical fitness in patients with AS and controls AND to explore associations between physical fitness and disease activity in the patient group	No	n=149, 92M Age = 49.4±11 AS duration = 23	n=133, 77M Age = 52.6±11.3	once
Jennings *et al.* (30)	2015	To evaluate the effects of aerobic exercise in patients with AS	Yes (2 groups: aerobic exercise + stretching *vs.* stretching alone), randomised	n=70, 49M Age = 41.5±9.6 AS duration = 14.7		2 years
Karapolat *et al.* (31)	2009	To compare the effects of conventional exercise, swimming and walking on pulmonary function	Yes (3 groups: swimming + conventional exercise *vs.* walking + conventional exercise *vs.* conventional exercise alone), randomised	n=45, 27M Age = 48.5±11.8 AS duration = 18.9		6 weeks
Lubrano *et al.* (32)	2006	To determine the effects of a combination treatment including rehabilitation and etanercept *vs.* rehabilitation only, on function, disability, and quality of life in a group of patients with active AS.	Yes (for all patients: intensive standardised exercise program), cross-over design	n=19, 16M Age = 41.3±8.6 AS duration = 9.3		9 months
Mangone *et al.* (14)	2011	To assess whether pelvis shoulder coordination during walking in AS patients differs from that in healthy subjects	No	n=17, 15M Age = 47±21.9 AS duration = 15	n=10, 9M Age = 38.7±14.5	once

Study	Year	Main objective	Intervention	AS characteristics (with gait measurements)	HC characteristics (if included)	Length of follow-up
Mengshoel *et al.* (43)	2004	To examine whether there are any associations between walking time, quadriceps muscle strength and cardiovascular capacity in patients with RA and AS	No	n=26, 15M Age = 42±9 AS duration = 16		once
Ortancil *et al.* (33)	2009	To determine the effects of a 6 week home-based exercise program on the respiratory muscle and energy cost in AS	Yes (for all patients: breathing and upper extremity exercises)	n=22, 17M Age = 42.4±9 AS duration = 7		6 weeks
Rocha-Munoz *et al.* (34)	2015	To evaluate the effect of anti-TNF agents plus synthetic disease modifying anti-rheumatic drugs (DMARDs) *vs*. DMARDs alone for ankylosing spondylitis (AS) with reduced pulmonary function vital capacity (FVC%).	Yes (2 groups: DMARDs + anti-TNF *vs*. DMARDs alone), not randomised	n=36, 28M Age = 42.8[a] AS duration = 12.78		2 years
So *et al.* (35)	2012	To evaluate the effect of combining incentive spirometer exercise (ISE) with a conventional exercise (CE) on patients with AS stabilised by TNF	Yes (2 groups: conventional exercises + incentive spirometer exercises *vs*.conventional exercises), randomised	n=46, 44M Age = 36.3±7.5 AS duration = 12.55		16 weeks
Souza *et al.* (36)	2017	To evaluate the effectiveness of a progressive muscle strengthening program using a Swiss ball for AS patients	Yes (2 groups: medical treatment + Swiss ball exercises *vs*. medical treatment alone), randomised	n=60, 44M Age = 44.4±10 AS duration = 9.2		16 weeks
Zebouni *et al.* (13)	1992	To compare gait pattern of 12 patients with AS with axial disease with that of 11 healthy controls	No	n=12, 8M Age = 46.5 (28-70)[a] AS duration = 14	n=11, 9M Age = 39.5 (26-60)	once
Zhang *et al.* (17)	2019	To investigate the gait deviations of AS patients with hip involvement.	No	n=18, 18M Age = 40.2±6.4 AS duration = 14.1	n=18, 18M Age = 40.7±5.3	once

[a] Values are mean ±standard deviation, except for studies with [a] which is median associated to 1st and 3rd quartile
AS: ankylosing spondylitis; HC: healthy controls; M: male; NR: not reported.

Table II. Frequency of study design of included studies (n=21).

Study design	Number of studies (%)	Studies
Observational study	2 (9.5)	Er (41), Mengshoel (43)
Observational prospective cohort	0	
Observational case-control study	7 (33.3)	Brambila-Tapia (39), Cinar (27), Del Din (16), Halvorsen (42), Mangone (14), Zebouni (13), Zhang (17)
Experimental cross over study	1 (4.8)	Lubrano (32)
Experimental non randomised open label uncontrolled study	1 (4.8)	Ortancil (33)
Experimental non randomised open label controlled study	2 (9.5)	Rocha-Munoz (34), Coksevim (40)
Experimental randomised open label controlled study	5 (23.8)	Durmus (29), Karapolat (31), So (35), Basakci Calik (37, 38)
Experimental randomised controlled study with a blind evaluator	2 (9.5)	Jennings (30), Souza (36)
Experimental randomised double blind study	1 (4.8)	Barkham (28)

with interquartile ranges or first and third quartiles were extracted.

Two reviewers (JS and CA) independently extracted these data from each included study and compared the data for consistency. Any discrepancies between the two reviewers (JS and CA) were resolved at a consensus meeting. If disagreement persisted, a third reviewer (JV) was consulted to reach a final decision.

Results

The application of the search strategy described above lead to 192 records, 24 full-texts were reviewed, and, of those, 21 were finally included in the review (Fig. 1). The characteristics of the 21 studies are presented in Table I, representing a total of 859 patients with AS that had gait assessment.

For most of the 21 included studies, gait assessment was not the primary objective as only 4 had specific gait-based objective (13, 14, 16, 17) and 1 had balance-based objective (27). Most of other studies were experimental and used gait as a secondary outcome of intervention effectiveness. Half of the studies (n=12) had a longitudinal follow-up from 6 weeks to 2 years (28-36) but they were all associated to an intervention. Supplementary Figure S1 shows the number and frequency

Table III. Description of the tests and protocols used in studies with clinical measurements of gait (n=16).

Study	Year	Tests and protocols descriptions
Basakci Calik *et al.* (37)	2018	"Exercise capacity was measured using the 6MWT) The test was performed in a 30-m corridor in accordance with the testing guidelines [ATS guidelines]. Prior to the test, perceived resting heart rate, resting peripheral oxygen saturation, and resting blood pressure were measured."
Basakci Calik *et al.* (38)	2020	"Exercise capacity was measured using the 6MWT. The test was performed in a 30m corridor in accordance with the test guidelines [ATS guidelines]. Prior to the test, perceived resting heart rate, resting peripheral oxygen saturation, and resting blood pressure were measured."
Brambila-Tapia *et al.* (34)	2013	« Functional capacity, related with cardiopulmonary function, was measured with the 6-min walk test »
Çınar *et al.* (27)	2015	Gait speed, 6MWT
Coksevim *et al.* (40)	2018	"The 6 min walk distance (6MWD) test was used as a test of objective assessment of functional performance and endurance. Subjects were given the same standard verbal instructions before each test and instructed to walk their maximum distance in a 6 min period."
Durmus *et al.* (29)	2009	6MWT: "Subjects completed this test on a 42.6-m walkway. Subjects were given the same standard verbal instructions before each test and instructed to walk their maximum distance in a 6-min period. The total distance covered in meters during the 6 min of walking was used as the score for each session."
Er & Angin (41)	2017	6MWT: "straight enclosed environment designated by cones on a track of 30m of length, which is not slippery and not containing material that would obstruct the individual. With the command "start", the individual walks on a track on a self-adjusted fast speed for 6 minutes. At the end of 6 minutes, they stop with the command "stop" and they are given a chair in the stopping point to rest. The distance covered by the individual in 6 minutes is calculated in units of meters and recorded"
Halvorsen *et al.* (42)	2012	"Walking in a figure-of-eight pattern was used to assess dynamic balance. This test was reported to have good interrater reliability (r=.98) and test-retest reliability (standard error of measurement=2) in a group of patients with moderate disability. Two double circles were put together to form a figure-of-eight, which was marked on the floor (the inner circles with a diameter of 1.5 m, the outer circles with a diameter of 1.8 m). The participants were asked to walk the figure-of-eight twice without shoes, and the number of steps on lines and outside the figure were counted as the score.
Jennings *et al.* (30)	2015	"The 6MWT was performed on a 22-m indoor track following the guidelines of the American Thoracic Society."
Karapolat *et al.* (31)	2009	"The 6MWT was performed at least four hours before cardiopulmonary exercise test. Participants walked up and down on a 20-m hallway for a period of six minutes at their own pace. Patients were permitted to stop and rest and were instructed to continue walking as soon as they felt able to do so. The distance walked by each subject was recorded in meters"
Lubrano *et al.* (32)	2006	6MWT: It was carried out on a level hallway, and was supervised by a physician. Patients were instructed to cover the greatest distance possible during the allotted time, at a self-administered walking speed, pausing to rest as needed. The total distance in meters during the 6MWT was recorded.
Mengshoel *et al.* (43)	2004	"Flat floor walking time was assessed by measuring the time it took the patients to walk 160 m as fast as they could without running on a flat floor (…) All the patients wore shoes during the tests."
Ortancil *et al.* (33)	2009	6MWT: "at a 20-m length corridor, with heart rate at the beginning and the end, walk as fast as they could"
Rocha-Munoz *et al.* (34)	2015	6MWT, no more precisions
So *et al.* (35)	2012	"The 6-min walk distance (6MWD) test was used to objectively assess functional performance and endurance. The 6MWD test was performed according to modified American Thoracic Society guidelines."
Souza *et al.* (36)	2017	6MWT: "6-minute walking test (6MWT) that is a functional test that assess distance walked over 6 min in a 22-meter indoor track."

