DOI 10.26724/2079-8334-2022-4-82-12-16
UDC 616.5-004.1-092

Obadeh Mahmoud Al-Omary
National Pirogov Memorial Medical University, Vinnytsia

OPTIMIZATION OF COMPLEX THERAPY OF PATIENTS WITH LOCALIZED SCLERODERMA

e-mail: dr.obadaomari@yahoo.com

In this article, we consider the most important aspects and features of the treatment of patients with a diagnosis of localized scleroderma. In the course of the disease, there is a violation of the metabolism of connective tissues with the development of hyperproduction of collagen by fibroblasts. One of the reasons for this condition is a violation of the ratio of oxidants and antioxidants. The aim of the work was to increase the efficiency of diagnosis and treatment of localized scleroderma based on the study of endothelial, endotoxic and pro-oxidant metabolic disorders in patients, their relationship with the severity of the disease and the effectiveness of pharmacotherapy. The paper investigates the role of endothelial disorders, oxidative stress and endotoxicosis in the pathogenesis of localized scleroderma. The connection of certain metabolic disorders with the severity of the disease and clinical forms of dermatosis was revealed. It should be noted that the use of complex therapy, which included the appointment of L-arginine, an antioxidant drug – thioctic acid, colloidal silicon dioxide, ultraphonophoresis with hyaluronidase, corrected metabolic disorders in the body of patients with localized scleroderma, reduced the levels of endothelial markers, manifestations of endotoxicosis, restored the balance in the system of pro- and antioxidants, reduced the intensity of free radical oxidation processes. The proposed complex therapy of dermatosis in comparison with other proposed methods of treatment of scleroderma shows high clinical effectiveness, shortens the treatment period and prolongs the clinical remission of dermatosis.

Key words: localized scleroderma, methods of diagnosis and treatment, endotoxicosis, oxidative stress, endothelial dysfunction, treatment results.

Обадех Махмуд Ал-Омарі

ОПТИМІЗАЦІЯ КОМПЛЕКСНОЇ ТЕРАПІЇ ХВОРИХ НА ВОГНИЩЕВУ СКЛЕРОДЕРМІЮ

У даній статті ми розглядаємо найважливіші аспекти та особливості лікування пацієнтів з діагнозом вогнещевої склеродермії. У перебігу захворювання відзначають порушення метаболізму сполучної тканин з розвитком гіперпродукції колагену фібробластами, причому, однією з причин данного стану є порушення співвідношення оксидантів та антиоксидантів. Метою роботи було підвищити ефективність діагностики та лікування вогнищевої склеродермії на основі вивчення ендотеліальних, ендотоксичних та прооксидантних метаболічних порушень у пацієнтів, їх зв'язку з важкістю захворювання та ефективністю фармакотерапії. У роботі досліджено роль ендотеліальних порушень, оксидативного стресу та ендотоксикозу в патогенезі вогнищевої склеродермії. Виявлено зв'язок окремих метаболічних порушень зі ступенем важкості захворювання, клінічних форм дерматозу. Слід відмітити, що застосування комплексної терапії, яка включала призначення L-аргініну, препарату антиоксидантної дії – тіоктова кислота, кремнію діоксиду колоїдного, ультрафонофорезу з гіалуронідазою коригувало метаболічні порушення в організмі хворих на вогнищеву склеродермію, зменшувало рівні ендотеліальних маркерів, прояви ендотоксикозу, відновлювало баланс в системі про- та антиоксидантів, зменшувало інтенсивність процесів вільнорадикального окиснення. Запропонована комплексна терапія дерматозу в порівнянні з іншими запропонованними методами лікування склеродермії виявляє високу клінічну ефективність, скорочує строки лікування та продовжує клінічну ремісію дерматозу.

Ключові слова: вогнищева склеродермія, методи діагностики та лікування, ендотоксикоз, оксидативний стрес, ендотеліальна дисфункція, результати лікування.

The work is a fragment of the research project "New aspects of diagnosis, course and development introduction into practice of modern methods of complex treatment of chronic dermatoses and STDs", state registration No. 0119U000712.

Localized scleroderma is the second most common, after lupus erythematosus, a disease from the group of diffuse connective tissue diseases. Its prevalence is 32–45 cases per 100000 population [1, 3].

