Cureus
Part of SPRINGER NATURE

Open Access Original Article

Comparative Effects of Cold and Warm Pelotherapy on Disease Activity and Function in Ankylosing Spondylitis: A Prospective Study

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Review began 10/22/2026
Review ended 10/30/2026
Published 11/02/2026

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DOI: 10.7759/cureus.119027

Abstract

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease associated with pain, functional impairment, and progressive limitation of spinal mobility. Balneotherapy and pelotherapy (PT) are frequently incorporated into multimodal rehabilitation programs; however, evidence regarding the potential influence of peloid temperature on clinical outcomes remains limited. The present study aimed to compare the short-term effects of cold and warm PT on disease activity, functional status, and spinal mobility in patients with AS.

Methods

A total of 63 patients undergoing a two-week multimodal rehabilitation program were included and allocated to cold PT (n = 26) or warm PT (n = 37). Clinical outcomes were assessed at admission and discharge using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), and Ankylosing Spondylitis Disease Activity Score based on erythrocyte sedimentation rate (ASDAS-ESR).

Results

No statistically significant differences between the cold and warm PT groups were identified at admission or discharge for any of the evaluated clinical parameters. Nevertheless, significant within-group improvements were observed in BASDAI, BASFI, and ASDAS-ESR in both treatment groups. BASDAI decreased significantly in the cold and warm PT groups (both $p < 0.001$), as did ASDAS-ESR (both $p < 0.001$), while BASFI also improved significantly ($p = 0.014$ and $p < 0.001$, respectively). In contrast, BASMI did not change significantly in either group. No treatment-related adverse events were reported.

Conclusions

These findings indicate that both cold and warm PT, when incorporated into a multimodal rehabilitation program, are associated with short-term improvements in disease activity and functional status in patients with AS. No significant between-group differences were detected; however, the study was not powered to establish equivalence between the two procedures, while the limited change in spinal mobility may reflect the lower responsiveness of structural and mobility-related parameters to short-term rehabilitation. Larger controlled studies with longer follow-up are warranted to determine whether peloid temperature independently influences therapeutic outcomes.

Categories: Therapeutics, Other, Physical Medicine & Rehabilitation
Keywords: ankylosing spondylitis, asdas-esr, balneotherapy, basdai, basfi, basmi, pelotherapy, rehabilitation, sapropelic mud

Introduction

Seronegative spondyloarthropathies (SpA) are a family of rheumatologic disorders including ankylosing spondylitis (AS), psoriatic arthritis, inflammatory bowel disease-associated arthritis or enteropathic arthritis, reactive arthritis, and undifferentiated spondyloarthropathies [1].

AS is a chronic immune-mediated inflammatory disease primarily affecting the axial skeleton and sacroiliac joints, typically characterized by seronegativity for rheumatoid factor and progressive structural changes. The disease primarily affects the sacroiliac joints and spine, but peripheral joints, including the hips and knees, as well as entheses, may also be involved. In addition to musculoskeletal manifestations, AS is

frequently associated with extra-articular involvement, such as inflammatory bowel disease, acute anterior uveitis, psoriasis, cardiovascular complications, or osteoporosis. The hallmark feature distinguishing AS from other forms of SpA is the presence of radiographic sacroiliitis. However, patients commonly experience chronic inflammatory back pain and other symptoms for several years before structural changes become radiologically detectable [2,3].

The global prevalence of AS ranges from 0.1% to 1.4%. Disease onset typically occurs in the third decade of life and demonstrates a clear male predominance, with an estimated male-to-female ratio of approximately 2:1 [2,3].

Early manifestations of AS are often subtle and nonspecific, leading to reduced healthcare-seeking behavior and considerable diagnostic challenges. Consequently, diagnosis is frequently delayed by several years. Disease activity, functional status, and structural damage are commonly assessed using validated instruments, including the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [4], Bath Ankylosing Spondylitis Functional Index (BASFI) [5], Bath Ankylosing Spondylitis Metrology Index (BASMI) [6], Bath Ankylosing Spondylitis Patient Global Score (BAS-G) [7], modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) [8], and Ankylosing Spondylitis Disease Activity Score (ASDAS) [9].

Patients with AS frequently experience impaired quality of life due to the chronic and progressive nature of the disease. Pain and stiffness represent the cardinal symptoms, while progressive limitation of spinal mobility leads to significant physical impairment. More than half of patients report persistent fatigue related to disease activity, and inflammatory pain contributes to sleep disturbances in approximately 86-91% of cases. Additionally, increased rates of work disability have been documented among individuals with AS. Collectively, these physical and psychosocial burdens substantially affect both the physical and mental dimensions of health-related quality of life [10].

Optimal management of AS requires regular assessment of disease activity. Among the most commonly used instruments are the ASDAS and BASDAI [11]. BASDAI is a patient-reported instrument assessing clinical manifestations, including fatigue, spinal pain, peripheral joint pain, enthesitis, and both the severity and duration of morning stiffness, using a visual analog scale (VAS) [12]. Due to its simplicity, rapid administration, and good reproducibility, BASDAI is widely used in routine clinical practice [11]. Previous studies have shown that BASDAI correlates strongly with cervical spine pain, whereas stiffness appears to correlate more closely with functional impairment assessed by BASFI [13].

To incorporate an objective component into disease activity assessment, ASDAS was developed. This composite index includes patient-reported measures of spinal pain (question two of BASDAI), duration of morning stiffness (question six), peripheral joint pain (question three), and patient global assessment of well-being, together with an acute-phase reactant, either C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR). ASDAS values of <1.3 indicate inactive disease, values from 1.3 to <2.1 indicate low disease activity, values from 2.1 to 3.5 indicate high disease activity, and values of >3.5 indicate very high disease activity [14].

ASDAS-CRP is the preferred measure, while ASDAS-ESR may be used when CRP is unavailable. The score has been validated for use in both daily clinical practice and clinical research settings [12].

Achievement of ASDAS remission has been shown to correlate with slower radiographic progression [15]. Moreover, accumulating evidence suggests that ASDAS is superior to BASDAI in assessing disease activity [16]. Among available disease activity indices, ASDAS demonstrates the strongest correlation with magnetic resonance imaging (MRI) changes at the level of the sacroiliac joints [16].

For the assessment of functional status, BASFI is the most widely used instrument. It is a self-administered questionnaire based on VASs and includes items evaluating the patient's ability to perform daily activities such as bending, reaching, changing position, standing, turning, and climbing stairs, as well as two items assessing the capacity to cope with everyday life. Each item is scored from 0 (no functional impairment) to 10 (severe functional limitation), and the overall score is calculated as the mean of the individual items. Due to its ease of administration, short completion time, and good reliability, BASFI represents a practical and robust tool for evaluating patients with AS [14]. It also demonstrates strong discriminatory capacity across patient groups and therapeutic interventions [12].

Spinal mobility in AS is commonly assessed using BASMI, which includes five clinical measurements: cervical rotation, tragus-to-wall distance, modified Schober test, lateral spinal flexion, and intermalleolar distance. Scores range from 0 to 10, with higher values indicating greater mobility impairment [12]. BASMI is easy to perform, time-efficient, and provides complementary information to other disease activity and functional indices [12].