6MWT: 6-minute walk test, ATS: American Thoracic Society.

of publication per year of the included studies on gait and AS.

Gait assessments were divided into two distinct categories: (1) clinical measurements of gait using variables extracted from clinical tests; and (2) laboratory measurements of gait using spatio-temporal or kinematic parameters, assessed with electronic walkway, inertial sensors, electrogoniometers or 3D motion analysis, and sometimes associated to ground reaction force dynamometer and/or electromyography. Among the 21 included studies, 16 (76.2%) used clinical measurements to describe gait (27, 29-43), while 5 (23.8%) studies used laboratory measurements (13, 14, 16, 17, 28). No study combined both clinical and laboratory measurements of gait.

Clinical gait measurements

Tests and protocols described in studies with clinical gait measurements are described in Table III. The descriptions of gait tests were heterogeneous, with some studies giving only the distance

Table IV. List and values of parameters used in studies with clinical measurements of gait (n=16).

Gait parameters	Number of studies (%)	Studies	Results	Sign.
6MWD (meters)	n=14 (87.5)	Basakci Calik *et al*. (37)	AS = 504.9±59.4	
		Basakci Calik *et al*. (38)	AS = 504.0 ±88.4	
		Brambila-Tapia *et al*. (39)	AS = 324[a], HC = 520[a]	$p<0.001$
		Çınar *et al*. (27)	AS = 407 ±142, HC = 599±98	NS
		Coksevim *et al*. (40)	AS = 560.7±65.3	
		Durmus *et al*. (29)	AS = 548.5±87.6	
		Er et AngIn (41)	AS = 445.88±99.5	
		Jennings (30)	AS = 433.0±57.8	
		Karapolat (31)	AS = 388.3±88.0	
		Lubrano (32)	AS = 242.2a	
		Ortancil (33)	AS =574.2±94.5	
		Rocha-Munoz (34)	AS =299.8	
		So (35)	AS =515.7±60.3	
		Souza (36)	AS = 441.43±57.2	
Number of oversteps in figure of eight	n=1 (0.07)	Halvorsen *et al*. (42)	AS = 2.0 ±0.59, HC = 2.5±0.24	NS
Gait speed at comfortable pace (m/s)	n=1 (0.07)	Çınar *et al*. (27)	AS = 0.9 ±0.2, HC = 0. ±0.1	NS
Time to walk 160 m at fast pace (s)	n=1 (0.07)	Mengshoel (43)	86±13	

Values are mean ±standard deviation with values of patients with AS / healthy controls, except for studies with [a] which is median.
Sign: significance with healthy controls; AS: patients with ankylosing spondylitis; HC: healthy controls; 6MWD: 6-minute walk distance.

walkways (29-31, 33, 36-38, 43), and others describing more precisely the walkways used (41, 42). Some studies clearly described the instructions gave to the participant before the trials (29, 31-33, 41-43), 4 studies (25%) mentioned that they followed the American Thoracic Society guidelines (30, 35, 37, 38) and 4 studies (25%) did not mention the instructions (27, 34, 36, 39). No study gave information on the precise instructions provided during the 6MWT.

Table IV depicts the list and values of parameters used in studies with clinical measurements of gait, with the number of studies and percentage out of the 16 studies using the same parameter. The 6-minute Walk Distance (6MWD) was the mostly used clinical gait parameter (27, 29-41). Among these 14 studies, only 2 made a comparison with a healthy control group (27, 39) yielding different conclusions. Indeed, the first one (39) found a significant reduction of 6MWD (39) in patients with AS compared to healthy controls, while the second one (27) did not report any significant difference between both groups.

Laboratory gait measurements

Table V describes the materials and protocols used in studies using gait laboratory measurements. Materials used for gait assessments were mainly well described (13, 14, 16, 17) except in one study (28). Walkways used and pace were described in three studies (14, 16, 17), two studies specified the number of trials collected (14, 17) and two studies specified the minimum number of steps included in the analysis (13, 14, 16).

In studies using laboratory measurements of gait, more than 100 different gait parameters (spatio-temporal, kinematic or electromyographic parameters) were reported.

Table VI gives the list and results of spatio-temporal gait parameters used in studies with laboratory measurements of gait. Only one study found that gait velocity (17) was significantly lower in patients with AS, and two studies found lower stride length (13, 17) in patients with AS compared to HC. One study used stride width/height parameter and reported significant higher values in AS compared to HC (17). The other spatio-temporal gait parameters were not significantly different between AS and HC.

Table VII provides joints ranges of motion during gait in AS and HC. A significant increase of trunk sagittal ranges of motion during gait cycle was found in AS, with an increase of extension found by Del Din *et al*. (16) and an increase of flexion found by Zhang *et al*. (17). Significant decrease of pelvic movements were found for AS (14, 16); with an anterior tilt for AS and a posterior tilt for HC (14), and a decrease of pelvic obliquity (16). A significant decrease of sagittal hip movements was reported, with a decrease of hip flexion reported in 3 studies (13, 16, 17) and a decrease of hip extension reported by 1 study (14). Two studies reported an increase of hip abduction in AS (16, 17). Analysis of knee movements show somewhat contradictory results: Del Din *et al*. (16) and Zhang *et al*. (17) reported, respectively, significantly decreased and increased knee flexion is AS, while no significant difference between AS and HC was observed by Zebouni *et al*. (13). Ankle angles of the sagittal plane were reduced in AS, with a decrease of dorsi flexion at initial contact (16) and a decrease plantar flexion during the gait cycle (17).

Supplementary Table S1 reports continuous estimate of relative phase, joint moments and peak vertical ground reaction force parameters. Only joint moments were reported by at least 2 studies (16, 17). Hip sagittal moments were decreased (in extension (16) or in flexion (17)) in AS. Hip abduction and external rotation moments were also decreased in two studies (16, 17) in AS. Knee moments were shown to decrease in extension (16) and to increase in flexion (17) in AS compared to HC.

Only one study reported surface electromyography parameters during gait (Suppl. Table S2) and correlated gait parameters with clinical values (disease duration, Bath Ankylosing Spondylitis Functional Index) (17).

Table V. Description of materials and protocols used in studies with laboratory measurements of gait (n=5).