The treatment of localized scleroderma is a difficult clinical task due to the complex pathogenesis of this pathology, so currently, the therapy of this disease is complex. It is carried out by taking into account the dominant clinical and pathogenetic phenotype [2, 4, 6]. Standard therapies currently used are not effective enough and have limited opportunities to improve the prognosis of scleroderma. Therefore, the task of studying and implementing new approaches to therapy remains relevant [2, 5, 8].

The purpose of the study was to investigate the methods of treatment of patients with localized scleroderma and optimize the approach to complex therapy.

Materials and methods. The study was performed on the basis of National Pirogov Memorial Medical University, Vinnytsia and "Vinnytsia Regional Clinical Skin and Venereological Center of the Vinnytsia Regional Council". Laboratory examinations were performed on the basis of the educational and scientific laboratory of the Bukovyna State Medical University (certificate of re-certification No. 55/17 dated 26.12.2017). The work is based on long-term clinical observation during the 1st from 2019 to 2021. All patients were divided into groups according to the specific goal, tasks, and also the method of treatment: 78 patients with localized

scleroderma (the main group, of which 40 received complex treatment, 38 people – basic treatment) and 35 practically healthy people (control group). We conducted a study where 78 patients with localized scleroderma aged 43.2±7.28 years, including 27 men and 51 women, were under prospective observation.

Basic treatment included the use of antifibrosis, detoxification, vasoactive drugs, vitamins according to standard methods. Physiotherapy methods were also used in the treatment of patients with localized scleroderma, and the effectiveness of the combined pharmacotherapeutic method of treating patients with localized scleroderma was studied, including traditional therapy, as well as additionally L-arginine, colloidal silicon dioxide, an antioxidant drug – thioctic acid, and ultraphonophoresis with hyaluronidase. In the comparison group (n=38, 48.7 %), treatment was prescribed in accordance with clinical recommendations for this nosology (penicillin-G 1 million units intramuscularly twice a day for 10 days, lidase 64 units 1.0 ml intramuscularly through day 10 doses, vitreous body 2 ml intramuscularly every other day 10 doses, vitamins A and E 1 capsule 1 time a day for 4 weeks, xantinol nicotinate 1t three times a day for 4 weeks. This group was also prescribed local treatment with hydrocortisone ointment twice a day for 4 weeks.). In the main group (n=40, 51.3 %), patients received basic treatment with the addition of L-arginine – tivortin (Yuria Pharm, Ukraine) 1 spoonful twice a day for 2 weeks, colloidal silicon dioxide – eliminal gel (Orisyl Pharm, Ukraine) 1 drop twice a day one hour before meals for 2 weeks, thioctic acid – alpha lipone (Kyiv Vitamin Factory, Ukraine) 300 mg once a day 30 minutes before breakfast for 2 weeks, as well as ultraphonophoresis with hyaluronidase 3000 IU (PB Serum, Spain) once a day for 7 procedures.

The effectiveness of the therapy was evaluated according to the dynamics of the international, highly valid scleroderma activity index mLoSSI (Modified Localized Scleroderma Severity Index). With the help of this index, it is possible to assess the severity of clinical symptoms of localized scleroderma.

A global assessment using a 100-mm Visual Analog Scale (VAS) was also conducted – Global assessment using a 100-mm visual analog scale (PhysGA-A). The direction was to define clinical and laboratory signs according to consensus. Disease activity was defined as the degree and severity of adverse manifestations.

Dermatology Life Quality Index – DLQI (Dermatology Life Quality Index) is a reliable and proven quality of life indicator, developed for use in patients with skin diseases. The DLQI consists of 10 questions about how the skin disease has affected the patient's quality of life in the past week, in each of 10 domains, with 4 possible answers with a score of 0–3 (score range 0–30).

For statistical analysis of the obtained results, we used Statistica for Windows version 6.0 (Stat Soft inc., USA) and Epi Info 2000 software package, version 3.3.2. The normality of the distribution was checked using the Kolmogorov-Smirnov test. Significance of difference was determined using Student's t-test and Fisher's F-test for parametric data.

The assessment of treatment effectiveness was carried out taking into account the effects of treatment, absolute (AR) and relative (RR) therapeutic effects, therapeutic benefit – difference in absolute risk (ARR), changes in relative risk (RRR), as well as the odds ratio (OR) of drugs, with the calculation of confidence intervals and reliability criterion for RR and OR. At $p<0.05$, differences were considered statistically significant [5].

Results of the study and their discussion. Data on the absolute, attributable, relative risk, as well as the odds ratio of developing localized scleroderma in women are shown in Table 1.