The aim of this study was to compare the effects of cold and warm sapropelic mud application (cold and warm pelotherapy [PT]) on disease activity, functional status, and spinal mobility in hospitalized patients with AS, while the other components of the two-week inpatient rehabilitation program were similar

between groups.

Materials And Methods

Study design

We performed a prospective, non-randomized, comparative, single-center study in which patients were monitored throughout a two-week inpatient rehabilitation program.

A total of 75 patients were assessed for eligibility. Nine patients were not enrolled: five declined participation and did not provide written informed consent, while four could not be enrolled because the required laboratory investigations were unavailable. Of the 66 patients who provided informed consent and were enrolled, three were subsequently excluded from the final statistical analysis due to incomplete clinical or outcome assessment data. Consequently, 63 patients (42 men and 21 women), aged 30-77 years, were included in the final analysis. The patient recruitment and selection process is illustrated in Figure *1*.

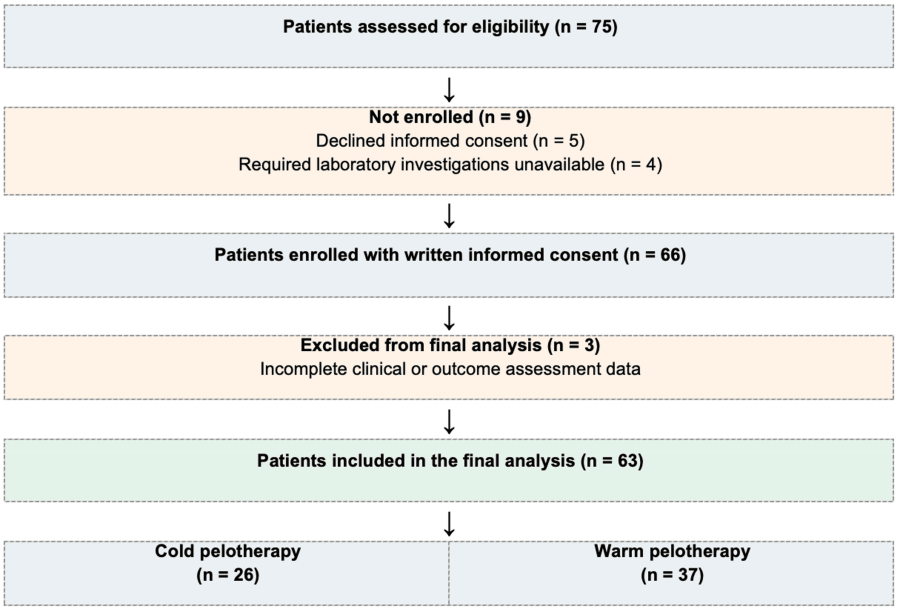


FIGURE 1: Flowchart of patient screening, enrollment, and inclusion in the final statistical analysis

The final study population comprised two groups according to the therapeutic intervention received. One group, consisting of 26 patients, underwent cold PT involving contrasting natural therapeutic factors, whereas the second group, comprising 37 patients, received warm PT, including mud packs, warm mud baths, or local mud applications, according to the medical prescription established at baseline.

Cold and warm PT are established therapeutic procedures in Romanian balneological practice, primarily distinguished by the temperature of mud application but also characterized by different treatment protocols and settings.

Cold PT is an alternating, physiologically demanding procedure performed outdoors on the shore of Lake Techirghiol, Romania, during the summer season. It consisted of the following sequence: initial sun exposure for 10-15 minutes; application of cold sapropelic mud, either generalized or limited to specific body regions; sun exposure for 30-60 minutes, during which the mud dried on the skin; immersion in the saline water of Lake Techirghiol for 10-15 minutes; a freshwater shower; and a final period of sun exposure. The mud was applied at ambient temperature, without prior heating. Warm PT was administered indoors and included general mud baths at 38°C, general or local mud packs at 38-39°C, and mud applications to restricted anatomical areas at 38-39°C. All warm PT procedures lasted 20 minutes. Cold PT was performed daily, seven days per week, for two weeks, as it is an outdoor procedure not dependent on the sanatorium's treatment schedule, whereas warm PT was administered five days per week, for two weeks, as indoor balneological procedures are not performed on weekends. The specific treatment modality was selected according to each patient's clinical condition and the medical prescription established at baseline. These two established therapeutic approaches differed in mud application temperature, application technique, treatment setting, and associated therapeutic factors.

The study aimed to investigate whether these two therapeutic approaches, characterized by different application temperatures and treatment protocols, were associated with differences in disease activity, functional status, and spinal mobility in patients with AS.

Ethical approval

The study was initiated after obtaining approval from the Ethics Committee of the Balneal and Rehabilitation Sanatorium of Techirghiol (approval no. 23a/04.04.2023). The research was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki for Medical Research Involving Human Subjects.

All participants received detailed information regarding the study objectives, procedures, and potential implications. Written informed consent was obtained from all patients prior to enrollment.

The study was performed at the department of adult rehabilitation, Balneal and Rehabilitation Sanatorium of Techirghiol, between March 2024 and February 2026.

Patients were not randomly allocated to the two treatment groups. Treatment assignment was determined primarily by the seasonal availability of the intervention. Cold PT, performed on the shore of Lake Techirghiol, is available exclusively during the summer season, whereas warm PT is administered within the sanatorium facilities using heated therapeutic mud.

Eligibility criteria

Inclusion Criteria

The inclusion criteria comprised a confirmed diagnosis of AS established by a rheumatologist and provision of written informed consent to participate in the study.

Exclusion Criteria

The exclusion criteria included the absence of a confirmed diagnosis of AS; refusal to participate or sign the informed consent form; initiation of biological therapy within the previous six months; severe mobility impairment preventing participation in the rehabilitation program; and contraindications to rehabilitation treatment.

Treatment

Participants were allocated to two treatment groups:

The cold PT group (n = 26) received therapy involving contrasting natural factors performed on the shore of Lake Techirghiol during the summer season. The intervention included heliotherapy, topical application of cold sapropelic mud, followed by immersion in Lake Techirghiol. This sequence combines thermal, chemical, and mechanical natural factors specific to the lacustrine environment.

The warm PT group (n = 37) received treatment administered within the sanatorium facilities, consisting of heated mud packs, warm mud baths, or local mud applications, according to medical prescription.

Treatment prescription was primarily determined by seasonal availability and secondarily tailored according to comorbidities and individual clinical characteristics.

In addition to PT, patients participated in a comprehensive rehabilitation program tailored to individual clinical needs. The majority of participants in both groups received similar adjunct therapies, including kinesiotherapy (approximately 45 minutes), massage therapy (approximately 15 minutes), and electrotherapy (15 minutes, depending on the prescribed modality).

Although minor variations in the rehabilitation protocol occurred according to the medical indication, the overall rehabilitation approach was comparable between the two groups, with PT representing the primary differentiating intervention.