Author	Year	Materials descriptions	Protocols description
Barkham *et al*. (28)	2010	« using an electronic walkway »	Not precised
Del Din *et al*. (16)	2011	"The instrumental assessment of gait was performed using a six cameras stereophotogrammetric BTS motion capture system (60–120 Hz) synchronised with two Bertec force plates (FP4060-10) and integrated with two Imago S.n.c plantar pressure systems (0.64 cm^2 resolution, 150 Hz). A full-body marker set was used [20, 25]: 24 reflective markers were placed on the subjects at anatomical landmarks of head, trunk, thigh, shank, foot, while 24 reflective markers were used for the six clusters (each formed by four markers) of pelvis, thigh and shank	"the subject was asked to perform independent barefoot gaits by walking along a 10-m walkway, at a self-selected speed, so that the target foot would naturally land on the compound instrument made with both the force and pressure plates. At least three left and right foot strikes were acquired."
Mangone *et al*. (14)	2011	"Gait analysis was performed using the ELITE stereophotogrammetric system (BTS, Milano, Italy), with 8 infrared video cameras for the acquisition of the kinematic variables. Kinematic data were acquired and digitised with a sampling rate of 100 Hz and were filtered using a fourth-order, zero lag, low-pass Butterworth filter with a cut-off frequency of 6 Hz."… "Three-dimensional marker trajectories during walking were obtained by means of a frame-by-frame tracking system (Tracklab, BTS, Milano, Italy), and joint angular excursion, defined as a rotation of the distal segment relative to the proximal segment in our biomechanical model [20], was calculated; joint excursion data were normalized to the stride duration and reduced to 100 samples over the GC." "Two strides in each trial were considered for the analysis. A stride was considered as the time between two consecutive heel-floor contacts of the same limb and was subdivided in a stance phase (from the 1st heel contact to toe-off) and a swing phase (from toe-off to the 2nd heel contact). The stance phase was further divided into the following sub-phases: loading response (LR) (0–12% of gait cycle [GC]); mid-stance (MS) (13–30% of GC); terminal stance (TS) (31–50% of GC) and pre-swing (PSw) (51–60% of GC).	"A standing trial was performed before each session started in order to determine the off-set angles. Subjects were then instructed to walk at a self-selected speed along a level surface approximately 10 m in length. Five trials were acquired for each subject in both groups, the mean values of the kinematic variables being used for the analysis."
Zebouni *et al*. (13)	1992	"The MIE gait analysis system was used, which measures hip and knee angles by electrogoniometers attached to the hips and knees." "The readings were relayed by a transmitter attached to a belt into a data analysis system which gave a digital and graphic display of the readings at each gait cycle. A minimum of two strides was used to calculate the mean of the data. Reproducibility studies were carried out using three stride lengths. This method of gait analysis needs the minimum of training, is easy to operate, and is practical to use in a general ward. The procedure took 50–60 minutes. At the end of the procedure the patient was disconnected from the measuring apparatus and timed while walking a short measured distance to calculate the stride length. The data were obtained during level walking."	The data were obtained during level walking.
Zhang *et al*. (17)	2019	"Kinematic data were acquired utilising a 10-camera, three-dimensional motion-capture system (Vicon, Oxford, UK, 100 Hz). This approach was combined with data derived from a ground reaction force dynamometer (Kistler, Switzerland, 1000 Hz) to derive three dimensional kinetics variables. A total of 51 reflective markers were placed on the subjects at the following anatomical landmarks: head, trunk, arms, pelvis, thighs, shanks and feet. Raw kinematic and kinetic data (C3D file format) were imported to Visual 3D software (C-Motion, Inc., USA) to filter and compute the gait parameters. Marker trajectories were filtered using a 4th-order zero-lag low-pass Butterworth filter, with a cut-off frequency of 10 Hz. (…) Kinetic parameters, including ground reaction force (GRF) and joint moments, were filtered using a 4thorder, zero-lag, low-pass Butterworth filter with a cut-off frequency of 50 Hz. Active surface electrodes (Trigno Wireless EMG System, Delsys, USA, sample rate 2000 Hz) were used to record surface electromyography (sEMG) signals. The sEMG for the bilateral gluteus maximus, gluteus medius, rectus femoris, biceps femoris, tibialis anterior and gastrocnemius of each patient was measured. The electrodes were placed on the muscle bellies of each muscle. The placement of the respective surface muscle electrode was according to the predecessor's reference. Integrated electromyography and root mean square amplitude were used to evaluate muscle function while the patient was walking in circles."	The gait test was performed across a distance of 10 m, as determined by the length of the laboratory. Participants were instructed to ambulate at a comfortable pace, and gait cycles for each limb were recorded across three trials at our laboratory. Patients were allowed to rest; however, they were not given any physical assistance during the test.

Discussion

In recent years, the evaluation of gait raises interest for a wide range of healthy and pathologic populations (*e.g.* see (25, 44, 45) for recent reviews), including patients with AS (Suppl. Fig. S1). The present systematic review aimed to compile published studies that have assessed gait in patients with AS, with clinical and/or laboratory measurements, to better understand AS consequences on gait pattern and to help researchers to use the most appropriate gait evaluation in this population. The following recommendations and suggestions for future studies on gait and AS can be outlined.

Study characteristics

For most of included studies, gait assessment was not the primary objective

as only 4 had specific gait-based objective (13, 14, 16, 17), and 1 had balance-based objective (27). Most of other studies were experimental and used gait as a secondary outcome of intervention effectiveness. Half of the studies had a longitudinal follow-up from 6 weeks to 2 years (28-36) but they were all associated to an intervention. By its heterogeneous evolution, AS appears hardly predictable (46), and no biomarkers have been reproducibly shown to predict outcomes in this population (47). Thus, the assessment of gait evolution could be helpful to allow prediction of disease and functional evolutions in patients with AS. Indeed, in the older adults and pathological populations, gait has been reported as a predictor of mortality (44), cognitive decline (45, 48), or fall risks (49–51).

Clinical gait measurements
– Tests and parameters used
By far, the 6MWT was the most commonly used test in included studies (27, 29-39, 41). As a measure of the submaximal level of functional capacity, the 6MWT appears to be an important clinical test in patients with AS. As patients are asked to choose their own intensity of exercise, the 6MWT captures patients' ability to carry out daily physical activities, at submaximal levels of exertion (52). The 6MWT evaluates exercises responses of numbers of systems in the human body, including cardiac and pulmonary systems (52). The pulmonary system is altered in 40 to 80% of patients with AS (53), mainly with a restrictive pattern (39, 53, 54). Factors, leading to AS pulmonary disabilities, are impaired spinal mobility and chest expansion (55), associated to interstitial lung disease, bronchiectasis and apical fibrosis (56). Besides, AS is associated to a significant increase in the risk of myocardial infarction, caused partly by systemic inflammation and high disease activity, that are increasing cardiovascular risks (57).
The 6MWT seems useful in AS follow-up and is applicable in clinical practice. Even if this test is valid (58) and reliable (59, 60) in healthy adults, the psychometric properties of these tests have not been specifically tested in patients with AS contrary to other pathologies, such as chronic obstructive pulmonary (61) or cardiac (62) diseases. Besides, no study assessed the minimal detectable change or the minimal clinically important difference on gait outcomes for patients with AS while this measure is useful for clinicians to estimate how much change in an outcome measure is clinically important and meaningful (63).

– Test protocols
There were major variations in procedures including tests used, protocols, distance and outcomes in studies using clinical gait measurements (Table III). A variety of tests and methods were used and may be dependent of tester preference and convenience (*i.e.* walkway or material available). Besides, a detailed description of materials and protocols used was lacking in most of the studies. Exact verbal instructions used were briefly described in the 6MWT, while this factor has been shown to significantly increase the six minute walk distance in patients with chronic heart failure and lung disease (64, 65). Thus, future studies should pay attention to use standardised protocols and to precisely describe the protocols and instructions provided to the participant.

