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B.D. Akhverdiev

Yevlakh Central District Hospital, Yevlakh, Azerbaijan

## FRAILITY 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  $69.5 \pm 0.6$  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  $9 \pm 0.3$ . 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  $69,5 \pm 0,6$  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  $9 \pm 0,3$ . 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 ( $r=0,203$ ,  $p=0,006$ ) і інтерлейкіну-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

of age is projected to double to 22 % of the total world population. By 2050, 80 % of older people will live in low- and middle-income countries [15].

In connection with the increase in the proportion of elderly people, the incidence of acute diseases of the abdominal organs, requiring surgical interventions is correspondingly growing. The tactics of surgical treatment of old patients are significantly different from operations in young people [5, 12]. One of the distinguishing criteria in old patients is frailty, which appears with age and is observed as a weakening of the intensity of the functions of various organs and functional systems. The frailty index (FI) measures the health status of aging people [7, 13].

Despite the growing interest in the frailty index among surgeons, information about the relationship between the pathophysiological changes in the inflammatory process underlying acute abdominal pathologies and frailty is rather contradictory. There is a variety of data demonstrating the role of pro-inflammatory cytokines, which can directly influence frailty by promoting protein degradation or indirectly by affecting important metabolic mechanisms. Some authors have identified a direct relationship between frailty and elevated levels of certain inflammatory markers, regardless of common chronic disease conditions [1, 3]. In contrast, other studies have found that these markers do not predict frailty in the elderly [9].

**The purpose** of the study was to reveal the relationship between the frailty index and inflammation markers in senile and elderly patients with acute abdominal pathologies requiring surgical intervention.

**Materials and methods.** The study involved 118 elderly and senile patients with acute diseases of the abdominal organs, who received treatment at the Yevlakh Central District Hospital (Yevlakh, Azerbaijan) in the period from 2020 to 2021. The mean age of the patients was  $69.5 \pm 0.6$  years (62–87 years). There were 77 men out of 118 (65.3 %), women 41 out of 118 (34.7 %). The period from the moment the first complaints appeared to hospitalization was  $7.1 \pm 0.5$  days. 101 patients out of 118 (86.6 %) were taken to the hospital privately by relatives, 16 out of 118 (14.4 %) by the ambulance. The distribution of patients according to diagnoses is presented in fig. 1.

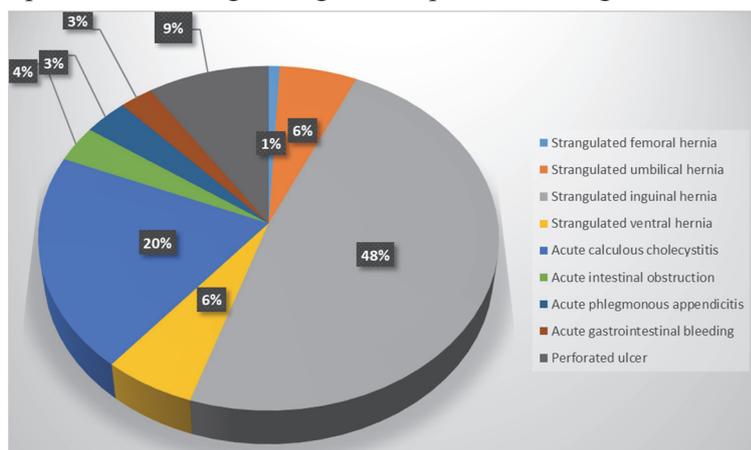


Fig. 1. The main diagnoses of patients with abdominal pathology

Immediately after admission, all patients underwent a general and biochemical blood test, urine and feces, radiological and additional studies according to indications. After preoperative preparation, all patients underwent surgery according to indications. Postoperative complications were studied according to the Clavien-Dindo classification [4].

Among the inflammatory factors, the levels of C-reactive protein (CRP) and interleukin-6 (IL-6) were determined by enzyme immunoassay as the most informative markers.

In addition, the frailty index (FI) was determined. The fragility index was calculated at the stage of inclusion of patients in the study: the Edmonton Frail Scale (EFS). The maximum allowable score is 17 [9]. A patient who scores 8 or more is considered frailty. According to the results obtained, 5 categories were distinguished: index  $\leq 5$  – absence of senile frailty; index within 6–7 – tendency to senile frailty; index within 8–9 – mild degree; index within 10–11 – average degree; within 12–17 – a severe degree of senile frailty.