Concomitant therapy and lifestyle control

Baseline pharmacological therapy for AS was continued throughout the study period. Patients were receiving standard treatments, including nonsteroidal anti-inflammatory drugs (NSAIDs), conventional synthetic disease-modifying antirheumatic drugs (e.g., sulfasalazine), and/or biologic agents (anti-tumor necrosis factor [anti-TNF] or anti-interleukin-17 [anti-IL-17]), according to their individualized regimens. No modifications to antirheumatic therapy were made during hospitalization.

During admission, all patients followed dietary regimens provided by the sanatorium's catering services and adapted according to comorbidities (e.g., low-sodium, diabetic, and vegetarian diets). Participants were advised to maintain their usual lifestyle habits throughout the study period.

Procedures and outcome assessment

All patients were evaluated at baseline (T0), upon admission, and at the end of the two-week hospitalization period (T1).

Disease activity was assessed using BASDAI and ASDAS-ESR. Functional status was evaluated using BASFI, while spinal mobility was assessed using BASMI. ASDAS was calculated using ESR, as CRP was available only qualitatively and was therefore unsuitable for quantitative scoring. ESR was measured using the Westergren method on blood samples collected at admission and discharge.

All clinical assessments were performed by the same physician to ensure consistency and minimize interobserver variability.

BASMI was calculated using the original three-point scoring method [6]: each of the five measurements (cervical rotation, tragus-to-wall distance, lateral lumbar flexion, modified Schober test, and intermalleolar distance) was scored as 0, 1, or 2, yielding a total score of 0-10. Measurements were performed using a standard measuring tape and a goniometer.

Sample size and statistical power

The final study sample comprised 63 patients with AS, including 26 patients in the cold PT group and 37 patients in the warm PT group.

Patients were selected from a larger population treated during the study period. Inclusion in the final analysis required complete BASDAI, BASFI, BASMI, and ASDAS-ESR assessments at both admission and discharge. Patients with incomplete assessment data were excluded.

No formal a priori sample size calculation was performed, as the sample size was determined by the availability of complete clinical data.

To evaluate the statistical sensitivity of the available sample, a sensitivity power analysis was performed using a two-sided independent-samples t-test approximation, with a significance level of 0.05 and a target statistical power of 80%.

Given the unequal group sizes (n = 26 and n = 37), the minimum detectable standardized between-group effect size was approximately Cohen's d = 0.73.

This calculation was intended to characterize the magnitude of between-group differences that could be detected under the specified assumptions. It does not establish adequate statistical power for all study outcomes, as the actual between-group analyses were performed using nonparametric tests.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics, version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive data and test statistics with corresponding p-values are presented in the tables. The normality assumption, assessed using the Shapiro-Wilk test ($p > 0.05$), was not met for all numerical variables in either the cold or warm PT groups at admission or discharge. Therefore, a nonparametric analytical approach was applied. The Mann-Whitney U test was used to examine differences in score distributions between the cold and warm PT groups, while the Wilcoxon signed-rank test was used within each group to assess changes between admission and discharge. Additionally, analysis of covariance (ANCOVA) was performed to compare clinical outcomes between the two treatment groups while adjusting for baseline differences. For each clinical assessment score (BASDAI, BASFI, BASMI, and ASDAS-ESR), the discharge value was considered the dependent variable, treatment group was included as a fixed factor, and the corresponding admission value was entered as a covariate. Adjusted between-group differences were reported with 95% confidence intervals. A p-value of <0.05 was considered to indicate a statistically significant difference.

Results

The descriptive statistics provide important insights for understanding and interpreting the study results, allowing the identification of baseline differences and potential prognostic factors between the analyzed groups.

Table *1* presents the descriptive statistics of disease activity, functional status, and spinal mobility parameters in the cold PT and warm PT groups at admission and discharge. No notable intergroup

differences were observed at baseline, although slightly higher median values were recorded in the warm PT group across most parameters, suggesting a trend toward greater disease burden.

Parameter	Group	n	Mean	SD	Range	Min	Max	Median (IQR: Q1-Q3)
BASDAI (A)	Cold PT	26	5.177	1.674	5.98	2.3	8.28	5.115 (3.775-6.405)
BASDAI (A)	Warm PT	37	5.742	2.131	9.08	0.7	9.78	6.150 (4.175-7.390)
BASDAI (D)	Cold PT	26	3.521	1.998	7.35	0.3	7.65	3.600 (2.050-4.988)
BASDAI (D)	Warm PT	37	4.047	2.314	9.08	0	9.08	3.850 (2.080-6.140)
BASFI (A)	Cold PT	26	3.981	2.273	7.3	1	8.3	3.500 (2.250-5.975)
BASFI (A)	Warm PT	37	4.916	2.412	8.8	0.7	9.5	5.200 (3.350-7.000)
BASFI (D)	Cold PT	26	3.365	2.537	8.1	0.2	8.3	2.800 (1.225-5.825)
BASFI (D)	Warm PT	37	4.178	2.784	9.5	0	9.5	4.300 (1.500-6.400)
BASMI (A)	Cold PT	26	4	1.575	6	2	8	4.000 (3.000-5.000)
BASMI (A)	Warm PT	37	4.811	2.39	9	1	10	5.000 (3.000-6.500)
BASMI (D)	Cold PT	26	4.115	1.633	6	1	7	4.000 (3.000-5.250)
BASMI (D)	Warm PT	37	4.405	2.242	9	1	10	4.000 (2.500-6.000)
ASDAS-ESR (A)	Cold PT	26	2.577	0.828	3.25	0.9	4.15	2.700 (2.135-3.200)
ASDAS-ESR (A)	Warm PT	37	2.944	0.876	4.19	0.81	5	2.880 (2.265-3.600)
ASDAS-ESR (D)	Cold PT	26	2.11	0.811	2.81	1	3.61	2.050 (1.575-2.600)
ASDAS-ESR (D)	Warm PT	37	2.409	0.86	3.71	1	4.4	2.450 (1.695-3.130)

TABLE 1: Descriptive statistics for BASDAI, BASFI, BASMI, and ASDAS-ESR scores at admission and discharge

Cold PT, cold pelotherapy; warm PT, warm pelotherapy; (A), admission; (D), discharge; n, number of patients in each group; SD, standard deviation; IQR, interquartile range (Q1-Q3); Q1, first quartile; Q3, third quartile; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; ASDAS-ESR, Ankylosing Spondylitis Disease Activity Score based on erythrocyte sedimentation rate

At discharge, both groups showed reduced median values for BASDAI, BASFI, and ASDAS, indicating improvement in disease activity and functional status within each group. In contrast, BASMI values remained relatively stable, with minimal changes observed between admission and discharge.

Variability measures (IQR) were comparable between groups, although slightly wider distributions were noted in the warm PT group, particularly for BASDAI and BASFI scores.

Tables *2*, *3* summarize the demographic and clinical characteristics of patients undergoing cold PT and warm PT. Overall, the two groups were broadly comparable, with minor variations observed between them.