Laboratory gait measurements
– Tests and parameters used
Five studies used laboratory gait measurements allowing the understanding of AS consequences on gait pattern (13, 14, 16, 17, 28). Gait was assessed with electronic walkway (28), electrogoniometers (13) or 3D cameras (14, 16, 17). One study assessed electromyography of lower limb muscles during gait (17). No study combined clinical and laboratory measurements of gait. The instrumentation of clinical tests (*e.g.* with the use of inertial sensors) allows objective capture of gait pattern that is sometimes called "clinical gait analysis" (66). Inertial sensors allow computation of spatio-temporal and kinematic parameters, either in clinical practice during clinical tests or in an ecological environment (home, work…) (20, 67).
In the included studies, the walkways used were of short distance (*i.e.* 10 meters, Table V) while long distances allow better classification of pathological gait such as diabetes or stroke (68, 69). Although it is now recognised that locomotion involves cognitive components (70) no study included in this review assessed the effects of a dual task on gait. Indeed, cognition may be affected in AS as structural changes in the nervous system and neurotransmitters have been highlighted in patients with inflammation and chronic pain (71, 72). Patients with AS often have fatigue symptoms, that are potentially associated with brain involvement (73). Previous studies also found that cerebral grey and white matter related to attention were thinner in patients with AS and fatigue (74).The gait dual tasking paradigm allows better classification and diagnosis in populations at risk such as patients with stroke (75), or fallers (76, 77), and could allow better classification of patients with AS.
The included studies used more than 100 different gait parameters, with spatio-temporal or kinematic parameters (Table VI, V, Suppl. Tables S1 and S2), and less than 20 were common between 2, 3 or the 4 studies (Table VI).

– Test protocols
Discrepancies were found with the protocols and their description in the different studies (Table V). The devices used were clearly described in some studies (13, 14, 16), but poorly described in another (28). Instructions were not described in all studies and the number of trials performed by each participant was indicated in only 2 studies (14, 17). To allow comparisons between studies and replications of the protocols, precise information regarding walkways, instructions, number of trials and number of steps in the analysis, should be implemented.

Gait characteristics in AS
The range of gait tests used across studies and the low number of studies that have involved a healthy control group did not allow us to pool data.
Three studies with clinical gait measurements included a healthy control

Table VI. List and values of spatio-temporal gait parameters used in studies with laboratory measurements to compare AS and HC groups (n=5).

Gait parameters	Number of studies	Study	Sign.	Results (mean ± SD) or direction of difference (↑↓)
		Spatio-temporal parameters		
Cycle time in seconds	1	Zebouni (13)	NS	AS = 0.59±0.05, HC = 0.58±0.04
Gait velocity in m/second	4	Del Din *et al*. (16)	NS	AS = 1.05±0.23, HC = 1.12±0.25
		Mangone *et al*. (14)	NS	AS = 0.94±0.2, HC = 0.96±0.2
		Barkham *et al*.	NA	AS = 1.10±0.23[a]
		Zhang *et al*. (17)	***p*=0.009**	**AS = 1.14±0.21, HC = 1.25±0.09**
Stride length in m	4	Del Din *et al*. (16)	NS	AS = 0.98±0.58, HC = 1.29±0.30
		Mangone *et al*. (14)	NS	AS = 1.09±0.1, HC = 1.14±0.2
		Zebouni *et al*. (13)	***p*<0.05**	**AS = 0.58±0.11, HC = 0.72±0.13**
		Barkham *et al*.	NA	AS = 1.25±0.18[a]
Left step length/height in m/m	1	Zhang *et al*. (17)	**0.009**	**AS = 0.34±0.06, HC = 0.38±0.19**
Right step length/height (m/m)	1	Zhang *et al*. (17)	**0.002**	**AS = 0.35±0.39, HC = 0.38±0.26**
Step length difference (m)	1	Zhang *et al*. (17)	**0.024**	**AS = 0.04±0.05, HC = 0.02±0.02**
Stride length/height (m/m)	1	Zhang *et al*. (17)	**0.002**	**AS = 0.70±0.97, HC = 0.76±0.42**
Stride width/height (m/m)	1	Zhang *et al*. (17)	**<0.001**	**AS = 0.08±0.06, HC = 0.04±0.01**
Cadence in steps/minute	2	Mangone *et al*. (14)	NS	AS = 102.4±13.3, HC = 101.4±8.7
		Zebouni *et al*. (13)	NS	AS = 102.6±9[a], HC = 103.2±6.6[a]
Gait cadence (/second)	1	Zhang *et al*. (17)	NS	AS = 0.95±0.09, HC = 0.94±0.04
Stride period in seconds	2	Del Din *et al*. (16)	NS	AS = 1.06±0.11, HC = 1.06±0.05
		Zhang *et al*. (17)	NS	AS = 1.19±0.13, HC = 1.15±0.05
Stance period in seconds	1	Del Din *et al*. (16)	NS	AS = 0.73±0.08, HC = 0.70±0.04
Left single stance period (%)	1	Zhang *et al*. (17)	NS	AS = 38.29±2.62, HC = 38.61±1.55
Right single stance period (%)	1	Zhang *et al*. (17)	NS	38.12±3.95 38.49 ±1.66

[a] Stride velocity has been converted from cm/s to m/s. Stride length has been obtained by multiplying step length by 2 and converted from cm to m. Cadence has been obtained from frequency (Hz) by multiplying by 60

Sign: Significance between patients with AS and healthy controls; NS: not significant, AS: ankylosing spondylitis; m: meters; HC: healthy controls; NA: not applicable; LR: loading response; PS: pre swing; gc: whole gait cycle.

group (27, 39, 42). One study found a significant reduction of distance during the 6MWT in patients with AS (39), that was not significant in another study (27), or with other clinical tests (*i.e*. number of oversteps in figure of eight or gait speed at comfortable pace) (27, 42).

In studies using spatio-temporal parameters, stride length was significantly decreased in patients with AS compared to controls in Zebouni *et al*. (13) and Zhang *et al*. (17), while the difference was not significant in Del Din *et al*. (16), and Mangone *et al*. (14). A lower gait velocity in AS compared to HC was reported in the study of Zhang *et al*. (17), but not in other 3 studies (14, 16, 28). Cadence was not significantly altered in patients with AS (13, 14, 17). When gait was assessed with kinematic parameters, significant differences were found between AS and HC in each study (Table VI, VII, Suppl. Tables S1 and S2) (13, 14, 16). Zebouni *et al*. found decreased angle of flexion at hip joint of patients with AS compared to healthy controls (13), in line with Del Din *et al*. where significant alterations in the sagittal plane at each joint (hip, knee, ankle) were found and associated with decreased hip and knee joint extension moments (16). Zhang *et al*. also found a significant decrease of hip and ankle sagittal movement associated to reduced hip moments and an increase hip abduction and external rotation in AS compared to HC. The decrease of hip flexion was partly explained as a combination of hip flexor muscle weakness, hip pain and hamstring muscle spasm (17). In contrast to the results obtained in Del Din *et al*. study (16), Zhang *et al*. found that patients with AS increased knee flexion during stance stage, decreased knee flexion during swing stage and increased knee moments (17). The patients included in Zhang *et al*. had hip involvement identified by radiography that was not the case in other studies and may explain the differences in decreased knee range of motion and increased knee moments as a compensation of reduced hip

Table VII. List and values of joint ranges of motion (in degrees) gait parameters used in studies with laboratory measurements to compare AS and HC groups (n=4).