Table 1

Absolute and relative risk of localized scleroderma development in female patients

Group	AR, %	ARR, %	RR [95 %CI]	OR [95 %CI]
Women (n=51)	65.0	50.0	1.31 [1.01–1.69] p	1.89 [1.03–3.48] p<0.05
Men (n=27)				

* AR – absolute risk; ARR – absolute relative risk; OR – odds ratio; RR – relative risk.

There was a significant relative risk (1.31 [1.01-1.69], $p<0.05$) and odds (1.89 [1.03-3.48], $p<0.05$) of developing localized scleroderma in women with an attributable risk of 50.0 % compared to men. The age of patients ranged from 10 to 81 years.

Interesting was the data on the number of young patients (under 20 years), whose share was 15.4 %, decreasing almost twice after 20 years and up to 35 (9.0 %). At the same time, the number of patients with localized scleroderma increased significantly after 35 to 55 years (23.5 %). The largest number, almost half of the sample, were elderly patients (55–70 years) – 43.6 %. Patients of senile age accounted for 9.0 % of the total sample of patients with localized scleroderma. In addition, by place of residence, urban residents prevailed over patients living in rural areas (56–71.8 % vs. 22–28.2 %), fig. 3.

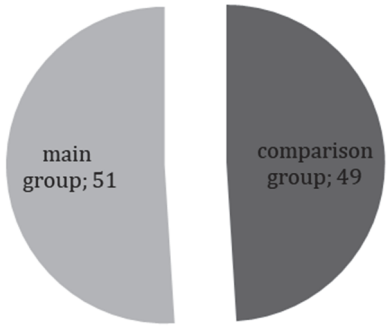

Fig. 1. Distribution of groups of patients with localized scleroderma (n=78) included in the study, depending on the prescribed treatment.

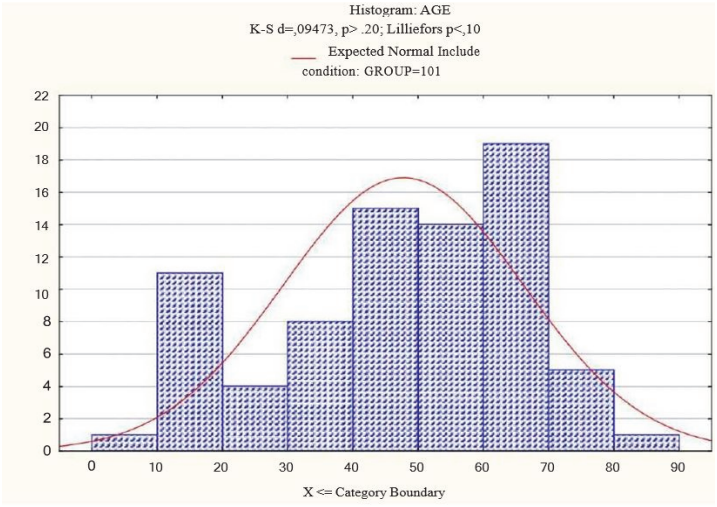

Fig. 2. Histogram of distribution of patients with localized scleroderma (n=78) by age groups.

The duration of the disease at the beginning of treatment was analyzed. It varied from 6 months to 10.5 years (mean 4.32±2.59 years). Patients with disease duration from 2 years to 6 years prevailed in the study (40 patients, 51.3 %). Less often it was more than 6 years (21 patients, 26.9 %). In some patients, the diagnosis was verified with the duration of the disease up to 2 years (17 people, 21.8 %). Thus, the data clearly indicate the late treatment and late diagnosis of the disease in 78.2 % of patients (Fig. 4).

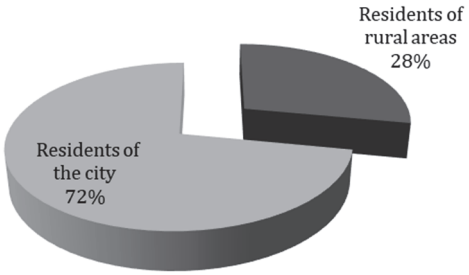

Fig.3. Distribution of patients included in the study by place of residence.