Characteristics	Cold PT (n = 26)	Warm PT (n = 37)
	Within cold PT, n (%)	Within warm PT, n (%)
Sex		
Male	20 (76.92%)	22 (59.46%)
Female	6 (23.08%)	15 (40.54%)
AS treatment		
Biologic therapy	4 (15.38%)	8 (21.62%)
Sulfasalazine	7 (26.92%)	11 (29.73%)
NSAIDs	12 (46.15%)	13 (35.14%)
No treatment	3 (11.54%)	5 (13.51%)
Occupational activity		
Active	8 (30.77%)	24 (64.86%)
Sedentary	11 (42.31%)	6 (16.22%)
Mixed	7 (26.92%)	7 (18.92%)
Smoking status		
Yes	12 (46.15%)	11 (29.73%)
No	14 (53.85%)	26 (70.27%)

TABLE 2: Demographic and clinical characteristics of the cold and warm PT groups

Cold PT, cold pelotherapy; warm PT, warm pelotherapy; AS, ankylosing spondylitis; NSAIDs, nonsteroidal anti-inflammatory drugs

Parameter	Group	n	Mean	SD	Range	Min	Max	Median (IQR: Q1-Q3)
Age (years)	Cold PT	26	53.038	9.211	33	37	70	54.500 (45.750-59.500)
Age (years)	Warm PT	37	57.081	12.045	47	30	77	57.000 (51.000-66.500)
BMI (kg/m²)	Cold PT	26	29.245	6.001	19.2	20	39.2	28.700 (23.880-34.755)
BMI (kg/m²)	Warm PT	37	27.245	4.279	20.1	16.5	36.6	27.600 (25.380-29.960)

TABLE 3: Age and BMI characteristics of the cold and warm PT groups

Cold PT, cold pelotherapy; warm PT, warm pelotherapy; n, number of patients; BMI, body mass index; SD, standard deviation; Q1, first quartile; Q3, third quartile; IQR, interquartile range

Demographic characteristics were relatively comparable between the two groups. The cold PT group had a slightly lower mean age (53.04 ± 9.21 years) than the warm PT group (57.08 ± 12.04 years). Similarly, mean BMI values were slightly higher in the cold PT group (29.24 ± 6.00 kg/m^2) than in the warm PT group (27.24 ± 4.27 kg/m^2).

In terms of sex distribution, males predominated in both groups, accounting for 20 (76.92%) patients in the cold PT group and 22 (59.46%) patients in the warm PT group. Female patients accounted for six (23.08%) and 15 (40.54%) patients, respectively.

Regarding pharmacological treatment, NSAIDs were the most frequently reported therapy in both groups, used by 12 (46.15%) patients in the cold PT group and 13 (35.14%) patients in the warm PT group. Sulfasalazine was used by seven (26.92%) and 11 (29.73%) patients, respectively, while biologic therapy was reported in four (15.38%) and eight (21.62%) patients. No pharmacological treatment was reported for three

(11.54%) patients in the cold PT group and five (13.51%) patients in the warm PT group.

Regarding occupational activity, active occupations were more frequent in the warm PT group, involving 24 (64.86%) patients compared with eight (30.77%) patients in the cold PT group. Sedentary occupations were reported in 11 (42.31%) patients in the cold PT group and six (16.22%) patients in the warm PT group. Mixed occupational activity was reported in seven (26.92%) and seven (18.92%) patients, respectively.

Smoking was reported in 12 (46.15%) patients in the cold PT group and 11 (29.73%) patients in the warm PT group. Conversely, 14 (53.85%) and 26 (70.27%) patients, respectively, were nonsmokers.

The median disease duration was 15 years (IQR: 6-24 years; n = 61), and 55 patients (87.3%) were HLA-B27 positive. The most frequently documented comorbidities were arterial hypertension (n = 26; 41.3%), degenerative spinal disorders (n = 21; 33.3%), peripheral osteoarthritis (n = 13; 20.6%), and osteoporosis or osteopenia (n = 11; 17.5%), while uveitis or iridocyclitis (n = 15; 23.8%) and psoriasis (n = 6; 9.5%) were also reported.

Quantitative CRP measurements were not available; therefore, ESR was used as the inflammatory marker for calculating ASDAS-ESR. Patient Global Assessment was recorded as a component of ASDAS-ESR but was not retained as a separate variable for statistical analysis. In addition to PT, patients received individualized rehabilitation interventions, including therapeutic exercise, massage therapy, and physical therapy modalities, according to their clinical indications and associated comorbidities. Background antirheumatic medication remained unchanged throughout hospitalization.

In addition to PT, patients in both groups received individualized rehabilitation interventions, including therapeutic exercise, massage therapy, and electrotherapy, according to their clinical indications and associated comorbidities, while their background antirheumatic medication remained unchanged throughout hospitalization.

Disease activity

BASDAI and ASDAS-ESR scores decreased from admission to discharge in both groups (Table *1*; Figures *2*, *3*). Although median disease activity scores were generally higher in the warm PT group, the between-group comparisons were not statistically significant at admission or discharge (Table *4*). Within-group reductions were statistically significant for both outcomes in each group (Table *5*).

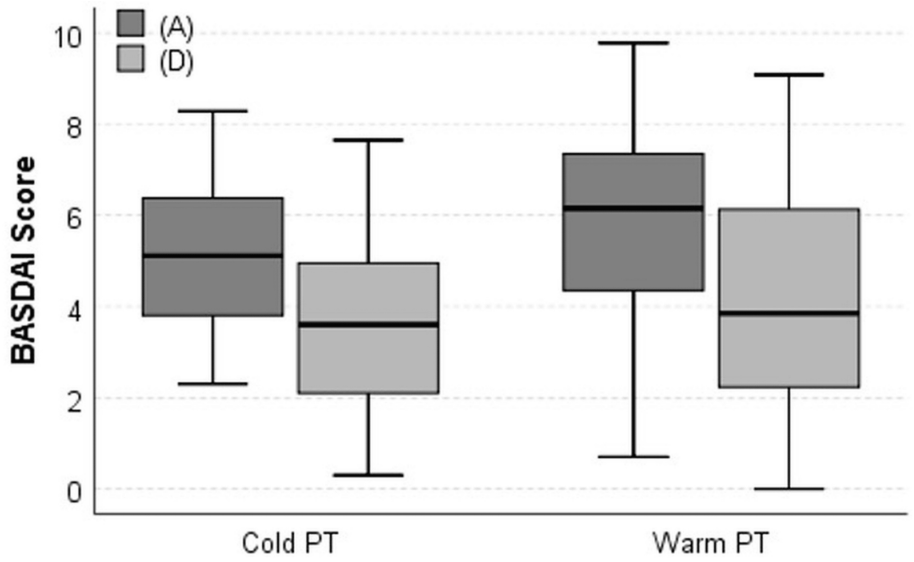


FIGURE 2: Box plot comparing BASDAI score distributions between the cold and warm PT groups at admission and discharge

(A), admission; (D), discharge; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; PT, pelotherapy