In cases where patients did not have the opportunity to answer questions, a close relative living with the patient was involved in the process. If the relatives of the patient did not give satisfactory information, the Edmonton index was studied as soon as the patients regained consciousness after anesthesia as soon as possible after the operation.

All parameters and data were collected in an Excel spreadsheet and then submitted for processing using the IBM SPSS-20 program. Continuous variables were expressed as mean  $\pm$  median ( $M \pm m$ ), and minimum (min) and maximum (max) values were reported. Categorical variables are expressed as actual numbers and their percentages. Statistical analysis was performed using the non-parametric Mann-Whitney U-test. Correlation relationships between the parameters were found out by the method of pair correlation (with the calculation of the Spearman coefficient). Values were considered statistically significant at  $p < 0.05$ .

**Results of the study and their discussion.** During the examination, the following concomitant diseases were revealed in patients: arterial hypertension – in 47 (39.8 %); chronic ischemic heart disease – 13 (11 %); diabetes mellitus – in 12 (10.2 %); obesity – 38 (32.2 %); prostate adenoma (in men) – in 3 (2.5 %); ovarian cyst (in women) – in 3 (2.5 %); chronic venous insufficiency of the lower extremities – in 3 (2.5 %); arterial occlusive disease – in 7 (5.9 %); anemia – in 2 (1.7 %); chronic bronchitis – in 79

(66.9 %); chronic obstructive pulmonary disease – in 1 (0.8 %); chronic kidney disease – in 2 (1.7 %); chronic liver diseases – 7 (5.9 %). Among the total number of patients, 1 concomitant disease was detected in 71 (60.2 %); 2 concomitant diseases – in 35 (29.7 %); 3 – in 9 (7.6 %); 4 – in 3 (2.5 %) examined.

All patients admitted with acute pathology underwent appropriate surgical intervention after diagnosis. The average duration of the intervention was 70.2±4.1 minutes, anesthesia – 105.3±4.2 minutes. General endotracheal anesthesia was used in 57 out of 118 (48.3 %) patients, local anesthesia with intravenous sedation – in 4 (3.4 %) patients, spinal anesthesia – in 57 (48.3 %) patients. The percentage of surgery interventions in patients with abdominal pathologies was shown in Table 1.

Table 1

#### Types of surgery in elderly and senile patients

Types of surgery	Absolute number	%
Open cholecystectomy	3	2.5
Appendectomy	4	3.4
Elimination of intestinal obstruction	1	0.8
Disconnection of adhesions, terminal ileostomy	1	0.8
Herniotomy, Hernioplasty	69	58.5
Herniotomy, colon resection, colostomy	1	0.8
Laparoscopic cholecystectomy	21	17.8
Resection of the stomach	1	0.8
Resection of the small intestine, ileostomy	3	2.5
Suturing a perforated ulcer	10	8.5
Opening of a perianal abscess	1	0.8
Ligation of a bleeding vessel	2	1.7
Ligation of a bleeding vessel, colostomy	1	0.8
Total	118	100.0

After the surgery, all patients were transferred to the general ward after treatment in the intensive care unit. Complications were noted in 31 patients out of 118 (26.3 %): in 5 out of 118 (4.2 %) the complication resolved without any intervention (Clavien-Dindo 1); intensive medical treatment was performed in 23 of 118 (19.5 %) (Clavien-Dindo 2); 13 patients out of 118 (11 %) needed small and medium surgical procedures.

Non-surgical complications were detected in 48 patients (40.7 %): renal failure (oligo-/anuria) – in 15 (12.7 %); thrombophlebitis of the lower peripheral veins – in 30 (25.4 %); atelectasis, pneumonia – in 10 (8.5 %); hemodynamic instability – in 29 (24.6 %); transient encephalopathy – in 7 (5.9 %); pulmonary heart failure – in 11 (9.3 %); multiple organ failure – in 5 (4.2 %). 44 patients had one complication; 17 had 2 different complications; 7 patients had 3 complications. Only one patient had 4 complications at the same time.

In-hospital mortality was noted in 5 patients out of 118 (4.2 %). The cause of death of patients was mainly toxic shock, multiple organ failure, progressing against the background of deep intoxication. The total duration of bed-days of surviving patients was 3.5±0.5 days, varying from 5 hours to 18 days after surgery. The analysis of blood parameters revealed the following changes (Table 2).

