HOW DO LIFE STYLE FACTORS INFLUENCE QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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1. **SUMMARY**

**Author:** Maria Angels Torrent Bagur  
**Title:** How do life style factors influence quality of life in patients with ankylosing spondylitis

**Background:** Ankylosing spondylitis is an axial spondyloarthropathy characterized predominantly by low back pain, stiffness and sacroileitis but it’s onset, presentation and prognosis is very variable from person to person. It can present as a simple back pain as well as a very invalidating pain with functional limitation. Therefore it is important to assess the quality of life perceived by the patient. The treatment that has shown the highest improvement and with better evidence are biological drugs, especially TNFα inhibitors. Several studies have shown how even a small amount of physical exercise can be beneficial for this patients. In addition, many patients report feeling much better after changing their diet although there is a lack of evidence to support this. There are many other factors that can have an effect in AS such as smoking, BMI, age at diagnosis… In this study we want to establish which is the relevance of all of them in quality of life in patients with AS.

**Aim:** To assess the quality of life of patients with AS in KK Klinikos and to evaluate which factors such as exercise, diet, smoking, BMI, age at diagnosis and use of biological treatment have a role in patient’s quality of life (QoL).

**Objectives:**
1. Study the relevance of age at diagnosis in ankylosing spondylitis presentation and perceived quality of life.
2. Study the effect and relevance of physical exercise in Quality of life of patients with AS, and if there is any difference between different modalities of exercise.
3. Study the effect and relevance of diet in Quality of life of patients with AS.
4. Study the effect and relevance of BMI in Quality of life of patients with AS.
5. Study the effect and relevance of smoking in QoL of patients with AS.
6. Study the relevance of biological treatment (presence or absence) in QoL of patients with AS.

**Methods:** Study done among AS patients in KK Klinikos using several questionnaires for above mentioned factors and evaluation of quality of life, activity of disease and limitation of function. Data analysis was performed using Microsoft Excel and SPSS program.

**Results:**
There is a weak positive correlation ($r=0.29; p=0.04$) between ASQoL scores and age at diagnosis (the oldest the patient at diagnosis, worse QoL at the moment). There is a significant difference between BASDAI, BASFI and ASQoL of patients with biological treatment, 52.08% (mean QoL 4.6) and the patients without biological treatment (mean QoL 8.95) with $p=0.0029$. The other factors studied didn’t show any statistically significant effect towards quality of life nor BASDAI or BASFI. When comparing patients who exercise vs. patients who don’t know statistically significant differences are found regarding QoL, however 72% of the patients claim that they feel better after exercising.

**Conclusions:**
Quality of life in our sample is positively affected by Biological treatment and by late diagnosis. The other factors studied: exercise, diet, BMI, smoking, didn’t show any statistically significant effect on our patient’s quality of life. The study potency was limited because of a small sample size and heterogeneous sample. The study could be repeated with a larger and more homogeneous sample to obtain more statistically significant conclusions.
2. ACKNOWLEDGEMENTS

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3. CONFLICT OF INTEREST

The author reports no conflicts of interest.

4. PERMISSION ISSUED BY THE ETHICS COMMITTEE
5. ABBREVIATIONS

AS – ankylosing spondylitis
SpA – Spondyloarthritis / spondyloarthropathy
QoL – Quality of life
ASQoL – Ankylosing spondylitis Quality of Life
BASDAI - Bath Ankylosing Spondylitis Disease Activity Index
BASFI - Bath Ankylosing Spondylitis Functional Index
NSAIDs – Non-steroidal Anti-inflammatory drugs
DMARDs – Disease modifying Anti rheumatic drugs
ESR – erythrocyte sedimentation rate
CRP – C reactive protein
WHO – World Health Organization
VAS – Visual analogue scale
GI – Gastro intestinal

6. TERMS

**Spondyloarthropathy**: It is the name for a family of inflammatory rheumatic diseases that cause arthritis. It involves the sites where ligaments and tendons attach to bones called entheses. Symptoms present in two main ways: The first is inflammation causing pain and stiffness of the spine. The second type is bone destruction causing deformities of the spine and poor function of the shoulders and hips.

**Ankylosis**: Fusion of a joint. It is an immobility and consolidation of a joint resulting from fibrous or bony union. In ankylosing spondylitis spinal vertebrae fuse together creating a rigid spine.
7. INTRODUCTION

Ankylosing spondylitis (AS) is an axial spondyloarthropathy characterized predominantly by low back pain, stiffness and sacroileitis but it’s onset, presentation and prognosis is very variable from person to person.

The cause is not known or clearly determined although the most common theory is the relation between genetic and environmental factors. Most of patients with AS are carriers of HLA B27, (there’s approx. a 5% of patients without HLAB27) and there is a belief that if they present an infection with GI bacteria having antigens with a very similar structure, it leads to a cross reaction, thus the body attacks self-molecules.

The main symptom is a dull diffuse pain in low back and buttocks, which can increase gradually over weeks or months. Generally it is a pain that increases with rest so it is worst in the morning and during the night, and can improve with some exercise. This pain can spread through the spine until the neck and to the ribs. There might also be affection of peripheral joints such as shoulders and hip (mostly), and knees and heels.

In advanced cases, the inflammation of vertebrae can cause ankylosis of the spine (bamboo spine) leaving it in an immobile position.

It’s also important to mention the presence of extra articular manifestations such as ocular (uveitis), cardiovascular, neurological, gastrointestinal, renal and respiratory, although they won’t be relevant subject of study for us.

On account of this, the presentation and prognosis of this disease can be determined by the age of patient at time of diagnosis (earlier onset, worse prognosis), by presence or absence of extraspinal and/or extraarticular manifestations, by the treatment given, and so on. It’s interesting how the same disease can express from a simple and mild back pain to a very strong pain and movement restriction which can even lead to disability.

Because of this variance, a very important part of the disease monitoring is not objective but the subjective concept of quality of life, the effect of the disease on the individual’s perception of his own state, which can be affected by a variety of factors.

Nowadays there are many reports from AS patients, claiming that some physical exercise or diet changes have benefits on their disease, so we are interested in examining if it significantly relates with disease activity and if it has an effect in their QoL. In addition to impact of diet and exercise in QoL, we suspect a negative influence by smoking exposure and high BMI. So in this study we aim to identify and investigate these factors together with treatment and their relation to quality of life of the patient.
8. **AIM AND OBJECTIVES**

**Aim:**

This study is aimed to assess the quality of life of patients with AS in KK Klinikos and to evaluate which factors such as exercise, diet, smoking, BMI, age at diagnosis and use of biological treatment have a role in patient’s quality of life (QoL).

**Objectives:**

1. Study the relevance of age at diagnosis in ankylosing spondylitis presentation and perceived quality of life.
2. Study the effect and relevance of physical exercise in Quality of life of patients with AS, and if there is any difference between different modalities of exercise.
3. Study the effect and relevance of diet in Quality of life of patients with AS.
4. Study the effect and relevance of BMI in Quality of life of patients with AS.
5. Study the effect and relevance of smoking in QoL of patients with AS.
6. Study the relevance of biological treatment (presence or absence) in QoL of patients with AS.
9. LITERATURE REVIEW

9.1. OVERVIEW OF ANKYLOSING SPONDYLITIS

AS commonly starts in the second or third decade of life and affects mostly axial joints. However, the clinical picture of early (juvenile onset) AS differs from that of adult onset by affecting peripheral joints more frequently. Men are affected approximately 2-3 times more frequently than women. The prevalence of AS is very variable depending on geography but in overall there’s a close correlation between the prevalence of HLAB27 and the prevalence of AS in a given population.

Sacroileitis is the earliest manifestation of AS being recognized. However, peripheral joints and extraarticular tissues can also be affected. In AS, subcondral tissues become granulomatous and infiltrated with lymphocytes, plasma cells, mast cells, macrophages and chondrocytes, so the affected joints show irregular erosion and sclerosis. Tissue is gradually replaced by fibrocartilage and becomes ossified. When this happens in the spine, the annular fibers are replaced by bone and vertebra become fused, forming a “bamboo spine”. Enthesitis, the inflammation of insertions of tendons and ligaments into bone is also a characteristic finding of AS.

Some authors believe that the interaction between HLA-B27 and T cell response is the key to pathogenesis of AS. As it happens with Reactive arthritis, bacterial infections are suggested to be triggering events in the pathogenesis of AS.

The close relationship between AS and inflammation of intestinal mucosa (IBD) suggest that normal intestinal bacteria and, thus, immune reaction directed against them may participate in the pathogenesis of AS.¹

A possible relation between AS and Klebsiella has been studied: The majority of AS patients possess HLA-B27 molecule, but also, during active phases of disease they have elevated levels of serum IgA, suggesting that a microbe from the bowel flora is acting across the gut mucosa. Biochemical studies revealed that Klebsiella has 2 antigen molecules with sequences resembling HLAB27. According to that, it has been suggested that Klebsiella found in the bowel flora might be the trigger factor in this disease and therefore reduction in the size of bowel flora could be of benefit in treatment of AS patients.³ However, cause is still being investigated and new studies have questioned this theory claiming that it should be reassessed.² A second theory is the “unfolded protein response” hypothesis and a third hypothesis is the “HLAB27 homodimer model”. These theories are also being questioned and need further investigation.²
9.2. TREATMENT

Goals of treatment:
1. Alleviation of pain
2. Recovery of physical functions related to daily life and occupational activities
3. Delay of structural damage responsible for physical impairments.