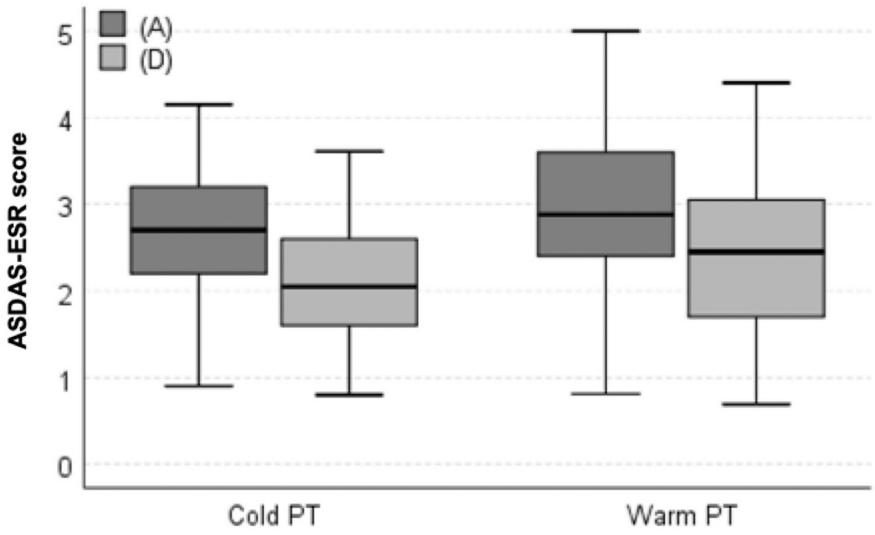


FIGURE 3: Box plot comparing ASDAS-ESR score distributions between the cold and warm PT groups at admission and discharge

(A), admission; (D), discharge; ASDAS-ESR, Ankylosing Spondylitis Disease Activity Score based on erythrocyte sedimentation rate; PT, pelotherapy

Outcome	Time point	Test statistic (U)	p-value
BASDAI	Admission	575.000	0.189
BASDAI	Discharge	548.000	0.350
BASFI	Admission	583.500	0.152
BASFI	Discharge	560.000	0.270
BASMI	Admission	570.500	0.204
BASMI	Discharge	500.000	0.788
ASDAS-ESR	Admission	577.000	0.180
ASDAS-ESR	Discharge	567.000	0.227

TABLE 4: Between-group comparisons of clinical outcomes

Cold and warm PT groups were compared using the Mann-Whitney U test. U is the test statistic; p-values are two-sided.

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; ASDAS-ESR, Ankylosing Spondylitis Disease Activity Score based on erythrocyte sedimentation rate

Outcome	Group	Test statistic (Z)	p-value
BASDAI	Cold PT	−4.086	<0.001
BASDAI	Warm PT	−4.994	<0.001
BASFI	Cold PT	−2.464	0.014
BASFI	Warm PT	−3.499	<0.001
BASMI	Cold PT	0.429	0.668
BASMI	Warm PT	−1.432	0.152
ASDAS-ESR	Cold PT	−3.675	<0.001
ASDAS-ESR	Warm PT	−4.975	<0.001

TABLE 5: Within-group changes in clinical scores from admission to discharge

Admission-to-discharge changes were analyzed using the Wilcoxon signed-rank test. Z is the standardized test statistic; p-values are two-sided.

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; ASDAS-ESR, Ankylosing Spondylitis Disease Activity Score based on erythrocyte sedimentation rate; cold PT, cold pelotherapy; warm PT, warm pelotherapy

ESR increased significantly in the Cold PT group, from a median of 10 mm/h at admission to 13 mm/h at discharge (p = 0.003). In the Warm PT group, ESR increased from 10 mm/h to 12 mm/h, without reaching statistical significance (p = 0.176). However, the between-group difference in ESR changes was not statistically significant (p = 0.334).

Functional status

BASFI scores decreased after the rehabilitation program in both groups, with statistically significant within-group changes (Tables *1*, *5*; Figure *4*). Between-group differences in BASFI were not statistically significant at either assessment (Table *4*).

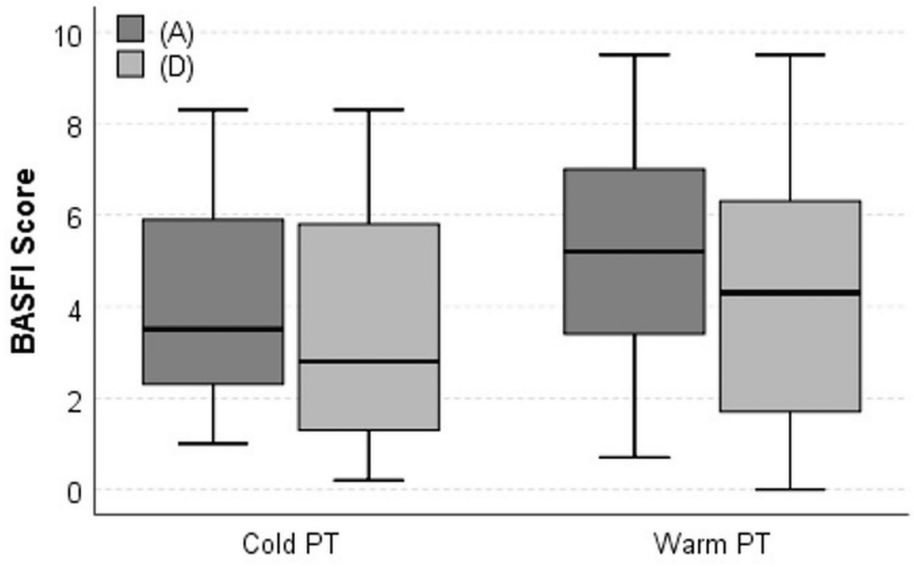


FIGURE 4: Box plot comparing BASFI score distributions between the cold and warm PT groups at admission and discharge

(A), admission; (D), discharge; BASFI, Bath Ankylosing Spondylitis Functional Index; PT, pelotherapy

Spinal mobility

BASMI scores showed little change over the two-week period, and neither group had a statistically significant within-group difference (Tables 1, 5; Figure 5). Between-group comparisons were also not statistically significant at admission or discharge (Table 4).

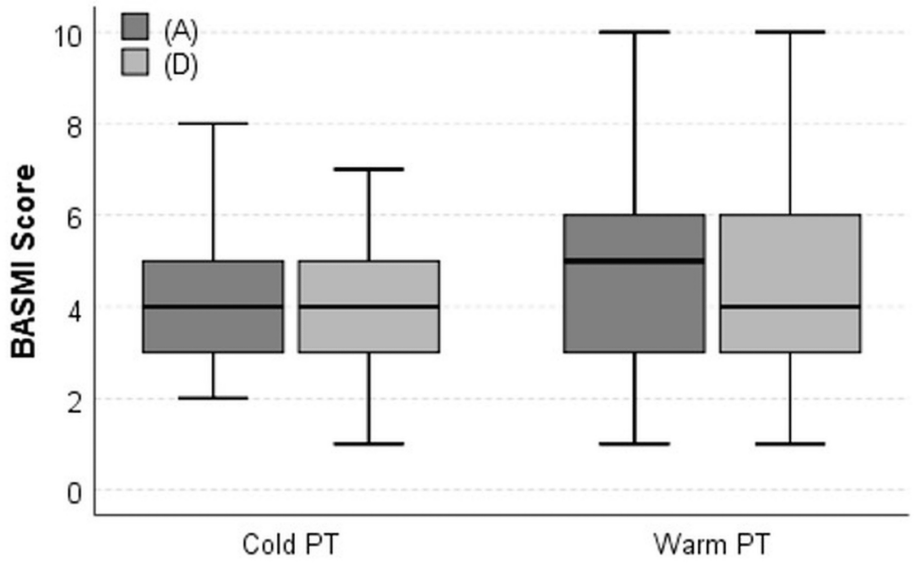


FIGURE 5: Box plot comparing BASMI score distributions between the cold and warm PT groups at admission and discharge

(A), admission; (D), discharge; BASMI, Bath Ankylosing Spondylitis Metrology Index; PT, pelotherapy

No patients withdrew from the study during the two-week hospitalization period. All participants completed the intervention and follow-up assessments. No adverse events related to the rehabilitation treatments were reported.