Table 2

#### The features of general and biochemical blood tests in elderly and senile patients

Indicators	min	max	M	m
Hb	5.10	16.20	11.37	0.17
Leukocytes	3.00	16.21	7.04	0.24
Erythrocytes	2.00	11.00	4.37	0.12
Lymphocytes	0.27	7.15	2.17	0.07
Neutrophils	2.2	21.0	7.2	0.26
Platelets	75.0	850.0	252.51	7.64
ESR	12.0	40.0	13.27	0.32
CRP	26.2	87.4	61.48	12.45
IL-6	3.5	23.7	11.15	4.25

Note: Hb – hemoglobin (mg/dl); Leukocytes ( $\times 10^9/l$ ); Erythrocytes ( $10^{12}/l$ ); Lymphocytes ( $10^6/\mu L$ ); Neutrophils (%); Platelets ( $\times 10^3$ ); ESR – Erythrocyte sedimentation rate (mm/h), CRP – C-reactive protein (mg/L), IL-6 – interleukin-6 (pg/ml).

When determining the frailty index, the following results were obtained. The mean FI value was 9±0.3, patients were divided into 5 categories: index ≤5 – in 14 patients (11.9 %); index within 6–7 – in 38 patients (32.2 %); index within 8–9 – in 26 (22 %); index within 10–11 – in 21 patients (17.8 %); index within 12–17 – in 19 operated patients out of 118 (16.1 %).

The next step of statistical processing was to identify correlations between FI and the studied markers of inflammation.

According to the results obtained, among the parameters of the general blood test, leukocytes ( $r=0.574$ ;  $p=0.000$ ), neutrophils ( $r=0.434$ ;  $p=0.000$ ) and ESR ( $r=0.210$ ;  $p=0.008$ ) had a positive correlation with FI. Analysis of biochemical markers of inflammation revealed that FI significantly correlated with markers of inflammation: with CRP ( $r=0.203$ ,  $p=0.006$ ); with IL-6 ( $r=0.347$ ,  $p=0.004$ ).

Frailty is a multidimensional geriatric syndrome characterized by increased vulnerability to disease. The clinical syndrome of frailty in the elderly is characterized by low physical activity, weakness, exhaustion, and impaired physiological reserves of several organ systems [3]. The activation of inflammation associated with acute diseases, as well as neuroendocrine dysregulation, naturally lead to an increase in frailty, as evidenced by our data. They are consistent with the results of a number of researchers who have studied fragility in elderly patients with various pathologies [7, 8, 10]. Frailty in the elderly is correlated with higher serum levels of inflammatory biomarkers, which are inversely correlated with poor physical activity, muscle weakness, and increased disability.

Thus, Van Epps P. et al. obtained data similar to ours when studying the prognostic value of some inflammatory cytokines (IL-6 and TNFR1) for predicting mortality in the elderly. They revealed that frailty status has a stronger association with inflammation [14]. Soysal P. et al reviewed the evidence for an association between inflammation and frailty through a systematic review where, after reviewing many studies in this field, they concluded that frailty and premature weakness were associated with higher levels of IL-6, as well as with an increased level of leukocytes and fibrinogen [11]. However, there are some works that do not support these conclusions, not revealing a significant relationship between these markers [2, 9].

It should be noted that in our study, only one scale for evaluating the “fragility” index from all those presented in the literature was used. In international practice, there are works using many different model of frailty (Fried model, FRAGIRE, IVCF-20 etc.) [6, 9]. Nevertheless, the assessment of the frailty index with their help, according to experts, have some limitations, which gives incomplete information about severity of the syndrome. Also, the measurement of some components of the syndrome requires specialized equipment and/or training, which makes it difficult to use in primary care. In addition, the choice of the Edmonton Frail Scale in our work was also dictated by the fact that its use is not associated with special instrumental studies; the list of questions in the questionnaire can be asked and evaluated by the doctor on his own, which simplifies its use.

In our view, the assessment of inflammatory markers in the setting of frailty in the elderly may represent a useful screening test and a potential target for further intervention. Of course, a high concentration of more than one inflammatory marker may be more likely to predict the onset of weakness than a high concentration of just one marker. In this situation, the measurement of CRP along with IL-6 and their complex assessment together with some indicators of the general blood test can play the role of a predictor for the detection of frailty in the elderly.

### Conclusion

The mean FI in elderly patients with acute abdominal disease requiring surgical interventions was  $9 \pm 0.3$ . Analysis of biochemical markers of inflammation revealed that FI significantly correlated with markers of inflammation: with CRP ( $r=0.203$ ,  $p=0.006$ ); with IL-6 ( $r=0.347$ ,  $p=0.004$ ).