Gait parameters	Nb studies	Study	Sign.	Results (mean ±SD) or direction of difference (↑↓) with phase (% of gc or name)
			Trunk angle parameters	
Trunk flexion/extension	2	Del Din *et al*. (16)	**10-100%: *p*<0.05** 0-10%: NS	**AS = 5.8±1.3, HC = 3.20±0.9 ;** **10-100%: ↑ ext**
		Zhang *et al*. (17)	***p*<0.001** ***p*<0.001** ***p*<0.001**	**Init contact: AS = 5.1±14.3 (↑ fl), HC = – 9.2±4.2** **Toe-off: AS = 5.0±14.4 (↑ fl), HC = – 10.5± 5.1** **gc: AS = 5.5±0.3 (↑ fl), HC = – 9.5±0.7**
Trunk adduction/abduction (for Del Din *et al*.) or obliquity (for Zhang *et al*.)	2	Del Din *et al*. (16)	NS	AS = 10.6±3.6, HC = 10.6±3.3
		Zhang *et al*. (17)	***p*=0. 028** NS: *p*=0.702 **<0.001**	**Init contact: AS =3.0±3.0 (↑ right), HC = 1.7±1.6** Toe-off: AS = 3.6±3.1, HC = 3.4±1.9 **gc: AS =3.1±0.2 (↑ right) , HC = 2.5±0.7**
Trunk internal/external (for Del Din *et al* or rotation (for Zhang *et al*.)	2	Del Din *et al*. (16)	NS	AS =13.8±7.3, HC = 12.8±8.9
		Zhang *et al*. (17)	***p*=0.012** NS: *p*=0.446 **<0.001**	**Init contact: AS =3.1±2.2 (↓rot), HC = 4.5±2.2** Toe-off: AS = 2.9±1.8, HC = 3.3±2.0 **gc: AS = 2.8±0.2 (↓rot), HC = 3.0±1.0**
Max flexion angle	1	Zhang *et al*. (17)	***p*=0.033**	**AS = 7.5±13.7 (↑fl), HC = – 7.5±4.6**
Max extension angle	1	Zhang *et al*. (17)	***p*<0.001**	**AS = – 3.2±14.5 (↓ext), HC = 12.4±4.6**
Maximal oblique angle	1	Zhang *et al*. (17)	NS: *p*=0.091	AS = 4.6±2.9, HC = 5.5±1.5
Minimal oblique angle	1	Zhang *et al*. (17)	***p*=0.005**	**AS = 1.9±3.2 (↑ min obl), HC = 0.2±0.7**
Maximal rotation angle	1	Zhang *et al*. (17)	***p*<0.001**	**AS = 4.5±2.1 (↓ max rot), HC = 6.1±1.3**
Minimal rotation angle	1	Zhang *et al*. (17)	**<0.001**	**AS = 1.0±1.5 (↑ min rot), HC = 0.0±0.0**
			Pelvis angles parameters	
Pelvic tilt	2	Del Din *et al*. (16)	NS	AS = 4.6±1.6, HC = 2.72±2.1
		Mangone *et al*. (14)	***p*=0.01** ***p*=0.029**	**LR : AS = 2.9±3.6, HC = -1.2±4.8 ;** **AS = anterior tilt, HC = posterior tilt** **PS : AS = 1.9±4.6, HC = -1.4±4.6** **AS = anterior tilt, HC = posterior tilt**
Pelvic obliquity	1	Del Din *et al*. (16)	0-30&50-100%: NS **30-50%: *p*=0.04**	**AS = 7.6±3.9, HC = 6.7±1.5** **30-50%: ↓**
Pelvic rotation	2	Del Din *et al*. (16)	NS	AS = 11.2±9.1, HC = 7.4±3.5
		Mangone *et al*. (14)	NS	LR: AS = 1.7±5.1, HC = 1.8±3.6 PS: AS = -3.3±3.4, HC = -3.1±3.8
			Hip angle parameters	
Hip flexion/extension	3	Del Din *et al*. (16)	**0-30&73-100%: *p*<0.05** 30-73%:NS	**AS = 34.6±6.6, HC = 44.5±3.9** **0-30,73-100%: ↓ flexion**
		Mangone *et al*. (14)	***p*=0.007** ***p*=0.05**	**LR: AS = 25.6±4.6, HC = 19.6±6.6** **AS: ↑ flexion** **PS: AS = -6.2±7.4, HC = -10.8±7.4** **AS: ↓ extension**
		Zhang *et al*. (17)	***p*<0.001** ***p*=0.030** ***p*<0.001**	**Init contact: AS =18.7±10.3 (↓fl), HC = 28.8±5.4** **Toe-off: AS = 1.9±11.3 (↓fl), HC = 5.3±6.2** **gc : AS = 7.8±8.8 (↓fl), HC = 15.5±13.0**
Hip flexion	1	Zebouni *et al*. (13)	***p*=0.04** NS: p *p*=0.57	**Right: AS = 22.7±8.5, HC = 29.2±8.6; ↓ fl** Left: AS = 26.7±9.0, HC = 27.5±6.2
Hip adduction/abduction	2	Del Din *et al*. (16)	0-87%: NS **87-100%: *p*<0.05**	**AS = 15.0 ±5.3, HC = 11.9±3.9;** **87-100%: ↑ abd**
		Zhang *et al*. (17)	NS: *p*=0.532 ***p*=0.002** ***p*<0.001**	Init contact: AS =4.3±5.6, HC = 3.8±3.7 **Toe-off: AS = 9.4±5.7, HC = 6.6±4.1** **gc: AS = 4.7±2.7 (↑ abd), HC = 1.2±3.8**
Hip internal/external	2	Del Din *et al*. (16)	NS	AS = 16.0±8.7, HC = 14.0±5.2
		Zhang *et al*. (17)	NS: *p*=0.092 NS: *p*=0.927 ***p*<0.001**	Init contact: AS = 7.3±9.4, HC = 4.9±6.1 Toe-off: AS = -1.5±6.8, HC = -1.6±6.7 **gc: AS = 0.8±2.6 (↑ int), HC = -1.3±2.8**

Gait parameters	Nb studies	Study	Sign.	Results (mean ±SD) or direction of difference (↑↓) with phase (% of gc or name)
Hip range	1	Zebouni *et al*. (13)	NS: *p*=0.5 NS: *p*=0.17	Right: AS = 30.2±8.7, HC = 35.5±5.5 Left: AS = 23.1±8.9, HC = 36.4±5.2
Max hip flexion angle	1	Zhang *et al*. (17)	**p<0.001**	**AS = 21.8±11.2 (↓fl), HC = 34.5±7.2**
Max hip extension angle	1	Zhang *et al*. (17)	NS: p=0.103	AS = 6.9±10.1, HC = 4.6±5.5
Max hip abduction angle	1	Zhang *et al*. (17)	***p*=0.007**	**AS = 10.9±5.7 (↑ abd), HC = 8.6±3.7**
Max hip adduction angle	1	Zhang *et al*. (17)	***p*<0.001**	**AS = 0.0±5.8 (add), HC = 4.6±3.6**
Max hip ext rotation angle	1	Zhang *et al*. (17)	NS: p=0.090	AS = 10.2±8.2, HC = 8.3±4.4
Max hip int rotation angle	1	Zhang *et al*. (17)	***p*=0.026**	**AS = 5.2±5.1 (int), HC = 7.3±5.1**
		Knee angle parameters		
Knee flexion/extension	2	Del Din *et al*. (16)	**0-30%: *p*<0.05** 30-73%: NS **73-100%: *p*<0.05**	**AS = 65.5±7.6, HC = 64.5±7.6** **0-30% and 73-100%: ↓ flexion**
		Zhang *et al*. (17)	NS: *p*=0.827 ***p*=0.003** ***p*=0.001**	Init contact: AS = 5.7±5.5, HC = 5.5±4.2 **Toe-off: AS = 53.3±10.6 (↑ fl), HC = 46.2±15.9** **gc: AS = 28.7±15.6 (↑ fl), HC = 26.4±20.4**
Knee flexion	1	Zebouni *et al*. (13)	NS: *p*=0.06 NS: *p*=0.16	Right: AS = 41±10.4, HC = 49±9.0 Left: AS = 42±9.1, HC = 48.4 ±8.6
Knee range	1	Zebouni *et al*. (13)	NS: *p*=0.05 NS: *p*=0.06	Right: AS = 39.9±9.2, HC = 49±9.9 Left: AS = 39.7±9.0, HC = 47.3±8.9
Max knee flexion angle	1	Zhang *et al*. (17)	NS: *p*=0.821	AS = 65.9±9.7, HC = 66.4±17.4
Min knee flexion angle	1	Zhang *et al*. (17)	NS: *p*=0.821	AS = 1.8±4.9, HC = 0.8±17.4
Knee fl/ext angle	1	Zhang *et al*. (17)	***p*<0.001** ***p*<0.001**	**Stance: AS = 21.3±10.0 (↑ fl), HC = 14.5±9.3** **Swing: AS = 42.7±14.7 (↓ fl), HC = 48.7±16.7**
		Ankle angle parameters		
Ankle dorsiflexion/plantarflexion	1	Del Din *et al*. (16)	**0-2%: *p*=0.048** 2-100%: NS	**AS = 29.3±8.1, HC = 29.0±5.7** **0-2%: ↓ dorsi**
		Zhang *et al*. (17)	NS: *p*=0.464 NS: *p*=0.626 ***p*=0.003**	Init contact: AS = – 5.1±29.9, HC = – 2.09±5.0 Toe-off: AS = – 13.5 ± 33.2, HC = – 11.2 ±9.5 **gc: AS =– 0.7±5.3 (↓ plant), HC = – 1.9±5.**1
Ankle eversion/inversion	1	Del Din *et al*. (16)	NS	AS = 2.1**±**2.2, HC = 13.8**±**3.7
Ankle internal/external	1	Del Din *et al*. (16)	0-10&30-73%: NS **10-30%: *p*=0.031** **73-100%: *p*<0.05**	**AS = 13.93 ±5.4, HC = 10.0 ±1.96** **10-30, 73-100%: ↑ internal rotation**
Maximal ankle dorsi angle	1	Zhang *et al*. (17)	NS: *p*=0.075	AS = 17.6±33.6, HC = 10.5±3.3
Maximal ankle plant angle	1	Zhang *et al*. (17)	***p*=0.018**	**AS = 27.9±28.0 (↑ plant), HC = 19.6±7.7**
		Shoulder angle parameters		
Shoulder rotation	1	Mangone *et al*. (14)	NS	LR: AS = -1.0±4.0, HC = -1.4±4.6 PS: AS = 1.1±3.9, HC = 1.2±3.2