The analysis revealed no statistically significant intergroup differences at baseline or post-intervention for any of the evaluated parameters at baseline or post-intervention.

No statistically significant between-group differences were observed at admission or discharge for any of the evaluated parameters. Both groups showed statistically significant within-group reductions in BASDAI, BASFI, and ASDAS-ESR scores, whereas changes in BASMI were not statistically significant in either group. To account for potential differences in baseline clinical status, ANCOVA was performed for all four assessment scores. After adjustment for the corresponding admission values, no statistically significant between-group differences were identified for BASDAI, BASFI, BASMI, or ASDAS-ESR at discharge (Table 6).

Clinical outcome	Adjusted mean difference (cold PT − warm PT)	95% CI	p-value
BASDAI	−0.065	−0.848 to 0.717	0.868
BASFI	0.144	−0.480 to 0.768	0.647
BASMI	0.303	−0.384 to 0.991	0.381
ASDAS-ESR	−0.0005	−0.248 to 0.247	0.997

TABLE 6: Baseline-adjusted comparison of clinical outcomes between the cold and warm PT groups

Adjusted mean differences were estimated using discharge scores as dependent variables, treatment group as the fixed factor, and corresponding admission scores as covariates. Positive differences indicate higher adjusted discharge scores in the cold PT group.

ANCOVA, analysis of covariance; CI, confidence interval; cold PT, cold pelotherapy; warm PT, warm pelotherapy

Discussion

The present study evaluated the effects of cold and warm PT on disease activity, functional status, and spinal mobility in patients with AS, highlighting several clinically relevant findings.

No statistically significant between-group differences were detected in the evaluated clinical outcomes at baseline. Although the warm PT group had slightly higher median values for BASDAI, BASFI, BASMI, and ASDAS, these differences did not reach statistical significance. Likewise, demographic characteristics, treatment regimens, smoking status, and body mass index were broadly comparable between groups.

A multimodal rehabilitation protocol similar to that used in our study has previously been implemented at the Techirghiol Balneal and Rehabilitation Sanatorium. The intervention consisted of a 10-day inpatient rehabilitation program combining hydrokinetotherapy, hydrothermotherapy with natural therapeutic factors from Lake Techirghiol, electrotherapy, massage, and therapeutic exercise. Saline water baths (35°C) and sapropelic mud baths (38°C) were alternated daily, each lasting 20 minutes, while the remaining rehabilitation procedures were individualized according to the patients' clinical status. Although this protocol was applied in patients with sarcopenia rather than AS, it illustrates the standardized multimodal rehabilitation approach routinely used at our institution [17].

One of the most important findings of this study was the significant reduction in BASDAI observed in both treatment groups. Because BASDAI incorporates several patient-reported domains, including fatigue, spinal pain, peripheral joint symptoms, enthesitis, and morning stiffness, the observed decrease suggests a global improvement in patients' perceived disease activity rather than improvement in a single symptom [18].

ASDAS-ESR also improved significantly following rehabilitation in both groups. Unlike BASDAI, ASDAS combines patient-reported outcomes with laboratory inflammatory markers, providing a more comprehensive assessment of disease activity. Therefore, the observed reduction suggests improvement in a composite measure integrating patient-reported disease activity with an objective inflammatory marker [18]. However, the mean reductions in ASDAS-ESR (−0.47 in the cold PT group and −0.54 in the warm PT group) were below the threshold for clinically important improvement (⩾1.1 units).

In the present study, ESR increased significantly in the cold PT group (median from 10 to 13 mm/h), whereas the increase observed in the warm PT group did not reach statistical significance, and the between-group difference in ESR changes was not statistically significant. This finding should be considered a potential safety signal. However, the absolute change was small, median values remained low, and the increase was not accompanied by clinical worsening, as BASDAI, BASFI, and ASDAS-ESR decreased and no adverse events were recorded. One possible explanation relates to the concept of hormesis, a biological phenomenon in which controlled exposure to mild stressors induces adaptive physiological responses. Gálvez et al. proposed that balneotherapeutic interventions may activate neuroendocrine and immunological regulatory mechanisms through thermal and biochemical stimuli, potentially contributing to their therapeutic effects [19]. Cold PT involves exposure to multiple contrasting natural factors, including cold mud application, solar radiation, and immersion in saline lake water. Compared with warm PT, this combination may represent a more complex physiological challenge, potentially eliciting a stronger adaptive stress response. Nevertheless, the observed ESR increase cannot be directly attributed to this mechanism, and this interpretation remains hypothetical. Future studies should monitor quantitative CRP and specific biomarkers of adaptive stress responses to clarify the significance of this finding.

Pain and fatigue represent two major and frequently reported manifestations of AS and contribute substantially to the overall disease burden. Fatigue has been reported in approximately 50-70% of patients and is closely associated with disease severity, functional impairment, global well-being, and psychological health. Both pain and fatigue are incorporated into BASDAI, emphasizing their contribution to the clinical assessment of disease activity in AS. Pain represents a complex multidimensional symptom that cannot be attributed exclusively to peripheral inflammation. Evidence suggests the coexistence of inflammatory and neuropathic components, while neuroimaging studies have demonstrated functional and structural alterations in brain networks involved in pain processing. Although pain and fatigue frequently coexist in AS, they appear to represent partially distinct clinical and neurobiological phenomena [20].

Functional improvement followed a similar pattern. BASFI decreased significantly in both groups, indicating better performance of activities of daily living after rehabilitation. BASFI is a validated patient-reported instrument that assesses functional ability and the capacity to cope with everyday activities, and its scores have been shown to correlate with clinical parameters, including pain and disease activity [21]. The observed improvement may therefore be related to the combined effects of pain reduction, decreased stiffness, and regular supervised exercise during hospitalization.

In contrast, spinal mobility assessed by BASMI did not show statistically significant changes in either group. This suggests that axial mobility may be less responsive to short-term rehabilitation or may require longer treatment duration to achieve measurable improvements. The lack of significant improvement in BASMI in our cohort may partly reflect the contribution of established structural changes to spinal mobility

impairment, as progressive ankylosis in AS results in increasing spinal rigidity that is unlikely to be substantially modified by a short-term rehabilitation intervention [22].

Perhaps the most relevant finding of the present study is that no statistically significant differences were observed between cold and warm PT. Despite differences in thermal exposure and application setting, both interventions were associated with improvements in disease activity and functional outcomes. These findings raise the possibility that the therapeutic effects of sapropelic mud involve mechanisms beyond thermal stimulation alone [23].