Optimal treatment of AS requires combination of non-pharmacological and pharmacological treatment\(^4\)

1. Non-pharmacological: Physical therapy and education (It will be discussed below in section “5. Exercise”)
2. Pharmacological treatment:

   **NSAIDS:** 1st line drugs for AS. Response and potency varies among patients. The drug should be administered continuously, not only on demand.\(^4\) If BASDAI is higher than 4 even after NSAIDs are used, other agents should be considered.\(^5\)

   **Analgesics:** Acetaminophen and opioid agents indicated for patients who complain of pain when being treated with NSAIDs or TNF\(_\alpha\) inhibitors but they are insufficient, contraindicated or not tolerated.\(^4,\,5\) In guidelines, recommendation of opioids is only by expert opinion with no evidence to reinforce it. Patients taking opioids are more likely to be older, have longer disease duration, greater functional impairment and less likely to be exercising regularly.\(^6\)

   **Disease modifying antirheumatic drugs (DMARDs):** Sulfasalazine and Methotrexate are not recommended (no evidence of efficacy) for axial diseases but they could be of worth in case of peripheral affection.\(^5\)

   **Biological therapies:**

   - **TNF\(_\alpha\) inhibitors** are effective in all disease stages so early use of TNF\(_\alpha\) inhibitors is widely recommended.\(^5\) It should be given to patients with persistent high disease activity (BASDAI>4) even if treated with NSAIDS, and when failure of >2 NSAIDS.\(^7\)
   
   Main agents: Infliximab, Etanercept, Adalimumab, Golimumab, Certolizumab.

   Main principles for use of TNF\(_\alpha\) inhibitors are:
   - If one agent is not effective, it can be replaced with other agents.
   - Response to biological agent should be evaluated at least 12 weeks after administration
   - Latent tuberculosis should be examined before administration, because the incidence could be increased due to TNF\(_\alpha\) inhibitors.\(^5\)
Other biological agents (non TNFα inhibitors): Interleukin inhibitors: Secukinumab (neutralizes IL-17A) is a major advance in treatment of AS. Janus kinase inhibitors: Tofacitinib, interferes in the inflammatory cascade of IL-17, IL-21 and IL-23.\textsuperscript{[2]}

3. Surgical treatment

According ASAS recommendations total hip arthroplasty should be considered in patients with refractory pain or disability and radiographic evidence of structural damage.\textsuperscript{[4]}

9.3. DIET

Regardless of development of biological therapy, many patients also look for complementary treatments such as dietary therapy. Diet plays an important role in the aetiology of diseases such as rheumatoid arthritis, cardiovascular diseases or cancer. The dietary patterns typical of industrialized countries (red meats, refined grain, fries, sweets, high fat, lower fruit and vegetables…) have been associated with an increased risk of Rheumatoid arthritis. Although some investigators have considered the evidence linking AS with diet, there have been no systematic assessments of the evidence.

Macfarlane et al.\textsuperscript{[9]} performed a systematic review in which they had few objectives and results, the most relevant were:

a) Observation of diet and severity of AS: The evidence was limited. In a study it was shown that 78% of AS patients believed that diet influenced the symptoms of their disease and one third of patients reported worsening of symptoms after intake of certain foods (most frequently: meats, coffee, sweets and sugar, citrus and apples).

Three studies reported data on relationship between consumption of dairy products and AS, but no association was found.

Another study reported that 82,7% of AS patients used dietary complementary and alternative medicine (CAM). The most common were fish oil, green tea and vitamin supplements. However, there were no differences between the dietary CAM users and non-users in most of the disease indices (ESR, CRP, BASDAI, BASFI, ASQoL, BASG).

b) Dietary interventions and AS symptoms: When diary products were eliminated in 25 patients, after 6 weeks 52% of the patients reported good improvement, out of which 62% were able to discontinue their NSAID therapy. After follow up of the patients was done at 3, 6 and 9 months, they were satisfied and had continued this dietary regime.\textsuperscript{[9]}

Sundstrom et al.\textsuperscript{[10]} compared a diet of high versus low-dose fish oil. There was a significant decrease in BASDAI scores in the high dose group and an increase in ESR in the low dose group, suggesting it could be beneficial, but without other significant differences.
In general the existing evidence about diet is pointed to a relationship between diet and AS, mostly in the subjective feeling of patients, but also in some disease markers. However it generally does not conclude with statistically significant results.

9.3.1 Theory of low starch diet:

As mentioned above, one of the suggested pathogenic theories suggested is that *Klebsiella* could be considered a triggering factor involved in the initiation and development of AS and it has also been studied that low starch diet leads to lower AS disease activity and lower presence of *Klebsiella pneumonia*.

Studies by Ebringer et al.\(^\text{[11]}\) suggest that subjects on low carbohydrate diets have lower levels of *Klebsiella* microorganisms in their stools. They compared faecal cultures of patients with a high carbohydrate diet, versus a group with a low carbohydrate diet; the mean of *Klebsiella* microorganisms was 30,000 per gram of faeces in the first group versus 700 per gram of faeces in the second group. In addition, the most probable source of the carbohydrate substrate for *Klebsiella* is dietary starch, because most normal people fail to absorb starch as it forms insoluble complexes with protein components while dietary mono- and disaccharides can be readily absorbed in the upper GI and consequently they are not available as substrate for *Klebsiella* in the colon. According to this, reducing starch in diet could be a way to decrease *Klebsiella* in colon and, assuming it to be a triggering factor of AS, decrease also the manifestations of ankylosing spondylitis.\(^\text{[11]}\)

Other four different studies regarding the relationship between starch and AS severity obtained different results where in general no association of daily starch intake with SF36, CRP or ESR, while on the other hand, there was an association with BASDAI, BASFI and BASG.\(^\text{[9]}\)

When it comes to other diet options such as alkaline diet, gluten free diet and their possible relation with QoL, BASDAI and other disease markers, no evidence has been found. No studies have been performed yet in this direction. Even though there is a suspicion that directs to the positive relation between diet characteristics and better outcomes of disease, there is not enough scientific evidence that a reduction in starch, lactose and other diet changes such as gluten-free products, alkaline diet or consumption of fish oils diminish AS symptoms; because there is a very low number of studies about this field and most of them are just observational. In the opposite site of this lack of scientific evidence, there is numerous amount of patients that claim to feel better, that their symptoms diminished and even disappeared after changing their diet, and because of that many AS associations and websites recommend these diet changes. Probably there should be further researches focusing on this area.
9.4. **SMOKING**

Cigarette smoking has been identified as one of the major environmental risk factors of rheumatic diseases such as Rheumatoid arthritis and Systemic lupus erythematosus. Fewer studies have been performed in ankylosing spondylitis, but smoking has been associated with increased disease activity and radiographic severity in some studies. \[12\]

It has not been established unquestionably that smoking is causally associated with poorer disease outcomes rather than being a marker for patients with generally poorer lifestyles. Several investigations examined the relationship between smoking and axial SpA and found that smokers have worse outcomes, more severe disease, and poorer quality of life. These associations have also been found in early disease, in which smokers experienced earlier onset of inflammatory back pain, higher disease activity, poorer function and evidence of increased axial inflammation and structural damage on imaging. \[13\]

There is weak evidence on smoking effect on pain level and overall assessment of health, and only one study has reported association between smoking and morning stiffness, suggesting that smokers have worse stiffness than non-smokers. In the case of disease activity (BASDAI) it has been established that current smokers have higher scores than non-smokers and that smoking is an independent variable for higher BASDAI score. In general, all the evidence points that smoker patients have poorer physical mobility than non-smokers, however there is no correlation with smoking quantity (cumulative exposure). \[12\]

In respect to Quality of Life most studies found that smoking and pack-years of smoking were positively and independently associated with the higher ASQoL scores. On the other hand there was no significant difference between smokers and non-smokers regarding SF36 subscale score.

In their study, Jones et al.\[13\] compared ever smokers versus never smokers reaching conclusions that ever smokers had poorer disease activity, function and metrology. There was no difference in the likelihood of having a history of extraspinal manifestations, however in ever smokers there was a 1.5 point increase in ASQoL score and thus a poorer specific quality of life.

Moreover, this study also provides a comparison of current versus ex-smokers with significant differences: ex-smokers were more likely to have a lower disease activity score than current smokers, and smoking cessation was associated with significant improvements in disease specific quality of life and some general measures of QoL. Overall, ex smokers experience less severe disease (including disease activity, function and quality of life) compared to current smokers. \[13\]

On the whole, all the evidence is directed to conclude that, not surprisingly, smoker AS patients have a worse quality of life, a worse disease activity and a worse disease course and thus have a poorer disease outcome. However this worsening in smokers can also improve after cessation of smoking.
9.5. **EXERCISE**

Exercise and physiotherapy have a positive effect in various physical and psychological domains in AS patients. Several studies suggest that even small amount of physical activity leads to improved health outcomes among patients when comparing with sedentary control groups. Exercise is shown in all studies as the most studied physiotherapy modality, with very few studies examining other physiotherapy modalities.