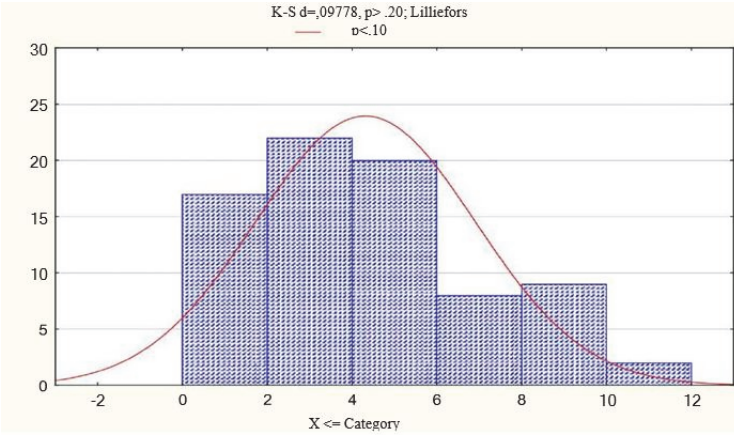

Fig.4. Histogram of distribution of patients with localized scleroderma by the disease duration.

Thus, it can be said that the primary occurrence of localized scleroderma is associated with the existing certain age peculiarity of this pathology – men are more likely to suffer at a young age, but after 55 years this disease is predominantly “female” (Table 2).

Table 2

Occurrence of localized scleroderma in men and women by age groups

Age	Women (n=51)		Men (n=27)		p
	Abs.	%	Abs.	%	
up to 20 years	6	11.8	6	22.2	<0.05
20–35	4	7.8	3	11.1	>0.05
35–55	6	11.8	12	44.5	<0.05
55–70	29	56.8	5	18.5	<0.05
Over 70	6	11.8	1	3.7	<0.05

Notes: p – the probability of difference between comparison groups.

In the work of Fomin O. A. et al. the results of the performed studies indicate the high clinical efficacy of extracorporeal photochemotherapy ECP in patients with localized scleroderma resistant to previous drug therapy. The greatest clinical effect was achieved in patients in the early stages of the disease, regardless of the severity of the pathological process. In 36.85 % of patients there was a complete disappearance of edema and peripheral corolla, a significant decrease in the density of the foci, in 63.15 % – pale reduction of the peripheral growth corolla and edema, a decrease in the density of the foci. In one

patient with signs of systemic disease, the density of the lesions remained, but the progression of the skin process stopped. All patients noted the disappearance of itching and skin tightness [5, 6].

The high efficacy of ECP was also demonstrated in a multicenter study in a comparative study with D-penicillamine. A significant reduction in the area of skin lesions after six months of treatment was found in 68 % of patients treated with ECP, and only in 32 % treated with D-penicillamine [1, 9]. R. Buense and colleagues [9] also noted a significant improvement in the skin and joint process in patients with localized scleroderma and a disease course of less than two years who received ECP in a randomized, double-blind, placebo-controlled study of 64 patients. A. X. Du et al. applied this method in the treatment of a patient with localized scleroderma and achieved a stable remission [10]. L. Pérez- Carmona et al. investigated the use of ECP in eight patients with systemic and localized scleroderma. As a result of treatment, an improvement in the course of the skin process was observed. A more pronounced clinical effect was obtained in patients with a duration of the disease not exceeding two years [8].

In the work of K. Krasagakis et al. improvement of the skin process after treatment with ECP was observed in 8 of 16 patients, with no changes – in three, in five patients the disease continued to progress, and its duration was more than two years. In five patients, immunosuppressive drugs could be discontinued on the background of ECP. As a result of the analysis, the authors concluded that ECP is an effective treatment if it is used in the initial stages of the disease [10].

Among other areas of treatment of localized scleroderma today is promising to influence the level of toxic and metabolic processes and antioxidant therapy. However, such works are rare. In particular, in the works of M. A. Ata, combined therapy in patients with localized scleroderma included both traditional therapy with penicillin G 5.0 million units intramuscularly for 10–12 days, and treatment with antioxidants – ascorbic acid 10.0 % 2.0 ml intramuscularly for 10–15 days; nicotinic acid 1 % 1.0 ml intramuscularly for 10–15 days. Locally, the researchers used external treatment with Traumel C, applications with a solution of dimexide 1:4 (according to the standards of therapy of localized scleroderma), as well as additionally Thiotriazoline 2.5 % 4.0 ml intramuscularly for 10–15 days and Cytoflavin 10.0 ml per 200.0 ml of saline intravenously drip for 10 days with subsequent transition to the tablet form. It has been proven that the introduction of complex therapy has a higher therapeutic efficacy (68.2 %) compared to the use of the components of the method and is accompanied by an improvement in the general condition of patients [5, 8, 10]. The criteria for the effectiveness of treatment of cutaneous scleroderma are the cessation of disease progression, reduction of erythema, edema, reduction of thickening and thickening of the skin, as well as other symptoms; elimination or reduction of subjective sensations [7, 9].