From a clinical perspective, these findings suggest that both cold and warm PT may represent well-tolerated options in rehabilitation programs for patients with AS. The absence of adverse events and the full adherence of patients to the treatment protocol further reinforce the feasibility and tolerability of these interventions. However, a recent systematic review and meta-analysis found that the available evidence regarding the safety of balneotherapy in rheumatic diseases remains inconclusive, highlighting the need for larger, well-designed studies to establish its safety profile [24].

The present findings are consistent with previous randomized controlled trials evaluating balneotherapy in AS. Several studies have demonstrated significant reductions in BASDAI and BASFI following spa rehabilitation programs, while improvements in BASMI have generally been smaller or absent. Although treatment protocols differed regarding mineral composition, treatment duration, and rehabilitation procedures, the overall direction of the results is remarkably consistent with our observations.

Ciprian et al. investigated 30 patients with AS receiving stable TNF inhibitor therapy for at least three months [25]. The study population consisted predominantly of men (28 men and two women), with a mean age of 47.2 years and a mean disease duration of 13.5 years. Patients were randomly assigned in a 1:1 ratio to either combined spa therapy and rehabilitation or a control group continuing anti-TNF treatment alone.

The intervention consisted of 10 treatment sessions administered over a two-week period. Each session included a 15-minute mud-pack application to the entire spinal region at 40-45°C, followed by a 10-minute thermal bath at 37-38°C. Patients subsequently participated in a one-hour supervised group rehabilitation session in a thermal pool at 32-34°C, including spinal mobilization, trunk strengthening, and respiratory exercises.

A significant and sustained improvement in functional status was observed in the intervention group, with BASFI remaining significantly lower than baseline not only immediately after treatment but also at three- and six-month follow-up.

Spinal mobility, assessed by BASMI, improved significantly immediately after treatment and remained improved at three months, although the difference was no longer significant at six months.

Despite the substantial clinical benefits provided by TNF inhibitors, residual limitations in spinal mobility and functional capacity may persist, supporting the continued role of nonpharmacological rehabilitation strategies in the management of AS.

The sustained improvement in BASFI suggests that adding spa therapy and thermal rehabilitation to stable anti-TNF treatment may provide additional functional benefits. The absence of significant changes in the control group further supports the contribution of the combined rehabilitation intervention rather than pharmacological treatment alone [25].

Aydemir et al. evaluated 28 patients with AS diagnosed according to the modified New York criteria [26]. The study population was predominantly male (27 men and one woman), with a mean age of 24.4 years and a relatively short mean disease duration of 4.7 years. All participants had been receiving stable treatment with sulfasalazine and indomethacin for at least six months.

Patients underwent a three-week spa treatment program consisting of 30-minute sessions in a 37°C therapeutic pool, five days per week. The pool sessions included underwater exercises and were followed by 20 minutes of respiratory exercises and 20 minutes of postural exercises.

Although disease activity and several individual measures of spinal mobility showed numerical improvement following treatment, most changes did not reach statistical significance. Notably, BASMI was the only clinical outcome to demonstrate a statistically significant improvement, decreasing from 3.23 before treatment to 2.29 at follow-up [26].

Altan et al. conducted a randomized controlled study including 60 patients with AS diagnosed according to the modified New York criteria [27]. Patients had moderate pain and stiffness and were randomly assigned to receive either balneotherapy combined with exercise or exercise alone.

Patients in the balneotherapy group received 30-minute sessions in a therapeutic pool at 39°C once daily for three weeks, in addition to a daily 30-minute home exercise program consisting of respiratory, postural, and dorsal and lumbar extension exercises. The control group followed the same exercise program without balneotherapy.

The addition of balneotherapy to exercise resulted in greater short-term improvements in disease activity and several patient-reported outcomes compared with exercise alone. Significant between-group differences at three weeks favored combined treatment for BASDAI, pain-related and physical domains of quality of life, fatigue, sleep, and both patient and physician global assessments.

The superiority of combined balneotherapy and exercise was less evident during longer-term follow-up. At 24 weeks, significant between-group differences persisted only for patient global assessment and the modified Schober test, despite sustained within-group improvements in several clinical outcomes [27].

Yurtkuran et al. conducted a prospective randomized study including 61 patients with AS [28]. Patients were allocated to three treatment groups: balneotherapy alone (n = 21), balneotherapy combined with NSAID therapy (n = 20), or NSAID therapy alone (n = 20). Patients with active peripheral arthritis or other systemic involvement were excluded.

All three groups followed the same daily respiratory and postural exercise program throughout the six-month study period, allowing the additional effects of balneotherapy and/or NSAID therapy to be evaluated against a common exercise-based rehabilitation background.

Balneotherapy alone resulted in significant improvements in pain, morning stiffness, functional status, and several measures of spinal mobility. Importantly, most of these benefits remained evident six months after treatment, suggesting that the clinical effects of a relatively short course of balneotherapy may persist beyond the immediate treatment period.

At six-month follow-up, improvements in several symptomatic and mobility-related outcomes were greater in both balneotherapy groups than in patients treated with NSAIDs alone. Moreover, the overall response to balneotherapy alone was broadly comparable to that observed with combined balneotherapy and NSAID treatment [28].

Balneotherapy comprises a range of therapeutic interventions based on natural resources, including immersion in thermal mineral waters, mud applications, and other balneological procedures. These interventions are frequently incorporated into comprehensive spa-based rehabilitation programs and may be combined with health education, physical activity, and other rehabilitation strategies [23].

Current ASAS-EULAR recommendations emphasize that the optimal management of AS requires an individualized combination of pharmacological and nonpharmacological interventions [29]. Although the introduction of TNF inhibitors and other biologic agents has substantially improved disease outcomes, residual disease activity and functional impairment frequently persist, providing a rationale for complementary rehabilitation strategies such as balneotherapy and PT [30].

Recent evidence further supports the role of nonpharmacological interventions, with physiotherapy-based and complementary rehabilitation approaches demonstrating significant improvements in pain, functional status, and disease activity, thereby reinforcing their value as adjunctive components of comprehensive AS management [31].

Balneotherapy should be considered part of a comprehensive and individualized rehabilitation strategy. Such interventions should be integrated into a personalized care plan and delivered under appropriate medical supervision. Importantly, balneotherapy should not replace standard pharmacological treatment, but rather complement it, contributing to improved clinical outcomes and overall patient well-being [25,28].

Balneotherapy is generally considered a safe and well-tolerated intervention. Adverse events are uncommon, and most clinical studies have not reported exacerbation of inflammatory disease activity during treatment [32].

Moreover, balneotherapy has been proposed as a potentially cost-effective rehabilitation strategy capable of improving clinical symptoms and soft tissue involvement in patients with AS [28]. This concept is supported by a randomized controlled trial showing that spa therapy, when added to standard treatment, achieved favorable cost-effectiveness and cost-utility ratios compared with conventional management alone [33].