The main goals of exercise in AS patients are preventing and delay stiffness, pain control and improve physical function, usually focusing on aerobic exercise, kinesiotherapy, strengthening, and stretching.\(^{[14, 15, 16]}\)

It has been proved that applying a structured theoretical and exercise education program in patients with AS provides benefits in general condition and improves scores of BASFI, BASDAI and ASQoL.\(^{[17]}\)

When comparing supervised group exercise program versus a home exercise program: both significantly improve BASFI and pain score however the improvement is not significant in QoL and BASDAI and there were no differences between groups.\(^{[18]}\) Therefore we can conclude that even a minimal amount of home exercise can have a positive result.

9.5.1. **Aerobic vs. stretching exercise**

In order to assess the effectiveness of aerobic training in AS patients the following study was performed.\(^{[19]}\) The intervention group performed 3 sessions a week of 80 min consisting of aerobic exercise (walking) followed by stretching for 30 min. The control group was performing only 3 sessions a week of stretching exercises during 30 min.

By the end of the study there was an improvement in BASFI, HAS-Q and BASMI compared to the beginning, but without significant difference between groups. In SF36, only the functional capacity improved in both groups. There was no change of CRP or ESR over time.

Overall, the study showed an improvement in both groups. In conclusion there was a positive effect of physical activity in functional capacity, mobility and disease activity but without a significant difference between aerobic and stretching exercises.\(^{[19]}\)
9.5.2. Different modalities of exercise: Water exercise

Aquatic (water-based) exercise has a beneficial effect in various musculoskeletal conditions and some studies reflect the beneficial effect on AS patients too.

While comparing the additive effect of water exercise to patients under standard drug therapy:

Fernández et al. \[20\] compared an intervention group, which underwent aquatic fitness plus relaxation program with a control group (only under drugs), and observed that there was a significant improvement in pain, stiffness, disease activity, functional capacity and quality of life in the group performing hydrokinesiotherapy, stretching exercises and relaxation techniques, comparing to the control group. Aydemir et al. also found a statistically significant improvement in pain and BASMI in the intervention group (water), however the improvement was not significant in BASDAI. \[21\]

While comparing water exercise with land exercises two studies are relevant:

In Dundar et al.’s study \[22\] patients with AS were assigned to receive either home-based exercise or aquatic exercise treatment protocol. The intervention resulted in improvement in both groups concerning pain, BASFI, BASMI, BASDAI and QoL; in addition to that, the water exercises lead to higher improvement in pain score and quality of life compared to home-based exercises.

Karapolat et al. compared 3 groups: G1 – conventional exercise + swimming, G2 – conventional exercise + walking and G3 – conventional exercise only. In the 3 groups there was an improvement on QoL, pain score and mobility, but aerobic exercises (swimming and walking) further increased functional capacities of patients. \[21\]

In conclusion, most studies showed a significant improvement on pain, disease activity, mobility, functionality, cardiorespiratory function, depression and QoL. \[21\]

By comparing supervised group exercise program (SGEP) and non supervised home exercise program, it showed that SGEP is more effective than home exercise, which can also be effective if performed more often, because it has a limited effect due to poor compliance or incorrect understanding.

Combined exercises (aerobic, stretching, range of motion) are more beneficial than range of motion (ROM) exercises alone. The review results also suggest that water exercise has an additive beneficial effect on pain, mobility, functionality and QoL, when compared with land exercise, due to the special properties of water (enabling environment of movement and pain relief). On the whole, land and water exercise are both proven to be beneficial for patients with AS and should always be an important part of the treatment prescribed. \[21\]
However, while it is clear that exercise in different modalities is relevant in AS treatment there is no information to guide an exercise planning, it is not clear which exercise program which duration, frequency or intensity should be better for these patients, because of that J.R Millner et al. performed a systematic review in order to formulate 10 final recommendations for practice of therapeutic exercise, obtaining the following: Assessment (individual exercise prescription), monitoring, safety, disease management, AS specific exercise (emphasis on spinal mobility), physical activity (interrupt sedentary activities), dosage (exercise frequency, intensity, duration), adherence and exercise setting. \[23\] See annex 1 – Image summarizing these recommendations and exercise framework. Further explanation of recommendations.\[23\]

9.6. **BMI**

Obesity in general population is associated with an increase in overall mortality, accelerated cardiovascular risk, impaired functional capacity and increase rate of malignancy, diabetes and depression.

In rheumatoid arthritis increased adiposity is protective against radiological progression, however in AS the prevalence of obesity and its relationship to disease-specific features needs further investigation. The role of adipose tissue in AS has not been widely investigated, however indirect results suggest that there is a connection between excess adipose tissue and inflammation in AS.\[24\] Preobesity (BMI 27.1 to 29.9) in AS patients lead to an increase in disease activity, deterioration of functional condition and significant decline in quality of life compared with healthy individuals.\[24\]

When compared disease characteristics, perceptions regarding exercise, and functional limitations in overweight patients to those with a normal BMI, significant differences between groups were established considering QoL, perceived barriers to exercise and BASFI and BASDAI. No differences were established between groups in their pain scores, stiffness and fatigue severity indexes. The overweight and obese patients had less positive perception about benefits of exercise and greater awareness of barriers. They also had a lower sense of overall wellbeing and increased BASDAI and functional limitation; concluding that increased body mass index (BMI) in patients with AS is associated with a greater burden of symptoms and poor perception of the benefits of exercise.\[25\]

Another study concluded that BMI has an influence on CRP levels, only in female patients, and this influence was of limited clinical relevance. But contrarily to other studies they found that BMI did not have a significant influence on any patient reported outcome or ASDAS.\[26\]

Being female and/or overweight or obese is associated with a lower rate of TNFα inhibitor treatment success. This is explained because adipose tissue produces adipokines, which influence the immunological process of disease.
Ibáñez Vodnizza et al. [27] performed a study in which a higher body fat content (measured not by BMI, but by fat percentage, fat mass and FMI (fat mass index)) was associated with less chance to achieve a clinically important response to treatment with a TNFα inhibitor, according to ASDAS-CRP and BASDAI changes. In the other hand, they did not find that high BMI was related with a worse response to treatment, so BMI (which does not distinguish between muscle and fat mass) is not capable to identify the effect of body composition on disease.

9.7. GENERAL MEASURES OF QUALITY OF LIFE AND AS MEASURES.

The WHO [28] defines Quality of Life as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment.

WHO’s Quality of Life domains include:

- Physical health (energy and fatigue, pain and discomfort, sleep and rest)
- Psychological (appearance, negative and positive feelings, self esteem, thinking, memory)
- Level of independence (mobility, activities of daily living, dependence on medical substances, work capacity)
- Social relationships (personal relations, social support, sexual activity)
- Environment (financial resources, freedom, home environment, health accessibility and quality, physical environment (pollution, noise, traffic)…)
- Spirituality (religion, personal beliefs)

9.7.1. Quality of life in Ankylosing spondylitis

Quality of life domains above mentioned that have a higher relevance in spondyloarthritis are: Negative feelings (due to existence of an invalidating and painful disease), activity of daily living (the reduced mobility and functionality hampers the daily activities of the patient), energy and fatigue, pain and discomfort, personal relationships, work and capacity, and mobility.

In spinal SpA is also more relevant (than in peripheral arthritis) the general level of independence and the burden of treatment which affects financial resources because there are less options of treatment and they are much more expensive (biological drugs). [29]

Within ankylosing spondylitis patients, physical functioning and disease activity are associated with both physical and mental aspects of QoL: the patients most frequently report high
levels of pain, fatigue, sleep disturbances, depression and anxiety and all of them lead to a worsening of daily life and thus of quality of life.

In general, patients with AS show poorer QoL than the general population. Because of the particularities of determinants for QoL in AS, a more specific questionnaire for QoL is developed for these patients, the ASQoL questionnaire, which assesses the mobility, the ability to perform daily tasks, and the emotional domains of these patients.

Some non-modifiable risk factors that can be related with poor QoL in patients with AS are: Female sex, increasing age, deprivation areas, and lower education. All of them can be determinants for poorer QoL in general population, but they are significant in patients with AS.

Meanwhile, potentially modifiable characteristics in AS patients include the following facts:
- Ex/current smokers have a higher risk of poor QoL than never smokers (as in general population).
- High disease activity (BASDAI >4), poor physical function (BASFI >4) and poor spinal mobility have also higher risk of poor QoL. But they can be corrected by the appropriate treatment and thus QoL can be improved.