Clinicians evaluating elderly patients with acute abdominal disease should always consider in the differential diagnosis that elevated serum levels of CRP and IL-6 may be part of an underlying chronic inflammatory process associated with frailty syndrome in the elderly. The strategies applied in the prevention of fragility will undoubtedly have a significant positive impact on the prevention of adverse socio-economic consequences, both at the individual and at the population level.

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**O.M. Babii, N.V. Prolom, B.F. Shevchenko, A.M. Halinska, N.V. Poliak, O.V. Pakholka**  
SI "Institute of Gastroenterology of NAMS of Ukraine", Dnipro

## DIAGNOSIS AND CORRECTION OF COMPLICATIONS OF INSUFFICIENCY OF ANTI-REFLUX FUNCTION OF THE PHYSIOLOGICAL CARDIA IN HIATAL HERNIAS

e-mail: Aleksandr\_babiy@ukr.net

To improve the diagnosis and treatment of complications of the insufficiency of the antireflux function of the physiological cardia in hiatal hernias, an examination was performed on 78 patients. All patients underwent X-ray examination with determination of the type of hiatal hernia and endoscopic examination with detection of non-erosive reflux esophagitis – in 9 (11.5 %) patients, erosive reflux esophagitis in 16 (20.8 %), ulcers of the lower third of the esophagus in 3 (3.8 %), peptic stricture of the lower third of the esophagus in 3 (3.8 %), and Barrett's esophagus in 3 (3.8 %) patients. It is proposed to stage the treatment of complications of insufficiency of the antireflux function of the physiological cardia in hiatal hernias with the use of conservative therapy, hydrostatic balloon dilatation or argon plasma coagulation and prepare the patient for the second stage of treatment – antireflux surgery.

**Key words:** hiatal hernia, gastroesophageal reflux disease, reflux esophagitis, Barrett's esophagus, argon plasma coagulation, hydrostatic balloon dilatation.

**О.М. Бабій, Н.В. Пролом, Б.Ф. Шевченко, А.М. Галінська, Н.В. Поляк, О.В. Пахолка**

## ДІАГНОСТИКА ТА КОРЕКЦІЯ УСКЛАДНЕНЬ НЕДОСТАТНОСТІ АНТИРЕФЛЮКСНОЇ ФУНКЦІЇ ФІЗІОЛОГІЧНОЇ КАРДІЇ ПРИ ГРИЖАХ СТРАВОХІДНОГО ОТВОРУ ДІАФРАГМИ

Для покращення діагностики та лікування ускладнень недостатності антирефлюксної функції фізіологічної кардії при грижах стравохідного отвору діафрагми проведено обстеження у 78 хворих. Усім пацієнтам проведено рентгенологічне дослідження зі встановленням типу грижі стравохідного отвору діафрагми та ендоскопічного дослідження з виявленням неерозивного рефлюкс-езофагіту – у 9 (11,5 %) пацієнтів, ерозивного рефлюкс-езофагіту у 16 (20,8 %), виразки нижньої третини стравоходу у 3 (3,8 %), пептичної стриктури нижньої третини стравоходу у 3 (3,8 %) та стравоходу Барретта – у 3 (3,8 %) пацієнтів. Запропоновано етапність лікування ускладнень недостатності антирефлюксної функції фізіологічної кардії при грижах стравохідного отвору діафрагми із застосуванням консервативної терапії, балонної гідродилатації чи аргоноплазмової коагуляції та підготувати хворого до другого етапу лікування – антирефлюксного оперативного втручання.

**Ключові слова:** грижа стравохідного отвору діафрагми, гастроєзофагеальна рефлюксна хвороба, рефлюкс-езофагіт, стравохід Барретта, аргоноплазмова коагуляція, ендоскопічна балонна гідродилатація.

*The work is a fragment of the research project "To study the features of the complicated course of the hiatal hernia, gastroesophageal reflux disease, esophageal achalasia, stenosis of the gastroduodenal zone of ulcer genesis and to improve the methods of their surgical correction with the use of endolaparoscopic technologies", state registration No. 0119U102471.*

Cardia is an anatomical and functional formation of the gastroesophageal junction (crura of diaphragm, Laimer-Bertelli connective membrane, Gubarev valve, gastric bubble, angle of His) that provides its pulp-valve function. Insufficiency of the physiological cardia is accompanied by pathological reflux of gastric contents into the esophagus: gastroesophageal reflux disease (GERD), migration of a part of the stomach into the chest cavity – hiatal hernia (HH) [1, 2].