It should also be remembered that the treatment of each patient should be selected individually, depending on the form, stage and severity of the disease, as well as the localization of lesions [9]. The aim of therapy is to prevent the further development of sclerosing inflammation [6, 7]. In the active process, the number of courses should be at least 6, with an interval of 1–2 months; if the process has stabilized, the interval between courses of treatment is increased to 4 months; in case of residual clinical manifestations and for prevention purposes, therapy is carried out 2–3 times a year with drugs that improve microcirculation [10].

Conclusion

It has been established that the primary occurrence of localized scleroderma is not only gender-related, but there are also certain age characteristics of this pathology - men are more often affected at a young age (up to 20 years, 22.2 % of the examined), but at the age of 55–70 and among patients women over the age of 70 likely predominated (56.8 % versus 18.5 %, 11.8 % versus 3.7 %). The absolute risk of BC at the age of 55 among men reached 78.0 %, (RR – 2.48 [1.58–3.90], OR – 7.66 [2.59–22.6], $p<0.05$). The average duration of the disease at the time of initial treatment was 4.32±2.59 years. In general, among all the examined, a late referral for localized scleroderma was established – 78.2 % (after 2 or more years after the onset of the disease). Women applied earlier, compared to men – 29.4 %, among men the proportion of early applications was only 7.4 % (hypertensive disease (20.5 %), diabetes (10.3 %) and diseases gastrointestinal tract – (17.9 %), chronic pyelonephritis (2.6 %) and chronic bronchitis (5.1 %) are among the foci of chronic infection. Among the clinical forms of focal scleroderma, the largest part of cases (70.5 %) was the plaque form. In several cases, a linear form was observed (15.4 %). Some patients were diagnosed with scleroatrophic lichen (9.0 %) and idiopathic Pazini-Pierini atrophoderma (5.1 %). Based on the analysis of the gender characteristics of the clinical forms of scleroderma, it was established that the plaque form of scleroderma prevailed significantly more often in women (80.3%), the linear form and scleroatrophic lichen – in men (22.2 % each). According to the stages of development of the pathological process, most patients (61.0 %) had a thickening stage, and some patients – had an atrophy stage (8.0 %). The number of lesions on the skin varied from 1 to 5 (average number of foci 2.8±1.12). Almost half of the patients had three foci (34 people, 43.6 %). There were 23.1 % of patients with one focus (18 people), with two –16.7 % (13 people), four – 11.5 % (9 people), and 4 patients had five or more foci (5.1 %).

References

1. Adler S, Huscher D, Siegert E, Allanore Y, Czirják L, DelGaldo F et.al. Systemic sclerosis-associated interstitial lung disease – individualized immunosuppressive therapy and course of lung function: results of the EUSTAR group. Arthritis Res Ther. 2018; 20: 17. doi: 10.1186/s13075-018-1517
2. Albuquerque JV, Andriolo BN, Vasconcellos MR, Civile VT, Lyddiatt A, Trevisani VF. Interventions for morphea. Cochrane Database Syst Rev. 2019; 7 (7): CD005027.
3. Antoniou KM, Trachalaki A, Tzouvelekis A, Poletti V, Vasarmidi E, Sfikakis et.al. A role of antifibrotics in the treatment of Scleroderma-ILD. Pulmonology. 2020; 26 (1): 1-2. doi: 10.1016/j.pulmoe.2019.08.004.
4. Berger M, Steen VD. Role of anti-receptor autoantibodies in pathophysiology of scleroderma. Autoimmun Rev. 2017; 16(10): 1029-1035. doi: 10.1016/j.autrev.2017.07.019. Epub 2017 Aug 1.
5. Jordan S, Distler JH, Maurer B. EUSTAR Rituximab study group. Effects and safety of rituximab in systemic sclerosis: an analysis from the European Scleroderma Trial and Research (EUSTAR) group. Ann Rheum Dis. 2013; 74(6): 1188-94. doi:10.1136/annrheumdis-2013-204522
6. Kajihara I, Jinnin M, Honda N. Scleroderma dermal fibroblasts overexpress vascular endothelial growth factor due to autocrine transforming growth factor β signaling. Mod. Rheumatol. 2013; 23 (3): 516-524. doi: 10.1007/s10165- 012-0698-6.
7. Shroff A, Mamalis A, Jagdeo J. Oxidative Stress and Skin Fibrosis. Curr. Pathobiol. Rep. 2014; 2 (4): 257-267. doi: 10.1007/s40139-014-0062-y
8. Thakkar V, Patterson KA, Stevens W. Increased serum levels of adhesion molecules ICAM-1 and VCAM-1 in systemic sclerosis are not specific for pulmonary manifestations. Clin Rheumatol. 2018; 37(6):15631571. doi: 10.1007/s10067-018-4081-7.
9. Tolkachjov SN, Patel NG, Tollefson MM. Progressive hemifacial atrophy: a review. Orphanet J Rare Dis. 2015; 10: 39. doi: 10.1186/s13023-015-0250-9.
10. Tsou PS, Sawalha AH. Unfolding the pathogenesis of scleroderma through genomics and epigenomics. J. Autoimmun. 2017; 83: 73-94. doi: 10.1016/j.jaut.2017.05.004.