The most important elements that can present a patient with AS and that have been independently associated with a substantially higher risk of poor QoL are the following: 
- Fatigue: it is a major component of high disease activity, which affects to about a 60% of the patients. Fatigue is associated with global well-being feeling, higher disease activity, lower functional ability, and mental health status. Because of that fatigue negatively influences different aspects of quality of life. 
- Chronic widespread pain: It is a very invalidating factor because pain increases the existing structural limitation, hampering daily life, but it also has a very important psychological part, as it its very likely to let patients down and even lead to depression.
- Physical function limitations: The combination of fatigue, chronic pain, inflammation, stiffness, and structural damage of joints leads to a decrease in physical functions that impede the patient to perform daily life activities normally.
- Spinal mobility: in early disease is reduced because of inflammation, in more advanced disease it is reduced because of structural damage, but in both cases it limits spinal movements and can cause worsening of patient’s autonomy.

All of them condition the daily life of the patient in several manners: reduced the capability of perform daily and routine activities by reducing the range of movement necessary for them, causing unbearable pain or by many other ways.
Moreover, work disability is another important determinant for quality of life. Many patients with AS are unable to work or have a decreased productivity because of functional impairment, fatigue, chronic pain and psychological factors such as depression. In addition, this unemployment leads to economic burden and emotional affection, which further decreases the quality of life.\[32,34\]

9.7.2. **THE MEASURES OF ANKYOSING SPONDYLITIS**\[31\]

9.7.2.1. **ASQOL (Ankylosing Spondylitis Quality of Life)**

Used to assess the impact of ankylosing spondylitis on the quality of life of patient, with emphasis on ability of the person to fulfill their needs. It contains 18 items about impact of pain on sleep, mood, motivation, ability to cope, and activities of daily living, independence and social life. It has yes (1) and No (0) answers with a range of 0-18 being the higher scores worse quality of life.

9.7.2.2. **BASDAI (Bath ankylosing spondylitis disease activity index)**

Used to define disease activity status in patients with AS. It consists of 6 VAS for measuring severity of the 5 major symptoms: fatigue, spinal pain, peripheral pain/swelling, localized tenderness and morning stiffness. Score 0 is no symptoms and 10 is very severe symptoms. At the end a mean score is measured from the 6 scores. Higher scores show greater disease activity.

9.7.2.3. **BASFI (Bath ankylosing spondylitis functional index)**

It defines and monitor functional ability by asking patient’s perception of their ability and how well they are able to function in everyday life. It gives 10 items with 0-10 VAS scales being 0=easy and 10= impossible. Mean of the 10 scales is measured and gives a final score. High scores reflect a low physical functioning.

9.7.2.4. **BAS-G**

Used to make a global assessment of the wellbeing of the patient (their perspective) over a period of time. It consists of 2 questions about the effect of AS on their well being during last week and last 6 month marked on a 0-10 VAS being 0=none and 10= very severe effect.

9.7.2.5. **BASMI**

Used to assess the axial status of patients with ankylosing spondylitis and define clinically significant changes in spinal movement. This is not a self-reported as all the previous measures. It is assessed by physicians, performing an examination of 5 clinical measures: cervical rotation, tragus to wall distance, lumbar side flexion, lumbar flexion and intermalleolar distance. The range of severity 0-10 reflects mild to severe disease activity and functional ability in the spinal column.\[31\]
10. RESEARCH METHODOLOGY AND METHODS

Research planning (organization)
The research was divided in 4 stages:

1. Collection of literature and theoretical knowledge of the disease and factors.
2. Literature review, creation of questionnaires and collection of permissions.
3. Collection of data: giving questionnaires to our population.
4. Statistical analysis, results and presentation preparing

Object of study and Participant selection
The research was carried in Kauno Klinikos, LSMU hospital Rheumatology department, in which we have a population of patients suffering from Ankylosing spondylitis. During the period from 5 of November until 12 of December a sample of 48 patients was taken out of this population by handing a questionnaire to the patients coming to the office for consultation, check-up, or receiving their treatment. Inclusion criteria: Patients in rheumatology department with ankylosing spondylitis, more than 18 years old who answered the questionnaire correctly.

Research methods
The data presented in this thesis is taken from the several questionnaires we used, which were answered by our sample. In these questionnaires the following determinants were investigated: ASQoL, disease activity and function (BASDAI; BASFI), and the exposure to factors: age, BMI, exercise, smoking, diet, treatment.

For quality of life, BASDAI and BASFI we ask the patient to determine how well he identifies himself with the proposed statements. In the questionnaires we want to obtain data about patient’s age, BMI, smoking history, physical exercise routines, diet peculiarities, age at diagnosis and treatment being used, we ask some questions about each topic. (See annex 2)

All patients who agreed to complete the questionnaire and signed their consent, being previously informed that it would be anonymous, were included in the study. Out of these 48 patients, 3 more patients were excluded for not answering the whole questionnaire.

Methods of data analysis
After all the data of the questionnaires was collected, it was analysed by using Microsoft Excel and SPSS software. Descriptive statistics were used to describe the study sample: analysis of each of the variables in the database is carried out, for which a frequency table (number of cases and percentages) is calculated and shown as a graphic representation in the mode of the graph of sectors. Inferential statistics tests such as correlation, t-Student, Multivariate analysis of variance and chi-
square tests were used to analyse the sample, detect differences according patient’s exposure to different factors and reach conclusions.

11. RESULTS AND DISCUSSION

DESCRIPTIVE RESULTS OF SAMPLE

1. Sex
In the Figure 1 we show the percentage of males and females in our sample. Out of the 48 patients who answered our questionnaires there were 16 females (33.33%) and twice as much men, 32 (66.67%).

2. Age
The mean age of the population was 45.21 years with a standard deviation of 13.43. The youngest patient was 21 years old and the oldest was 72 years old. Mode of age was 36 years old.

3. Age at diagnosis
The mean age of diagnosis was 35.48 with a standard deviation of 11.97. The youngest diagnosis was at 16 years old while the oldest was at 67 years old.

4. BMI
If we classify the patients in groups by BMI ranges, the most numerous group was Overweight (BMI 25-30) with a 41.7%, followed by the group with a normal healthy weight (33%). 18.8% of the patients were Obese and 6.3% were Severely Obese. See figure 2.
5. Physical exercise

When we asked our patients if they perform any kind of physical exercise 43 of them (89.58%) answered “yes”, while only 5 (10.42%) answered “No”. This is shown in Fig. 3.

If we ask our patients how do they feel about their capability to perform physical exercise, 8 of them (16.67%) claimed that they were unable to exercise. A bigger group of patients claimed that they were in a good condition to exercise, and it was not painful (18 patients, 37.5%). While the most numerous group, a 45.83% of the patients, claimed that they were able to perform physical activity but it was painful for them. This is shown in figure 4.

The 43 patients who perform some physical exercise, were divided in three groups according the frequency of exercise (in days a week); the most numerous group (41.86%) was exercising 1-2 days a week, the rest of results are shown in figure 5:

With regard to the time expended in each exercise session, the major group of patients (39.53%) expended between 20 and 40 minutes. The rest of the patients were distributed in 4 more groups: 9 patients only exercise for less than 10 minutes, 7 patients exercise about 10-20 min, 8 patients exercise about 40-60 min, and only 2 patients claimed to exercise for more than one hour. This is shown in figure 6.
When it comes to the modality of exercise executed by our patients it was varied, and there were a number of patients who combined different kinds of exercise:

The most practiced exercise is Walking, chosen by 21 (48.84%) patients; from them, 11 did strictly walking while the rest combine it with other kinds of exercises such as stretching, running… (these can be seen in table 4). It is followed by Stretching exercises, practiced by 20 patients (46.51%), 12 of them only stretch while 8 combine it: 6 patients combine stretching with walking, and 2 patients combine it with swimming. Only 2 patients marked running as their exercise, and both of them combine it with another exercises. Swimming is the option of 9 patients (20.93%), and aerobic is the choice of 2 patients (4.65%). There were 2 patients who marked the option “Other exercise” but didn’t specify which.