Values are round to the nearest tenth. For Mangone *et al*. study (14), pelvic anterior tilt, flexion and right side anterior (with respect of left side for rotations) give positive values. For the Zhang *et al*. study (17), flexion, abduction and external rotation of hip and knee, dorsiflexion of ankle and right obliquity of shoulder-pelvic give positive values.
Sign: significance between patients with AS and healthy controls; NS: not significant; AS: ankylosing spondylitis, m: meters; HC: healthy controls; NA: not applicable; LR: loading response; PS: pre swing; gc: whole gait cycle; init: initial; max: maximal; min: minimal; fl: flexion; ext: extension; abd: abduction; add: adduction; int: internal; ext: external; plant: plantar flexion; dorsi: dorsiflexion.

movement during gait (17). Besides, a reduction of pelvic obliquity (16), and an altered pelvis shoulder coordination in transitions from stance to swing (14), were found and may be explained as a strategy of patients to reduce sacroiliac joints torsion if they have experienced sacroiliac pain (14). Del Din et al. found that patients with AS had lower variability in terms of gait pattern compared to healthy controls, explained by spine rigidity which is the main feature of this pathology (16). Even only few studies used laboratory gait measurements, gait pattern of patients with AS

was described as more cautious (13, 16), and less stable (14, 16), with less variability (16) than healthy controls, associated to decreased lower limbs angles in the sagittal plane (13, 16, 17), and pelvic tilt (14, 16), that could lead to higher energy consumption (14). However, these results should be taken with caution as case-control studies sample sizes were small (Tables I and II), and comparisons between studies were rather difficult as protocols and parameters used were different.

Conclusion and recommendations

This review included 21 studies relevant to gait and AS. Published data evidence that no consensus exists regarding gait analysis methods for patients with AS. The methodology used to assess gait as well as the description of the testing procedures is quite variable. The 6MWT was the most commonly used clinical test in patients with AS. However, only 2 studies with clinical gait measurements had a healthy control group and, hence, did not allow us to conclude on clinical gait alterations in AS patients.

These clinical tests could benefit of (1) the addition of wearable sensors (*e.g.* smartphone-based sensors) (78), and (2) the use of the dual task paradigm to better capture gait characteristics (79, 80). Indeed, gait of patients with AS was associated with decreased stride length, pelvic movements and lower limbs angles in the sagittal plane, and increased hip abduction and external rotation in 4 studies with laboratory measurements of gait (13, 14, 16, 17) and no study assessed the effect of a dual-task. Besides, no study assessed the evolution of gait pattern in patients with AS along with the natural evolution of the pathology. We can reasonably expect that the combination of both clinical and laboratory measurements of gait in patients with AS would strengthen the capacity to monitor disease's evolution and to predict changes in patients' physical function (81). As observed in other diseases, gait could be a valuable biomarker to predict outcomes in this population.

Based on the results of this review, published studies are encouraging as they provide us the opportunity to propose guidelines to improve the design and methodology for future studies on gait and AS. Future studies should focus on the following recommendations regarding the development of gait assessments in patients with AS:

- Study design: prospective case-control studies and studies assessing psychometric properties of gait tests;
- Outcomes: clinical and laboratory gait measurements parameters;
- Tests: 6MWT, and gait assessment in a single and dual task paradigm;
- Protocols: full description of materials, walkway, environment, instructions gave to the participants, and their footwear.

We hope that these recommendations will help to better identify gait characteristics in patients with AS.