Стаття надійшла 11.12.2021 р.

DOI 10.26724/2079-8334-2022-4-82-16-20
UDC 616.38–089:316.346.32-053.9

B.D. Akhverdiev
Yevlakh Central District Hospital, Yevlakh, Azerbaijan

FRAILTY INDEX AND INFLAMMATORY MARKERS IN ELDERLY PATIENTS WITH ACUTE SURGICAL ABDOMINAL PATHOLOGIES

e-mail: mic_amu@mail.ru

The purpose of the study was to reveal the relationship between the frailty index and inflammation markers in elderly patients with acute surgical abdominal pathologies. 118 elderly and senile patients (average age was 69.5±0.6 years) were involved in the study. Immediately after admission, the levels of C-reactive protein and interleukin-6 were determined. In addition, at the stage of inclusion of patients in the study, the frailty index was determined using the Edmonton scales. Mean frailty index was 9±0.3. Leukocytes (r=0.574; p=0.000), neutrophils (r=0.434; p=0.000), erythrocyte sedimentation rate (r=0.210; p=0.008), C-reactive protein (r=0.203, p=0.006) and interleukin-6 (r=0.347, p=0.004) had a positive correlation with frailty index. Clinicians evaluating elderly patients with acute abdominal disease should always be aware that elevated serum levels of C-reactive protein and interleukin-6 may be part of the chronic process associated with frailty syndrome in the elderly.

Key words: frailty index, C-reactive protein, interleukin-6, Edmonton scales, acute abdominal diseases.

Б.Д. Ахвердієв

ІНДЕКС «КРИХКОСТІ» І МАРКЕРИ ЗАПАЛЕННЯ У ХВОРИХ ПОХИЛОГО ВІКУ З ГОСТРОЮ ХІРУРГІЧНОЮ АБДОМІНАЛЬНОЮ ПАТОЛОГІЄЮ

Метою дослідження було виявлення зв'язку між індексом «крихкості» та маркерами запалення у хворих похилого віку та літнього віку з гострими абдомінальними патологіями, що потребують оперативного втручання. До дослідження було залучено 118 хворих похилого та старечого віку із гострими захворюваннями органів черевної порожнини (середній вік склав 69,5±0,6 років). Відразу після надходження визначалися рівні С-реактивного білку та інтерлейкіну-6, а також індекс «крихкості» із застосуванням шкали Едмонтон. Середнє значення індексу «крихкості» склало 9±0,3. Лейкоцити (r=0,574; p=0,000), нейтрофіли (r=0,434; p=0,000), швидкість осідання еритроцитів (r=0,210; p=0,008) С-реактивний білок (r=0,203, p=0,006) 6 (r=0,347, p=0,004) мали позитивний кореляційний зв'язок з індексом «крихкості». Клініцисти, які проводять оцінку пацієнтів похилого віку з гострими захворюваннями органів черевної порожнини, повинні враховувати, що підвищені рівні С-реактивного білка та інтерлейкіну-6 у сироватці можуть бути пов'язані з «крихкістю» пацієнтів.

Ключові слова: індекс «крихкості», С-реактивний білок, інтерлейкін-6, шкала Едмонтон, гострі абдомінальні захворювання.

Recently, there has been an increase in the number of elderly and senile people worldwide. According to the World Health Organization, people aged 65 and over now make up more than 10 % of the world's population, with 125 million people over the age of 80. The average life expectancy is 74.4 years for men and 81.8 years for women. Between 2015 and 2050, the share of the population over 60 years