Table 1. Answers of the patients about which kind of exercise performed

<table>
<thead>
<tr>
<th>Modality of exercise</th>
<th>Pts</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Walking</td>
<td>11</td>
<td>25.58</td>
</tr>
<tr>
<td>2. Stretching</td>
<td>12</td>
<td>27.91</td>
</tr>
<tr>
<td>3. Running</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>4. Swimming</td>
<td>5</td>
<td>11.63</td>
</tr>
<tr>
<td>5. Aerobic</td>
<td>1</td>
<td>2.33</td>
</tr>
<tr>
<td>6. Others</td>
<td>2</td>
<td>4.65</td>
</tr>
<tr>
<td>Walk + Stretch</td>
<td>6</td>
<td>13.95</td>
</tr>
<tr>
<td>Walk + Run</td>
<td>1</td>
<td>2.33</td>
</tr>
<tr>
<td>Walk + Swim</td>
<td>2</td>
<td>4.65</td>
</tr>
<tr>
<td>Stretch + Swim</td>
<td>2</td>
<td>4.65</td>
</tr>
<tr>
<td>Walk + Run + Aerobic</td>
<td>1</td>
<td>2.33</td>
</tr>
<tr>
<td>Total</td>
<td>43</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Table 2. Total of patients for each kind of exercise

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Pts</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking</td>
<td>21</td>
<td>48.84</td>
</tr>
<tr>
<td>Stretching</td>
<td>20</td>
<td>46.51</td>
</tr>
<tr>
<td>Running</td>
<td>2</td>
<td>4.65</td>
</tr>
<tr>
<td>Swimming</td>
<td>9</td>
<td>20.93</td>
</tr>
<tr>
<td>Aerobic</td>
<td>2</td>
<td>4.65</td>
</tr>
<tr>
<td>Others (unspecified)</td>
<td>2</td>
<td>4.65</td>
</tr>
</tbody>
</table>

Fig 7. Condition of patients after exercise

When we asked the patients to evaluate their condition after performing physical exercise, most of the patients claimed they feel better afterwards (31 patients, 72%), a group of 11 patients claimed that they do not feel any difference with their condition before and after exercise, and only one patient feels worse afterwards.
6. Diet

Regarding diet recommendations: From our 48 patients, only 27% were recommended to change their diet after being diagnosed. The rest (73%) didn’t receive any recommendation about diet. However, 44% of the patients have changed their diet after being diagnosed and 56% didn’t change it.

About diet peculiarities we asked about: alkaline diet, gluten, lactose and starch intake. A 27% of the patients claimed to know about or at least heard about the alkaline diet, but only 4% of the patients followed it.

In the matter of gluten-containing diet, most of the patients eat gluten products; only 7 patients followed a gluten-free diet, this is a 15%. As for lactose, most of the patients also consumed it, and only 11 patients (23%) followed a lactose free diet.
In the case of low starch diet, there were 19 patients, a 40%, following it, while 60% doesn’t follow it as shown in figure 14. We also asked about gastrointestinal diseases, obtaining the results in figure 15, showing that 11 of the patients with AS also had a GI disease (Crohn, Ulcerative Colitis, IBS…), but the majority, 37 of the patients, don’t suffer digestive tract diseases.

7. **Smoking habit**

In regards to the smoking habits of our patients, the majority of them, 45,83%, were former smokers and a 31,25% never smoked. Only 11 (22,92%) of them are currently smokers. The mean of cigarettes per day of the currently smokers was 14,85 and a mean of 245,55 packs per year. All of the smokers (100%) use normal cigarettes, none of them use electronic cigarrete.

8. **Treatment and Management**

When asking about treatment we gave the patients 3 options representing 3 groups of treatments: Anti-inflammatory drugs, Biological drugs and DMARDs (Sulfasalazine, MTX) allowing to mark all the treatments received at the moment. All the options marked by patients are shown in figure 18. The total of patients using anti-inflammatory drugs is 25 (52,08%). From these patients, 18 of them are taking anti-inflammatory drugs exclusively, 3 patients are taking them in combination with Biological drugs and 4 patients use them in combination with DMARDs. This is shown in figure 19. The total of patients using Biological drugs is 25 (52,08%). From these patients 20 are taking...
biological drugs exclusively, while 3 are taking them in combination with anti-inflammatory (as mentioned above), and 2 patients are taking them in combination with DMARDs. See figure 20. The total of patients using DMARDs is 7 (14.58%). From these only 1 patient is using sulfasalazine exclusively, the rest are taking it in combination with Anti-inflammatory and biological drugs, 4 and 2 respectively (as mentioned above). See figure 21.

![Fig 17. Total of patients taking each group of drugs (alone or combined)](image)

![Fig 18. Distribution of all treatment options](image)

![Fig 19. Pattern of treatment of patients taking antiinflammatory drugs (25)](image)
As for the management with physiotherapy, a 65% of the patients had resort to physiotherapy in some moment, while 35% never used physiotherapy. Those who used physiotherapy did it in different frequency; the majority (14 patients, 45% out of the 31 using physiotherapy) only went few times to the physiotherapist, the second biggest group only went from 1 to 5 times in a year. A group of 4 persons went from 5 to 10 times a year, and the remaining two persons went once a month and once a week respectively.
9. **Disease activity and functionality of patient: BASDAI and BASFI**

**BASDAI**

The mean BASDAI score was 4.60 with a standard deviation of 2.16. The maximum score obtained was 10 and the minimum score was 1.

We divided the patients in two groups according to the interpretation of the score, when it was more than 4 we considered it high (disease is highly active) and when it was less than 4 we considered it low. 25 patients (52.08%) obtained a BASDAI score ≥4 and thus have a highly active disease. In this group the mean score is 6.26. The rest of the patients, 22 (45.83%) obtained a BASDAI score <4. The mean score in this group is 2.71. There was one patient (2.08%) who didn’t answer the BASDAI VAS.

**BASFI**

The mean BASFI score was 3.99 with a standard deviation of 2.37. The maximum score obtained was 10 and the minimum score was 1.

In this case we also divided the patients in two groups according the BASFI score, being BASFI ≥ 4 a high function impairment and BASFI <4 a low function impairment:

A total of 30 patients (62.5%) had a BASFI score less than 4 meaning they had a low functional limitation. The average score in this group was 2.47.

The rest of the patients (17 patients, 35.42%) had a BASFI score higher than 4, and the average score in this group was 6.68. Again there was one patient who didn’t answer the BASFI VAS.

10. **AS Quality of Life questionnaire**

The mean QoL score was 6.64 with a standard deviation of 5.17. The minimum score obtained was 0 and the maximum was 17 (the maximum possible is 18).

In the QoL results we decided to divide the patients in three groups:

- Good-medium quality of life when ASQoL < 4 - there were 16 patients (33.33%)
- Poor quality of life when ASQoL = 4 - 10 - there were 19 patients (39.58%)
- Very poor quality of life when ASQoL ≥10 – there were 12 patients (25%)

There was one patient who didn’t answer the ASQoL questionnaire.
ANALYTIC RESULTS AND DISCUSSION

First of all, let us understand that this research had few limitations:

To start with, the potency of the study has been diminished by the low number of participants; a small sample can prevent us from finding the searched differences (there is a higher $\beta$ risk), which with a larger number of participants might be found. Therefore it is possible that in our study we reach conclusions that with a larger sample would turn out differently.

Furthermore, the fact of analysing many factors at the same time can make some of them interfere with each other, as they are all related to the outcome and this could make our conclusions less significant than they would be if sample had been larger and more homogeneous. For instance, out of the 48 patients in this study, we have 43 patients who exercise vs. only 5 patients who don’t, but at the same time they are differently exposed to diet, BMI, treatment; if sample were more homogeneous it would gain potency and precision.

Being these few things clear we can present our results:

In first place we established the Pearson correlation between each of the indexes we use to evaluate the disease presentation: BASDAI, BASFI and ASQoL. As expected BASDAI, BASFI, and ASQoL are significantly and strongly correlated. Correlation between BASDAI and BASFI is strong with an $r=0,77$ as well as correlation between BASDAI and ASQoL with an $r=0,79$. In all cases $p$ value $< 0,00005$.

1. AGE AT DIAGNOSIS

We found that in our sample there was a weak positive Pearson’s correlation ($r=0,29$), which was statistically significant ($p = 0,04$) between ASQoL scores and age at diagnosis. This means that for an older age at diagnosis, the patients presented a higher score of ASQoL (worse quality of life) at the moment of the questionnaire. The same happens with BASDAI ($r = 0,18$) and in case of BASFI we could already consider a medium correlation ($r=0,30$). In clinical terms there is a correlation between the age of diagnosis and the disease activity and functional limitations in a way that as older age at diagnosis, higher disease activity and limitations at the moment of the questionnaire.

This somehow contradicts our expectations because of existing literature that establishes an early onset of the disease as a worsen prognosis predictor; this would made us expect a negative correlation instead of a positive one. Nevertheless, we are not dealing with the end prognosis but with the quality of life perceived at the moment of questionnaire, and in a sample with very different patients, so it is not strictly contradicting the literature as we mention, and probably we should see how this correlation would turn out in a more homogeneous and larger sample.
2. BMI

Unexpectedly, as we were studying the relevance of BMI we couldn’t find any statistically significant correlation (r) between BMI and the results of BASDAI, BASFI, nor QoL. The results are shown in table 3. On the other hand, if we divide the patients in groups according their BMI, and then we compare the mean of BASDAI, BASFI and QoL of each group, we can see that there are clinical differences; in the case of QoL, for instance, the mean in normal BMI group is 4,81 and it increases in each group; Overweight 6,73 and obese 8,44 reaching a mean of 10,33 in the severely obese group. A similar progression happens with BASDAI and BASFI. All the results can be seen in table 4.

Table 3. Pearson’s Correlation between BMI and BASDAI, BASFI, QoL.

<table>
<thead>
<tr>
<th></th>
<th>BASDAI</th>
<th>BASFI</th>
<th>ASQoL</th>
</tr>
</thead>
<tbody>
<tr>
<td>r</td>
<td>0,1708</td>
<td>0,2438</td>
<td>0,2131</td>
</tr>
<tr>
<td>P</td>
<td>0,251</td>
<td>0,0986</td>
<td>0,1504</td>
</tr>
</tbody>
</table>

Table 4. Means of BASDAI, BASFI and QoL by groups according BMI.