References

1. DEAN LE, JONES GT, MACDONALD AG, DOWNHAM C, STURROCK RD, MACFARLANE GJ: Global prevalence of ankylosing spondylitis. *Rheumatology* (Oxford) 2014; 53: 650-7.
2. PROFT F, PODDUBNYY D: Ankylosing spondylitis and axial spondyloarthritis: recent insights and impact of new classification criteria. *Ther Adv Musculoskelet Dis* 2018; 10: 129-39.
3. ARIZA-ARIZA R, HERNÁNDEZ-CRUZ B, NAVARRO-SARABIA F: Physical function and health-related quality of life of Spanish patients with ankylosing spondylitis. *Arthritis Rheum* 2003; 49: 483-87.
4. HEIJDE DM VAN DER, REVICKI DA, GOOCH KL *et al*.: Physical function, disease activity, and health-related quality-of-life outcomes after 3 years of adalimumab treatment in patients with ankylosing spondylitis. *Arthritis Res Ther* 2009; 11: R124.
5. KHANITTANUPHONG P, TIPCHATYOTIN S: Correlation of the gait speed with the quality of life and the quality of life classified according to speed-based community ambulation in Thai stroke survivors. *NeuroRehabilitation* 2017; 41: 135-41.
6. PEREZ-LLORET S, NEGRE-PAGES L, DAMIER P *et al*.: Prevalence, determinants, and effect on quality of life of freezing of gait in Parkinson disease. *JAMA Neurol* 2014; 71: 884-90.
7. PRICE R, CHOY NL: Investigating the relationship of the functional gait assessment to spatiotemporal parameters of gait and quality of life of individuals with stroke. *J Geriatr Phys Ther* 2018.
8. WARSCHAWSKI Y, ELBAZ A, SEGAL G *et al*.: Gait characteristics and quality of life perception of patients following tibial plateau fracture. *Arch Orthop Trauma Surg* 2015; 135: 1541-46.
9. AYDOG E, DEPEDIBI R, BAL A, EKSIOGLU E, UNLU E, CAKCI A: Dynamic postural balance in ankylosing spondylitis patients. *Rheumatology* (Oxford) 2006; 45: 445-8.
10. BOT SD, CASPERS M, VAN ROYEN BJ, TOUSSAINT HM, KINGMA I: Biomechanical analysis of posture in patients with spinal kyphosis due to ankylosing spondylitis: a pilot study. *Rheumatol Oxf* 1999; 38: 441–3.
11. KOCA TT, GÖĞEBAKAN H, KOÇYIĞIT BF, NACITARHAN V, YILDIR CZ: Foot functions in ankylosing spondylitis. *Clin Rheumatol* 2018.
12. HELLIWELL PS, SMEATHERS JE, WRIGHT V: Shock absorption by the spinal column in normals and in ankylosing spondylitis. *Proc Inst Mech Eng* 1989; 203: 187-90.
13. ZEBOUNI L, HELLIWELL PS, HOWE A, WRIGHT V: Gait analysis in ankylosing spondylitis. *Ann Rheum Dis* 1992; 51: 898-9.
14. MANGONE M, SCETTRI P, PAOLONI M, PROCACCIANTI R, SPADARO A, SANTILLI V: Pelvis-shoulder coordination during level walking in patients with ankylosing spondylitis. *Gait Posture* 2011; 34: 1-5.
15. BIANCHI L, ANGELINI D, ORANI GP, LACQUANITI F: Kinematic coordination in human gait: relation to mechanical energy cost. *J Neurophysiol* 1998; 79: 2155-70.
16. DEL DIN S, CARRARO E, SAWACHA Z *et al*.: Impaired gait in ankylosing spondylitis. *Med Biol Eng Comput* 2011; 49: 801-9.
17. ZHANG G, LI J, XIA Z, XU W: The gait deviations of ankylosing spondylitis with hip involvement. *Clin Rheumatol* 2019; 38: 1163-75.
18. MURO-DE-LA-HERRAN A, GARCIA-ZAPIRAIN B, MENDEZ-ZORRILLA A: Gait analysis methods: an overview of wearable and non-wearable systems, highlighting clinical applications. *Sensors* 2014; 14: 3362-94.
19. CIMOLIN V, GALLI M: Summary measures for clinical gait analysis: a literature review. *Gait Posture* 2014; 39: 1005-10.
20. IOSA M, PICERNO P, PAOLUCCI S, MORONE G: Wearable inertial sensors for human movement analysis. *Expert Rev Med Devices* 2016; 13: 641-59.
21. SOULARD J, VUILLERME N, VAILLANT J: Gait characteristics in patients with ankylosing spondylitis: protocol for a systematic review. *JMIR Res Protoc* 2019; 8: e12470.
22. MOHER D, LIBERATI A, TETZLAFF J, ALTMAN DG, PRISMA GROUP: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; 6: e1000097.
23. VERHOEVEN F, GUILLOT X, PRATI C *et al*.: Aerobic exercise for axial spondyloarthritis - its effects on disease activity and function as compared to standard physiotherapy: A systematic review and meta-analysis. *Int J Rheum Dis* 2018.
24. ZÃO A, CANTISTA P: The role of land and aquatic exercise in ankylosing spondylitis: a systematic review. *Rheumatol Int* 2017; 37: 1979-90.
25. BOYER KA, JOHNSON RT, BANKS JJ, JEWELL C, HAFER JF: Systematic review and meta-analysis of gait mechanics in young and older adults. *Exp Gerontol* 2017; 95: 63-70.
26. STEBBINS J, TRINLER UK, BAKER R, BRUNNER R, WREN T, THEOLOGIS T: Recommendations for reporting gait studies. *Gait Posture* 2015; 41: 339-40.