The precise mechanisms underlying the therapeutic effects of balneotherapy have not yet been fully elucidated. Current evidence suggests that its clinical benefits result from the combined action of thermal stimulation, the mineral composition of the water, and the physical and chemical properties of peloids,

rather than from a single mechanism alone. Thermal stimulation induces both local and systemic vasodilation, improving blood circulation and potentially facilitating the removal of cytokines and other inflammatory mediators from affected tissues. Heat exposure also reduces muscle tone and muscle spasm while increasing the pain threshold, contributing to symptom relief. Intense thermal stimulation, such as whole-body mud application, may activate the neuroendocrine system by promoting the release of pituitary hormones and endogenous opioid peptides. These responses are thought to contribute to the analgesic effects observed following balneotherapy. The primary objectives of these interventions are to reduce stiffness, preserve spinal mobility, prevent progression toward ankylosis, and maintain muscle strength in patients with AS [32].

Besides heat-induced vasodilation, the interaction between the biologically active constituents of peloids and the skin has been proposed to play an important role. Since the skin acts as a selectively permeable interface, the distinct changes in its electrical properties following mud application compared with water exposure suggest that peloid-skin interactions may involve biological effects beyond simple heat transfer. However, the relative contributions of these thermal and biochemical mechanisms remain to be fully elucidated [34].

The effects of Techirghiol sapropelic mud have been attributed to the combined mechanical, thermal, and chemical properties of the natural therapeutic environment. Moreover, its complex biochemical composition and the interactions among its multiple components make it difficult to attribute its biological activity to a single mechanism. Clinical benefits of Techirghiol sapropelic mud have also been reported in other musculoskeletal disorders, with reductions in pain and improvements in functional status observed following multimodal rehabilitation programs incorporating PT. In patients with knee osteoarthritis undergoing a two-week multimodal rehabilitation program including physiotherapy, hydrotherapy, and warm PT, Iliescu reported a marked reduction in pain intensity together with an improvement in general functional status [35].

Mud-bath therapy has a long history of use in the management of rheumatic diseases and musculoskeletal complaints. It generally consists of the application of therapeutic mud to the body surface, followed by immersion in mineral-rich thermal water. The therapeutic benefits of mud-bath therapy have traditionally been attributed, at least in part, to its analgesic and muscle-relaxing effects. The role of mud-bath therapy in inflammatory rheumatic diseases remains less clearly established. While thermal stimulation may be inappropriate during acute inflammatory phases, experimental evidence suggests that mud-bath therapy may exert beneficial effects in chronic articular inflammation. The biological effects of mud-bath therapy may extend beyond thermal stimulation. Experimental evidence suggests potential anti-inflammatory and antioxidant actions, including reductions in TNF alpha (TNF-α) and IL-1 levels following mud-bath applications. Mud-bath therapy may be particularly relevant in chronic inflammatory rheumatic diseases characterized by predominant axial involvement. In AS, thermal applications may reduce paravertebral muscle spasm and interrupt the pain-spasm-pain cycle, thereby contributing to an analgesic effect [30].

The influence of application temperature on the therapeutic effects of PT remains incompletely understood. Recent evidence suggests that the clinical response may not increase proportionally with increasing thermal intensity. In a randomized study comparing mud-pack applications at different temperatures, significant improvements were observed across all treatment groups. No significant differences were found between the 42°C and 45°C interventions. These findings suggest that, beyond a certain thermal threshold, further increases in temperature may not provide additional clinical benefit. Although these results were obtained in patients with knee osteoarthritis, they provide relevant evidence that temperature alone may not be the main determinant of the therapeutic response to PT [36].

Beyond their symptomatic effects on musculoskeletal disorders, thermal mineral waters and mud therapy may also influence inflammatory and immune pathways. Experimental studies suggest that hydrogen sulfide (H_2S)-containing compounds exert anti-inflammatory, antioxidant, and anticatabolic effects by reducing inflammatory mediators such as IL-6, TNF-α, prostaglandin E2 (PGE2), and nitric oxide (NO), while modulating cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), nuclear factor kappa B (NF-κB) signaling, and matrix metalloproteinase (MMP) activity. However, these effects appear to depend on H_2S concentration and exposure duration, indicating that the biological response may not be uniformly anti-inflammatory. Clinical studies further support a potential systemic immunomodulatory effect of balneotherapy. Reductions in circulating pro-inflammatory mediators, including TNF-α, IL-1 beta (IL-1β), PGE2, leukotriene B4 (LTB4), and CRP, together with increased insulin-like growth factor 1 (IGF-1), have been reported following balneotherapy or mud therapy. Changes in cellular immune responses have also been described. Importantly, these effects are not limited to osteoarthritis or rheumatoid arthritis; modifications of the pro-inflammatory cytokine network have also been reported in patients with AS following whole-body hyperthermia and speleotherapy [23].

Within this neuroendocrine-immune network, peripheral serotonin and dopamine have attracted particular interest because of their roles in both neuroendocrine regulation and immune function. Recent randomized controlled evidence further supports the existence of a systemic neuroendocrine response, demonstrating reductions in salivary cortisol accompanied by improvements in psychological distress and well-being following balneotherapy. However, post-treatment cortisol concentrations did not differ significantly

between treatment modalities, suggesting that the biological response is likely driven by the interaction of multiple therapeutic stimuli rather than by temperature alone [37,38]. Nevertheless, the available evidence remains limited and heterogeneous, and differences in treatment temperature, treatment duration, biomarker assessment, and patient characteristics may partly explain the variability observed across studies.

Limitations of the study

Several limitations should be acknowledged. First, the relatively small sample size, particularly in the cold PT group, may have limited the statistical power to detect modest between-group differences. The sensitivity analysis indicated that only between-group differences of approximately Cohen's d = 0.73 could be detected, and the 95% confidence intervals for the adjusted between-group differences were wide (e.g., up to approximately 0.85 BASDAI units). Therefore, the absence of significant differences does not establish equivalence or non-inferiority between the two procedures, and a formal non-inferiority margin should be prespecified in future trials. Second, treatment allocation was nonrandomized and largely determined by seasonal availability, introducing the possibility of selection bias and seasonal confounding. Third, the two treatment modalities differed not only in temperature but also in treatment setting and associated therapeutic components. Therefore, the independent effect of peloid temperature cannot be isolated. In addition, some heterogeneity existed within the warm PT protocol, which included mud baths, mud packs, or local mud application according to individual medical prescription. Also, the absence of a control group receiving rehabilitation without PT prevents the independent effects of mud treatment from being distinguished from those of the other components of the multimodal rehabilitation program.

The two-week intervention period allows assessment only of short-term effects and may be insufficient to detect changes in relatively stable domains such as spinal mobility. Finally, the absence of long-term follow-up prevents assessment of the persistence of the observed clinical improvements.

Conclusions

Cold and warm PT, when incorporated into a multimodal rehabilitation program, may represent valuable complementary approaches to the management of patients with AS. Both modalities were associated with short-term improvements in disease activity and functional status, although the present study did not establish the superiority of either approach.

These findings support further investigation into the potential role of different peloid application techniques and temperatures in rehabilitation outcomes. Larger randomized controlled trials with longer follow-up periods are needed to determine whether clinically meaningful differences exist between cold and warm PT and to evaluate their long-term effects.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Ethics Committee of the Balneal and Rehabilitation Sanatorium of Techirghiol issued approval No. 23a/04.04.2023. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have

declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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