<table>
<thead>
<tr>
<th></th>
<th>Mean BASDAI</th>
<th>Mean BASFI</th>
<th>Mean ASQoL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal BMI</td>
<td>3,972</td>
<td>3,58</td>
<td>4,81</td>
</tr>
<tr>
<td>Overweight</td>
<td>4,721</td>
<td>3,66</td>
<td>6,737</td>
</tr>
<tr>
<td>Obese</td>
<td>4,97</td>
<td>4,61</td>
<td>8,44</td>
</tr>
<tr>
<td>Severely obese</td>
<td>6,017</td>
<td>6,417</td>
<td>10,33</td>
</tr>
</tbody>
</table>

The results in table 3 and therefore reaching the conclusion that statistically there is no correlation between BMI and BASDAI, BASFI or QoL contradicts previous existing literature that established a worsening of disease activity, physical function in overweight and obese patients who also report a lower sense of overall wellbeing and worse QoL.\[^{24,25}\]

On the other hand, when we divided the sample in groups by BMI, we could clearly see the pattern in which as the BMI increases, the indexes and ASQoL increase as well. If we interpret the BASDAI as low <4 and high >4, we obtain a low disease activity only in the normal BMI group, and from the overweight group, all the groups have high disease activity. It happens similarly in BASFI. All this clinical differences are more consistent with the existing evidence, and the fact that there is a pattern (which in this case is not statistically significant) tells us that if we had a larger sample that could increase the research potency maybe the correlation would be statistically significant.

Nonetheless, we can’t conclude that in our sample the BMI has a statistically significant effect on the Quality of life in patients with AS.
3. EXERCISE

First of all, we compared the mean of indexes and quality of life of patients who exercise vs. patients who don’t. The results are shown in table 5. In any of the cases we could not find a statistically significant benefit from exercising. The mean of QoL in patients who exercise and in patients who don’t was 6.54 and 7.4 respectively, with a p value = 0.731. The differences weren’t statistically significant in BASDAI or BASFI either. We can establish that in our sample there are no statistically significant differences between the mean values of patients who exercise and patients who don’t.

Table 5. Mean scores in BASDAI, BASFI, QoL according exercise (t- Student test)

<table>
<thead>
<tr>
<th>Mean of</th>
<th>Patients who exercise</th>
<th>Patients who don’t exercise</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASDAI</td>
<td>4.07</td>
<td>4.66</td>
<td>0.569</td>
</tr>
<tr>
<td>BASFI</td>
<td>4.00</td>
<td>3.88</td>
<td>0.914</td>
</tr>
<tr>
<td>ASQoL</td>
<td>6.54</td>
<td>7.4</td>
<td>0.731</td>
</tr>
</tbody>
</table>

In previous literature it is shown how a minimal exercise, even a small amount at home, improved the outcomes and studies showed a significant improvement of BASFI and pain scores, while only if the patients were in an exercise education program there was improvement of BASDAI, BASFI, and ASQoL.

However, in our study we didn’t find differences between patients who exercise and patients who don’t, which according to the literature we were expecting to find; we didn’t ask our patients if they performed the exercises by themselves or if they have any tutoring of the exercise, a trainer or any person supervising the exercise, so we could not establish this difference as in the literature, although we did ask the frequency of exercise and the time of exercise, and this could bring some different conclusions.

In second place we took the group of patients who exercise, and then we compared the mean of BASDAI, BASFI, ASQoL in three different groups of patients according frequency of exercise as shown in table 6. In this case we could not find any statistically significant difference either.

In third place, from the group of patients who exercise, we compared the mean of BASDAI, BASFI and ASQoL between five groups of patients according the time they were expending in each exercise session. This is shown in table 7, and again, we weren’t able to reach any statistically significant difference.

As for frequency or time of exercise we didn’t have any previous data and any study had reflected the relevance of frequency/time of exercise that we could compare our results to.
Table 6. Mean scores of BASDAI, BASFI, ASQoL according frequency of exercise (ANOVA test)

<table>
<thead>
<tr>
<th></th>
<th>1-2 days/week</th>
<th>2-4 days/week</th>
<th>&gt; 5 days/ week</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BASDAI</td>
<td>4.3</td>
<td>4.7</td>
<td>5.1</td>
<td>0.678</td>
</tr>
<tr>
<td>Mean BASFI</td>
<td>3.935</td>
<td>4.16</td>
<td>3.86</td>
<td>0.633</td>
</tr>
<tr>
<td>Mean ASQoL</td>
<td>5.70</td>
<td>6.25</td>
<td>8.66</td>
<td>0.974</td>
</tr>
</tbody>
</table>

Table 7. Mean score of BASDAI, BASFI, ASQoL according time of exercise (ANOVA test)

<table>
<thead>
<tr>
<th></th>
<th>&gt;10 min</th>
<th>10 -20 min</th>
<th>20 -40 min</th>
<th>40 -60 min</th>
<th>&gt; 1 h</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BASDAI</td>
<td>4.77</td>
<td>5.01</td>
<td>4.49</td>
<td>4.43</td>
<td>4.14</td>
<td>0.586</td>
</tr>
<tr>
<td>Mean BASFI</td>
<td>4.70</td>
<td>4.07</td>
<td>4.15</td>
<td>2.87</td>
<td>4.02</td>
<td>0.67</td>
</tr>
<tr>
<td>Mean ASQoL</td>
<td>7.88</td>
<td>5.57</td>
<td>6.625</td>
<td>6</td>
<td>5.5</td>
<td>0.754</td>
</tr>
</tbody>
</table>

The fact that neither the exercise itself, nor the frequency nor the time of exercise were statistically significant for us, made it impossible to extract any positive relevant conclusion about exercise exposure and it wasn’t necessary to compare the modality of exercise, referring to which the literature supports the additional benefit of water exercises and the superiority of aerobic vs. stretching/ROM. [21, 22]

To sum up, in our sample the exercise did not show to have an important role in BASDAI, BASFI and ASQoL. Even if evidence has shown a benefit from exercising in our study we cannot reach the same conclusion.

We would also like to point out that, when we asked the patients to evaluate their condition after performing physical exercise, most of the patients (72%) claimed they feel better afterwards, and this could serve as to draw a different conclusion: exercise didn’t show to have a role in BASDAI, BASFI or ASQoL, but it has a role in the subjective short-term feeling of the patients.

If we take into consideration literature that supports that supervised exercise can obtain better results compared to home exercise, [21] and the fact that our sample didn’t obtain a statistically significant effect of exercise, we could open a door to consider the introduction an exercise program for AS patients in Lithuania, in order to optimize their exercise and improve these results.
4. DIET

When it comes to diet, we compared in first place those patients who changed their diet in any non-specific way since their diagnosis, to those who didn’t make any change to their diet. This didn’t lead to any statistically significant difference: BASDAI was 4.79 in patients who changed diet and 4.45 in patients who didn’t (p=0.59), ASQoL mean was 6.7 in patients who changed diet and 6.59 in patients who didn’t.

In second place we compared the means of BASDAI, BASFI, ASQoL according some different diet options: In the case of alkaline diet, which in the descriptive results we saw that it is a very unknown and even less followed diet in Lithuania (27% of the patients had heard some time about the diet, and only 4% follow it), we didn’t obtain any statistically significant difference between patients following it and patients not following it, however if we take a look to the results, we can appreciate clinical differences between them: The mean of BASDAI in patients following alkaline diet is 2.9 versus 4.67 in patients not following them which clinically translates into low activity AS in the first group vs. a highly active disease in the second group. The same happens in BASFI in which means of patients following alkaline diet and patients not following it are 1.8 and 4.092 respectively; and in ASQoL the means are 2 and 6.84 respectively. In patients who follow alkaline diet their physical function seems better and their QoL also seems better. This of course is not statistically significant (all p values > 0.05) but clinically we could draw a pattern in which this could be relevant. There is no evidence to compare our results with.

Subsequently, we compared patients eating gluten-containing diet with the patients with a gluten-free diet and we didn’t find any statistically significant difference between them. So we can’t conclude that gluten has a role in patients with AS. The results are shown in table 8.

To continue with, we compared patients with a lactose containing diet with patients with a lactose free diet and, as it happened with gluten, we didn’t find any statistically significant difference between them. Lactose didn’t show to have any relevant role in patients with AS. Some studies didn’t find significant differences with lactose either but in one study the removal of diary products resulted in improvement and even discontinued NSAID treatment of half of the patients.

Regarding all those diet options there barely is evidence related to AS, we couldn’t find any reference to them in the literature associating diet and AS, in addition our results were not statistically significant, so we can’t conclude neither exclude there is a relation between them.
In any case, to prove it, further investigation should be done and new studies should be performed, more accurately, to reach a statistically significant conclusion.