27. ÇINAR E, AKKOÇ Y, KARAPOLAT H, DURUSOY R, KESER G: Postural deformities: potential morbidities to cause balance problems in patients with ankylosing spondylitis? *Eur J Rheumatol* 2016; 3: 5-9.
28. BARKHAM N, COATES LC, KEEN H *et al*.: Double-blind placebo-controlled trial of etanercept in the prevention of work disability in ankylosing spondylitis. *Ann Rheum Dis* 2010; 69: 1926-8.
29. DURMUŞ D, ALAYLI G, UZUN O *et al*.: Effects of two exercise interventions on pulmonary functions in the patients with ankylosing spondylitis. *Jt Bone Spine Rev Rhum* 2009; 76: 150-5.
30. JENNINGS F, OLIVEIRA HA, SOUZA MC DE, CRUZ V DA G, NATOUR J: Effects of aerobic training in patients with ankylosing spondylitis. *J Rheumatol* 2015; 42: 2347-53.
31. KARAPOLAT H, EYIGOR S, ZOGHI M, AKKOC Y, KIRAZLI Y, KESER G: Are swimming or aerobic exercise better than conventional exercise in ankylosing spondylitis patients? A randomized controlled study. *Eur J Phys Rehabil Med* 2009; 45: 449-57.
32. LUBRANO E, D'ANGELO S, PARSONS WJ *et al*.: Effects of a combination treatment of an intensive rehabilitation program and etanercept in patients with ankylosing spondylitis: a pilot study. *J Rheumatol* 2006; 33: 2029-34.
33. ORTANCIL O, SARIKAYA S, SAPMAZ P, BASARAN A, OZDOLAP S: The effect(s) of a six-week home-based exercise program on the respiratory muscle and functional status in ankylosing spondylitis. *J Clin Rheumatol Pract Rep Rheum Musculoskelet Dis* 2009; 15: 68-70.
34. ROCHA-MUÑOZ AD, BRAMBILA-TAPIA AJL, ZAVALA-CERNA MG *et al*.: Influence of anti-TNF and disease modifying antirheumatic drugs therapy on pulmonary forced vital capacity associated to ankylosing spondylitis: a 2-year follow-up observational study. *J Immunol Res* 2015; 2015.
35. SO MW, HEO HM, KOO BS, KIM Y-G, LEE C-K, YOO B: Efficacy of incentive spirometer exercise on pulmonary functions of patients with ankylosing spondylitis stabilized by tumor necrosis factor inhibitor therapy. *J Rheumatol* 2012; 39: 1854-8.
36. SOUZA MC DE, JENNINGS F, MORIMOTO H, NATOUR J: Swiss ball exercises improve muscle strength and walking performance in ankylosing spondylitis: a randomized controlled trial. *Rev Bras Reumatol* 2017; 57: 45-55.
37. BASAKCI CALIK B, GUR KABUL E, TASKIN H *et al*.: The efficiency of inspiratory muscle training in patients with ankylosing spondylitis. *Rheumatol Int* 2018; 38: 1713-20.
38. BASAKCI CALIK B, PEKESEN KURTCA M, GUR KABUL E *et al*.: Investigation of the effectiveness of aerobic exercise training in individuals with ankylosing spondylitis: Randomized controlled study. *Mod Rheumatol* 2020: 1-9.
39. BRAMBILA-TAPIA AJL, ROCHA-MUÑOZ AD, GONZALEZ-LOPEZ L *et al*.: Pulmonary function in ankylosing spondylitis: association with clinical variables. *Rheumatol Int* 2013; 33: 2351-8.
40. COKSEVIM NH, DURMUS D, KURU O: Effects of global postural reeducation exercise and anti-TNF treatments on disease activity, function, fatigue, mobility, sleep quality and depression in patients with active Ankylosing spondylitis: A prospective follow-up study. *J Back Musculoskelet Rehabil* 2018; 31: 1005-12.
41. ER G, ANGIN E: Determining the relationship of kinesiophobia with respiratory functions and functional capacity in ankylosing spondylitis. *Medicine* (Baltimore) 2017; 96.
42. HALVORSEN S, VØLLESTAD NK, FONGEN C *et al*.: Physical fitness in patients with ankylosing spondylitis: comparison with population controls. *Phys Ther* 2012; 92: 298-309.
43. MENGSHOEL AM, JOKSTAD K, BJERKHOEL F: Associations between walking time, quadriceps muscle strength and cardiovascular capacity in patients with rheumatoid arthritis and ankylosing spondylitis. *Clin Rheumatol* 2004; 23: 299-305.
44. VERONESE N, STUBBS B, VOLPATO S *et al*.: Association between gait speed with mortality, cardiovascular disease and cancer: a systematic review and meta-analysis of prospective cohort studies. *J Am Med Dir Assoc* 2018; 19: 981-8.e7.
45. KIKKERT LHJ, VUILLERME N, CAMPEN JP VAN, HORTOBÁGYI T, LAMOTH CJ: Walking ability to predict future cognitive decline in old adults: A scoping review. *Ageing Res Rev* 2016; 27: 1-14.
46. LUKAS C, DOUGADOS M, COMBE B: Factors associated with a bad functional prognosis in early inflammatory back pain: results from the DESIR cohort. *RMD Open* 2016; 2.
47. REVEILLE JD: Biomarkers for diagnosis, monitoring of progression, and treatment responses in ankylosing spondylitis and axial spondyloarthritis. *Clin Rheumatol* 2015; 34: 1009-18.
48. BEAUCHET O, ANNWEILER C, CALLISAYA ML *et al*.: Poor gait performance and prediction of dementia: results from a meta-analysis. *J Am Med Dir Assoc* 2016; 17: 482-90.
49. ALLALI G, AYERS EI, HOLTZER R, VERGHESE J: The role of Postural instability/gait difficulty and Fear of falling in predicting falls in non-demented older adults. *Arch Gerontol Geriatr* 2017; 69: 15-20.
50. MARQUES NR, SPINOSO DH, CARDOSO BC, MORENO VC, KURODA MH, NAVEGA MT: Is it possible to predict falls in older adults using gait kinematics? *Clin Biomech Bristol Avon* 2018; 59: 15-8.
51. MORTAZA N, ABU OSMAN NA, MEHDIKHANI N: Are the spatio-temporal parameters of gait capable of distinguishing a faller from a non-faller elderly? *Eur J Phys Rehabil Med* 2014; 50: 677-91.
52. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002; 166: 111-7.
53. DINCER U, CAKAR E, KIRALP MZ, BOZKANAT E, KILAC H, DURSUN H: The pulmonary involvement in rheumatic diseases: pulmonary effects of ankylosing spondylitis and its impact on functionality and quality of life. *Tohoku J Exp Med* 2007; 212: 423-30.
54. SAMPAIO-BARROS PD, CERQUEIRA EMFP, REZENDE SM *et al*.: Pulmonary involvement in ankylosing spondylitis. *Clin Rheumatol* 2007; 26: 225-30.
55. BERDAL G, HALVORSEN S, HEIJDE D VAN DER, MOWE M, DAGFINRUD H: Restrictive pulmonary function is more prevalent in patients with ankylosing spondylitis than in matched population controls and is associated with impaired spinal mobility: a comparative study. *Arthritis Res Ther* 2012; 14: R19.
56. FENLON HM, CASSERLY I, SANT SM, BREATNACH E: Plain radiographs and thoracic high-resolution CT in patients with ankylosing spondylitis. *AJR Am J Roentgenol* 1997; 168: 1067-72.
57. MATHIEU S, SOUBRIER M: Cardiovascular events in ankylosing spondylitis: a 2018 meta-analysis. *Ann Rheum Dis* 2018.
58. PROESSL F, SWANSON CW, RUDROFF T, FLING BW, TRACY BL: Good agreement between smart device and inertial sensor-based gait parameters during a 6-min walk. *Gait Posture* 2018; 64: 63-7.
59. JANAUDIS-FERREIRA T, SUNDELIN G, WADELL K: Comparison of the 6-minute walk distance test performed on a non-motorised treadmill and in a corridor in healthy elderly subjects. *Physiotherapy* 2010; 96: 234-9.
60. MEYS R, SCHIEFER M, NIJS SB DE, BINDELS H, KRUIF MD DE: Measurement of dynamic hyperinflation during the 6-minute walk test using a mobile device. *Respir Care* 2019; 64: 182-8.
61. LIU Y, LI H, DING N, WANG N, WEN D: Functional status assessment of patients with COPD: a systematic review of performance-based measures and patient-reported measures. *Medicine* (Baltimore) 2016; 95: e3672.
62. BELLET RN, ADAMS L, MORRIS NR: The 6-minute walk test in outpatient cardiac rehabilitation: validity, reliability and responsiveness--a systematic review. *Physiotherapy* 2012; 98: 277-86.
63. FULK GD, HE Y: Minimal clinically important difference of the 6-minute walk test in people with stroke. *J Neurol Phys Ther JNPT* 2018; 42: 235-40.
64. GUYATT GH, PUGSLEY SO, SULLIVAN MJ *et al*.: Effect of encouragement on walking test performance. *Thorax* 1984; 39: 818-22.
65. WEIR NA, BROWN AW, SHLOBIN OA *et al*.: The influence of alternative instruction on 6-min walk test distance. *Chest* 2013; 144: 1900-5.
66. PAUL JP: Gait analysis. *Ann Rheum Dis* 1989; 48: 179-81.
67. ENGELHARD MM, DANDU SR, PATEK SD, LACH JC, GOLDMAN MD: Quantifying six-minute walk induced gait deterioration with inertial sensors in multiple sclerosis subjects. *Gait Posture* 2016; 49: 340-5.
68. NAJAFI B, KHAN T, FLEISCHER A, WROBEL J: The impact of footwear and walking distance on gait stability in diabetic patients with peripheral neuropathy. *J Am Podiatr Med Assoc* 2013; 103: 165-73.
69. CARVALHO C, SUNNERHAGEN KS, WILLÉN C: Walking speed and distance in different environments of subjects in the later stage post-stroke. *Physiother Theory Pract* 2010; 26: 519-27.
70. BAYOT M, DUJARDIN K, TARD C *et al*.:

The interaction between cognition and motor control: A theoretical framework for dual-task interference effects on posture, gait initiation, gait and turning. *Neurophysiol Clin Clin Neurophysiol* 2018; 48: 361-75.

71. SCHMIDT-WILCKE T, LEINISCH E, GÄNSSBAUER S *et al*.: Affective components and intensity of pain correlate with structural differences in gray matter in chronic back pain patients. *Pain* 2006; 125: 89-97.
72. SCHWARTZ M, KIPNIS J, RIVEST S, PRAT A: How do immune cells support and shape the brain in health, disease, and aging? *J Neurosci Off J Soc Neurosci* 2013; 33: 17587-96.
73. LI T, ZHOU L, ZHAO H *et al*.: Fatigue in ankylosing spondylitis is associated with psychological factors and brain gray matter. *Front Med* 2019; 6: 271.
74. WU Q, INMAN RD, DAVIS KD: Fatigue in ankylosing spondylitis is associated with the brain networks of sensory salience and attention. *Arthritis Rheumatol* (Hoboken NJ) 2014; 66: 295-303.
75. YANG L, LAM FM, HUANG M, HE C, PANG MY: Dual-task mobility among individuals with chronic stroke: changes in cognitive-motor interference patterns and relationship to difficulty level of mobility and cognitive tasks. *Eur J Phys Rehabil Med* 2018; 54: 526-35.
76. MONTERO-ODASSO M, MUIR SW, SPEECHLEY M: Dual-task complexity affects gait in people with mild cognitive impairment: the interplay between gait variability, dual tasking, and risk of falls. *Arch Phys Med Rehabil* 2012; 93: 293-9.
77. SPRINGER S, GILADI N, PERETZ C, YOGEV G, SIMON ES, HAUSDORFF JM: Dual-tasking effects on gait variability: the role of aging, falls, and executive function. *Mov Disord Off J Mov Disord Soc* 2006; 21: 950-7.
78. HANTON CR, KWON Y-J, AUNG T *et al*.: Mobile phone-based measures of activity, step count, and gait speed: results from a study of older ambulatory adults in a naturalistic setting. *JMIR MHealth UHealth* 2017; 5: e104.
79. MANOR B, YU W, ZHU H *et al*.: Smartphone app-based assessment of gait during normal and dual-task walking: demonstration of validity and reliability. *JMIR MHealth UHealth* 2018; 6: e36.
80. AUVINET B, TOUZARD C, MONTESTRUC F, DELAFOND A, GOEB V: Gait disorders in the elderly and dual task gait analysis: a new approach for identifying motor phenotypes. *J Neuroengineering Rehabil* 2017; 14: 7.
81. DORAN MF, BROPHY S, MACKAY K, TAYLOR G, CALIN A: Predictors of longterm outcome in ankylosing spondylitis. *J Rheumatol* 2003; 30: 316-20.