When it comes to low starch diet, evidence is also poor, but the small evidence existing points to a negative role of starch in patients with AS, and describes a benefit of following a low starch diet, finding an association between this diet and improvement of BASDAI and BASFI while no association with SF36 quality of life results; however our study didn’t repeat this results, as we couldn’t establish a statistically significant difference between patients with low starch diet and patients with normal diet. The mean BASDAI in low starch diet patients was 4,19 and in the other group of patients 4,87 with a p value = 0,297. BASFI results were similarly with a mean of 3,49 and 4,33 respectively with p= 0,2355. In QoL the means were 6,10 and 7 respectively.

Therefore, we can conclude that in our sample, the starch amount in diet doesn’t have any relevant role for activity, function and QoL of patients with AS.

Table 8. Mean of BASDAI, BASFI, ASQoL according different diets. (t-Student test)

<table>
<thead>
<tr>
<th>Diet Type</th>
<th>Mean if “yes”</th>
<th>Mean if “no”</th>
<th>P value</th>
<th>Mean BASDAI</th>
<th>Mean BASFI</th>
<th>Mean ASQoL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unspecific change of diet</td>
<td>4,7975</td>
<td>4,45</td>
<td>0,5912</td>
<td>4,112</td>
<td>3,907</td>
<td>6,7</td>
</tr>
<tr>
<td>Alkaline diet</td>
<td>2,9</td>
<td>4,673</td>
<td>0,2605</td>
<td>1,8</td>
<td>0,7730</td>
<td>0,944</td>
</tr>
<tr>
<td>Gluten containing diet</td>
<td>4,578</td>
<td>4,707</td>
<td>0,8865</td>
<td>3,88</td>
<td>4,61</td>
<td>6,55</td>
</tr>
<tr>
<td>Lactose containing diet</td>
<td>4,5902</td>
<td>4,6227</td>
<td>0,9658</td>
<td>4,127</td>
<td>3,559</td>
<td>6,611</td>
</tr>
<tr>
<td>Low starch diet</td>
<td>4,194</td>
<td>4,871</td>
<td>0,297</td>
<td>3,49</td>
<td>4,33</td>
<td>6,10</td>
</tr>
</tbody>
</table>

On the whole, diet in general didn’t show to have a relevant role for QoL in patients of our sample, as none of the t tests were statistically significant.

5. SMOKING

When we analysed smoking exposure results we divided by never smoker, formerly smoker, and current smoker, and we didn’t obtain any statistically significant difference between them. In ASQoL the mean in never smokers was 7,73, while in former smokers and current smokers were 6,47 and 5,45 respectively, with p = 0,759. These were quite surprising results as the mean of QoL was worst than in smokers and former smokers contrarily to what one would expect, nonetheless this is not statistically significant so we cannot establish any conclusion. Results are in table 9.
As for previous existing evidence we were expecting to find an improvement of QoL and BASDAI, as several studies establish that smokers with SpA have a more severe disease (higher BASDAI) and worse QoL, there are even studies that revealed smoking to be an independent variable for higher BASDAI score, and a positive and independent association of smoking and cumulative smoking exposure with lower quality of life. In addition to it, studies even found a difference between currently smokers and former smoker, which after cessation improved BASDAI and QoL.

Table 9. Mean of BASDAI, BASFI, ASQoL according smoking exposure. (ANOVA test)

<table>
<thead>
<tr>
<th></th>
<th>Never smoker</th>
<th>Former smoker</th>
<th>Current smoker</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BASDAI</td>
<td>3,84</td>
<td>4,62</td>
<td>5,11</td>
<td>0,228</td>
</tr>
<tr>
<td>Mean BASFI</td>
<td>4,62</td>
<td>3,75</td>
<td>3,58</td>
<td>0,345</td>
</tr>
<tr>
<td>Mean ASQoL</td>
<td>7,73</td>
<td>6,47</td>
<td>5,45</td>
<td>0,759</td>
</tr>
</tbody>
</table>

6. TREATMENT

In order to assess the relevance of the treatment we created a variable in which one group had biological treatment (alone or combined) and the other group didn’t have biological treatment at all (patients who have treatment with NSAIDs or DMARDs). The conclusions in this variable were statistically significant in the three measurements: BASDAI, BASFI and ASQoL. This is shown in table 10.

The mean ASQoL score in the Biological treatment group was 4,6 compared to a mean of 8,95 in the Non-biological treatment group. The difference between them was statistically significant with a p = 0,0029, and we can conclude that the patients using biological treatment have a better quality of life than those who don’t.

Table 10. Mean of BASDAI, BASFI, ASQoL according treatment. (t-Student Test)

<table>
<thead>
<tr>
<th></th>
<th>BIOLOGIC</th>
<th>NON BIOLOGIC</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BASDAI</td>
<td>3,594</td>
<td>5,78</td>
<td>0,0003</td>
</tr>
<tr>
<td>Mean BASFI</td>
<td>3,22</td>
<td>4,87</td>
<td>0,015</td>
</tr>
<tr>
<td>Mean ASQoL</td>
<td>4,6</td>
<td>8,95</td>
<td>0,0029</td>
</tr>
</tbody>
</table>
12. **CONCLUSIONS**

1. In our sample the quality of life was significantly influenced only by the age at diagnosis and biological treatment, while all the other factors didn’t show a statistically significant influence on quality of life. To answer our objectives:

   - **Study the relevance of age at diagnosis in ankylosing spondylitis presentation and perceived quality of life:** The older the patients were at diagnosis; the worse was the quality of life at the moment of questionnaire. There was a statistically significant weak positive correlation of $r=0.29$ between age at diagnosis and ASQoL score with $p=0.04$.

   - **Study the relevance of biological treatment (presence or absence) in QoL of patients with AS:** The patients who are treated with biological treatment (TNFa inhibitors) have a better quality of life, a lower disease activity and a lower function limitation. The mean of ASQoL in patients with biological treatment was 4.6 vs. a 8.95 in patients without biological treatment with a $p$ value $= 0.0029$. In case of BASDAI means were 3.59 vs 5.78 ($p=0.0003$) and means of BASFI were 3.22 vs 4.87 ($p=0.015$) respectively.

2. For the following objectives we didn’t obtain statistically significant results:

   - **Study the effect and relevance of physical exercise in Quality of life of patients with AS, and if there is any difference between different modalities of exercise:** Exercise in our sample is not relevant towards QoL. When we compared means of ASQoL, BASFI or BASDAI of patients who exercise and patients who don’t $p$ value was $> 0.05$ in all scores. It wasn’t significant either when we compare frequency or duration. The modalities of exercises were not compared, as none of the previous was significant. However, 72% of our patients claimed that they feel better after exercise. Also according literature, we could try to establish an exercise program for AS patients to optimize their exercise and results. And follow recommendations from J.R. Millner (see annex 1) could draw some more positive results.

   - **Study the effect and relevance of diet in Quality of life of patients with AS:** In our sample all the analysis turned out with no statistically significant differences between diets. Moreover, there is very poor amount of studies about relationship between diet and AS, more studies should be carried out in this direction. Especially in alkaline diet which in our results showed some positive clinical differences (QoL in alkaline diet patients was 2 vs 6.8 in non alkaline diet, although it was not significant $p=0.19$).
• Study the effect and relevance of BMI in Quality of life of patients with AS: The BMI showed no statistically significant correlation with quality of life ($r=0.21; p=0.15$), but when we compared the mean of ASQoL by groups of BMI (Normal 4.81, Overweight 6.73, Obese 8.44 and severely obese 10.33) results pointed to a possible correlation (Normal BMI patients had a better QoL and lower BASDAI, than overweight and obese) and the existing literature also supports these results.

• Study the effect and relevance of smoking in QoL of patients with AS: Contrarily to literature in which smoking is related with worse BASDAI and QoL, smoking didn’t show any relevance in QoL of our sample. The mean of ASQoL in smokers was 5.45, for former smokers was 6.47 and never smokers 7.73 with a $p=0.759$, so there were not statistically significant differences but the numbers obtained were far from what was expected.

3. To obtain further answers to our study objectives it’s also relevant to mention that this study was limited by the small sample. In some of the results that showed a positive pattern with differences that were not significant, study could be repeated with a larger sample to see if statistically significant differences would be obtained.
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14. ANNEXES


It summarises recommendations and relationships of these factors and may be useful in decision-making regarding exercise.

1. Assessment – individual exercise prescription according a thorough assessment of patient.
2. Monitoring – To achieve confidence and competence with exercise and to inform changing needs for exercise prescription.
3. Safety – especially for those with more severe disease, physical changes of AS should be considered: ankylosis, mobility changes, osteoporosis, …
4. Disease management – Even if being treated with antiTNFα patient should continue with regular exercise.
5. AS specific exercise: Mobility – Emphasis on spinal mobility and peripheral joints mobility, aiming to restoration or maintenance of ROM and posture.
7. Physical activity – regular physical activity should be encouraged. Interrupt sedentary activities.
8. Dosage – Exercise frequency, intensity, duration and type must be adapted to the assessment findings, goals and lifestyle of patient.
9. Adherence – important to assess regularly and encourage motivation.
10. Exercise setting – Priority should be given to patient preferences to enhance adherence.
Annex 2. Questionnaires

1. What is your age?
   Kiek jums metų?

2. What is your weight?
   Koks jusų svoris?

3. What is your height?
   Koks jusų ugis?

4. Physical exercise:
   1. Do you do any kind of physical exercise?
      Ar jūs darote kokį fizinį pratimą / sportuojate?
      a. YES/ Taip
      b. NO / Ne
   2. How many days a week do you exercise?
      Kiek kartų per savaitę sportuojate?
      a. From 1 to 2 / 1-2 kartus per savaitę
      b. From 2 to 4 / 2-4 kartus per savaitę
      c. 5 or more / Daugiau nei 5 kartus per savaitę
   3. How long do you exercise?
      Kiek laiko jus sportuojate?
      a. Less than 10 min / Mažiau nei 10 min.
      b. 10 – 20 min
      c. 20 - 40 min
      d. 40 – 60 min
      e. More than 1 h / Daugiau nei 1 val.
   4. Which kind of exercise do you perform?
      Kokios jūs darote?
      a. Walking / Vaikščioti
      b. Stretching / Ištempsti
      c. Running / Begti
      d. Swimming / Plaukti
      e. Aerobic classes / Aerobikos klasės
      f. Other / Kitas: ____________
   5. How do you feel after exercising?
      Kaip jūs jaučiātės po sporto ar mankedį?
      a. My symptoms get worse / Mano simptomai pablogėja
      b. I don’t feel a relevant difference / Aš nesijaučiu skirtumo
      c. My symptoms get better / Mano simptomai pagerėja
   6. How would you evaluate your capability to exercise lately?
      Kaip jūs vertinate savo galimybes sportuoti pastaruoju metu?
      a. I can’t exercise because I’m in pain / I have reduced mobility
         Aš negaliu sportuoti nes man skauda / aš sumažino judesiai
      b. I can exercise but I may feel pain during exercising
         Aš galiu sportuoti, bet man skauda kai sportuoju
      c. I’m in a good condition to exercise
         Aš esu geros būklės, galiu sportuoti

5. Smoking/ Rūkymas

Are you a smoker? Ar jūs rūkote?
   a. Never / Niekada
   b. Former / Anksčiau (Buves)
   c. Currently / Taip (šiuo metu)

- If yes, How many cigarretes a day? _____ Jei taip, kiek cigarečių per diena? _____
  For how long have you smoked? _____
  Kiek metų/jūs rūkote?
  Do you smoke electronic or usual cigarretes?
  Ar jūs naudojate elektroninę ar įprastą cigarečių?
6. Dieta:
1. Have you been recommended to change your diet?
   Ar jums buvo rekomenduota pakeisti dietą?
   a. Yes / Taip
   b. No / Ne
2. Have you changed your diet since you’ve been diagnosed of ankylosing spondylitis?
   Ar jūs pakeitėte savo dietą / mitybą, nes jums buvo diagnozuota ankilozinis spondilitas?
   a. Yes
   b. No
3. If yes, in which aspect did you change your diet?
   Jei taip, ką jūs pakeitėte?
4. Have you heard about the “alkaline diet”?
   Are jūs girdėjote apie šarminę dietą?
   a. Yes / Taip
   b. No / Ne
5. Do you follow it? Ar jūs laikotės šios dietos?
   a. Yes / Taip
   b. No / Ne
6. Do you eat gluten-containing products?
   Ar jūs valgote glitimo turinčius produktus?
   a. Yes / Taip
   b. No / Ne
7. Do you eat or drink lactose-containing products?
   Ar jūs valgote ar geriate laktozės turinčius produktus?
   a. Yes / Taip
   b. No / Ne
8. Do you follow a low starch diet?
   Ar jūs ribojate krakmolą savo maiste?
   a. Yes / Taip
   b. No / Ne
9. Do you have any gastrointestinal disease?
   Ar turite kokį nors virškinimo trakto ligą?
   a. Yes / Taip
   b. No / Ne

7. About your disease / Apie jusų ligą:
1. At what age were you diagnosed with ankylosing spondylitis?
   Kokį amžių jums buvo diagnozuotas ankilozinis spondilitas?
2. Which kind of medical treatment are you receiving now?
   Kokį gydymą jūs dabar gaunate?
   a. Anti-inflammatory: Indomethacin , Diclophenac, Celecoxib
      Prieš uždegiminis vaistas
   b. Biological drugs: Infliximab, Etanercept, Adalimumab, Golimumab
      Biologinis vaistas
   c. Sulfasalazine
   d. If a different drug please write: __________________________________________
      Jei kitas gydymas, prašau parašyti:________________________________________
3. Have you been treated by a physiotherapist?
   Ar jūs gydė fizioterapeutas?
   a. Yes / Taip
   b. No / Ne
4. If yes, how frequently?
   Jei taip, kaip dažnai?
   a. Only few times / tik kelis kartus
   b. 1-5 times a year / 1-5 kartus per metų
   c. 5-10 times a year / 5-10 kartus per metų
   d. Once a month / Vienas kartas per mėnesį
   e. Once a week / Vienas kartas per savaitę
The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

Please place a mark on each line below to indicate your answer to each question relating to the past week

1. How would you describe the overall level of **fatigue/tiredness** you have experienced?
   
   NONE ____________________________ VERY SEVERE

2. How would you describe the overall level of **AS neck, back or hip pain** you have had?
   
   NONE ____________________________ VERY SEVERE

3. How would you describe the overall level of pain/swelling in joints other than **neck, back, hips** you have had?
   
   NONE ____________________________ VERY SEVERE

4. How would you describe the overall level of **discomfort** you have had from any areas tender to touch or pressure?
   
   NONE ____________________________ VERY SEVERE

5. How would you describe the overall level of **morning stiffness** you have had from the time you wake up?
   
   NONE ____________________________ VERY SEVERE

6. How long does your morning stiffness last from the time you wake up?

   
   0 hrs  ½  1  1½  2 or more hours
Bath Ankylosing Spondylitis Functional Index (BASFI)

- **Putting on your socks or tights without help or aids (e.g. sock aid)**
- **Bending forward from the waist to pick up a pen from the floor without an aid**
- **Reaching up to a high shelf without help or aids (e.g. helping hand)**
- **Getting up out of an armless dining room chair without using your hands or any other help**
- **Getting up off the floor without help from lying on your back**
- **Standing unsupported for 10 minutes without discomfort**
- **Climbing 12–15 steps without using a handrail or walking aid, one foot on each step**
- **Looking over your shoulder without turning your body**
- **Doing physically demanding activities (e.g. physiotherapy exercises, gardening or sports)**
- **Doing a full day's activities whether it be at home or at work**
ANKYLOSING SPONDYLITIS QUALITY OF LIFE QUESTIONNAIRE

Please read each item and tick the one response that applies best to you at the moment.

Prašome perskaityti kiekvieną elementą ir pažymėti atsakymą kuris šiuo metu jums labiausiai tinka.

1. My condition limits the places I can go
   Dėl savo būklės negaliu lankyti kai kuriose vietose, kur norėčiau
   a. Taip
   b. Ne

2. I sometimes feel like crying
   Kartais aš jaučiuosi , lyg norėčiau verkti
   a. Taip
   b. Ne

3. I have difficulty dressing
   Man sunku apsirengti
   a. Taip
   b. Ne

4. I struggle to do jobs around the house
   Man sunku dirbti namuose
   a. Taip
   b. Ne

5. It’s impossible to sleep
   Neįmanoma miegoti
   a. Taip
   b. Ne

6. I am unable to join in activities with my friends/family
   Aš negaliu prisijungti prie veiklos su draugais / šeima
   a. Taip
   b. Ne

7. I am tired all the time
   Aš visada esu pavargęs
   a. Taip
   b. Ne

8. I have to keep stopping what I am doing to rest
   Turiu sustabdyti tai, ką darau, norėdamas pailsėti
   a. Taip
   b. Ne

9. I have unbearable pain
   Aš jaučiu nepakeliamą skausmą
   a. Taip
   b. Ne

10. It takes a long time to get going in the morning
    Ryte man reikia daug laiko, kol išsijudinu
    a. Taip
    b. Ne

11. I am unable to do jobs around the house
    Aš negaliu dirbti namuose
    a. Taip
    b. Ne

12. I get tired easily
    Aš greitai pavargstu
    a. Taip
    b. Ne

13. I often get frustrated
    Aš dažnai jaučiu musivylmą
    a. Taip
    b. Ne

14. The pain is always there
    Man visada skauda
    a. Taip
    b. Ne
15. I feel I miss out on a lot
   *Aš manau kad aš esu daug ko netiekęs dėl savo ligos*
   a. Taip
   b. Ne

16. I find it difficult to wash my hair
   *Man sunku išsilauti galvą*
   a. Taip
   b. Ne

17. My condition gets me down
   *Mano būklė mane žlugdo*
   a. Taip
   b. Ne

18. I worry about letting people down
   *Aš nerimauju, kad nuviliu aplinkinius žmones*
   a. Taip
   b. Ne

LABAI AČIU 😊