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Diagnostic significance of the lymphocyte-monocyte index in Dupuytren's contracture

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Abstract

Introduction World literature data indicate the involvement of inflammatory cells in the pathogenesis of palmar fascial fibromatosis. However, there are no data on possible changes in peripheral blood leukocyte indices in patients with Dupuytren's contracture (DC) in comparison with healthy people. **Aim** To assess the diagnostic significance of neutrophil-lymphocyte (N/L) and lymphocyte-monocyte (L/M) indices of peripheral blood in patients with CD. **Materials and methods** 162 medical records of patients admitted for surgical treatment were retrospectively studied. To compare the results of their peripheral blood tests with the norm, anonymous leukocytograms of 110 apparently healthy individuals (control) were used. **Results** In the group of healthy people and in patients with DC, sexual dimorphism of the absolute content of neutrophils was expressed. In DC males, a statistically significant decrease in the absolute content of lymphocytes ($p = 0.05$) was found, and in females, a significant increase in the absolute content of monocytes ($p = 0.00$) compared with the control, while in patients with DC there was no gender-related difference in these indicators, typical for healthy people. N/L ratio was elevated in DC males compared with controls ($p = 0.05$) and a subgroup of DC females ($p = 0.01$), but according to the results of ROC analysis, N/L ratio turned out to be diagnostically useless. For the model "L/M – degree of contracture" AUC 0.945, CI 0.918-0.970, $p = 0$, Se 90.12, Sp 93.21; optimal threshold L/M 3.102. In patients with low L/M (⩽ 3.0), the frequency of lesions in both hands and the frequency of grade III-IV contractures are higher by 27.75 % ($p = 0.02$) and 27.15 % ($p = 0.03$), respectively than in the high L/M subgroup. **Discussion** The multidirectional changes in the content of lymphocytes and monocytes in males and females is consistent with the literature data on dual gender-specific ways of regulating the immune system in healthy people and in patients with various diseases. **Conclusion** The findings of the studied sample of patients show that the lymphocyte-monocyte index is a useful additional laboratory indicator for identifying a risk group for severe fascial fibromatosis. It can be used in clinical practice at no additional cost along with the well-known Dupuytren diathesis criteria to identify a risk group for progression of Dupuytren's contracture.

Keywords: Dupuytren's contracture, diagnosis, neutrophil-lymphocyte index, lymphocyte-monocyte index

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INTRODUCTION

Dupuytren's disease is traditionally described as a benign fibromatosis of the palmar aponeurosis that can spread into the subcutaneous tissue and dermis [1]. At an early stage, the disease is manifested by the formation of nodules, followed by contractile fibrous chords covering part of the palmar fascia and causing limitation of extensor movements, and then persistent contractures of one or more fingers of the hand [2].

The incidence of Dupuytren's disease, according to current meta-analyses, affects on average 8 % of the world population [3] and 20 % of persons over 65 years of age [4]. Occasionally, the disease affects young people and even children [5]; but during the fifth or eighth decade of life, its incidence progressively increases. Males are affected 3-4 times more frequently [6]. According to the clinics of hand surgery, the contracture is detected only in 8 % of patients with palmar fascial fibromatosis older than 18 years [7]. However, conservative therapy of early manifestations of Dupuytren's disease does not have a sufficient evidence base [8].

A wide range of techniques has been developed for minimally invasive and open surgeries aimed at dissecting chords or removing pathological foci, as well as at hand deformity correction. However, the problems of postoperative complications and recurrence have not been solved so far [9]. Of particular difficulty is the treatment of patients with contracture stage III-IV [10].

Risk factors for the disease include bad habits, manual labor and hand trauma, epilepsy, diabetes, and genetic predisposition; however, the etiopathogenesis of fascial fibromatosis remains undiscovered, despite a significant number of publications on molecular biology and pathomorphology of fibromatosis [11].

The main role in the formation of collagen deposits and contraction of fibrous chords is played by fibroblasts and myofibroblasts [12, 13]. The pathogenetic significance of microvascular alteration and perivascular infiltration by inflammatory cells [14], as well as remodeling of small-caliber arteries that

perforate the palmar aponeurosis, and distal neuropathy of sensory nerves [15, 16] have been established. Immunohistochemical studies showed a correlation between the number of myofibroblasts and macrophages in fibromatous nodes; lymphocytes are typically located around fibromatous foci [17]. Based on examination of 21 DC patients, a correlation was established between the content of T- and B-lymphocytes in peripheral blood and the severity of the disease [18]. In ectopic fascial fibromatosis, Peyronie's disease, a correlation was found between the values of the peripheral blood neutrophil-lymphocyte index and the acute or stable stage of the disease [19]. However, in the available literature, we did not find data on possible changes in the ratios of neutrophils, lymphocytes, and peripheral blood monocytes in Dupuytren's contracture.

Purpose Assessment of the diagnostic significance of neutrophil-lymphocyte (N/L) and lymphocyte-monocyte (L/M) indices of peripheral blood in patients with Dupuytren's contracture (CD).

MATERIALS AND METODS

We retrospectively studied 162 medical records of DC patients who were surgically treated on at the Ilizarov National Medical Research Center for TO in the period from 2013 throughout 2020, analyzed the data of anamnesis and disease, their clinical and laboratory tests. To compare the results of peripheral blood tests with the norm, we used anonymized leukocytograms of 110 apparently healthy individuals obtained during periodic preventive medical examinations. Criteria for inclusion in the comparison group were a clinical DC diagnosis and histologically confirmed palmar fascial fibromatosis. Exclusion criteria were hand injuries, diabetes mellitus and chronic inflammatory diseases of the respiratory, digestive and genitourinary systems in the anamnesis. Criterion for inclusion in the control group was the absence of laboratory signs of acute or chronic inflammation.

The study was approved by the ethics board of the institution (protocol No. 2 (57) dated March 19, 2018), and was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki 2013.

Based on the literature data on the sexual dimorphism of the leukocyte formula [20] in healthy people, the comparison and control groups were divided into subgroups of males and females and stratified by age. Using their leukocytograms, the absolute number of neutrophils, lymphocytes and monocytes was calculated in the Excel 2010 program along with their ratios: neutrophil-lymphocyte and lymphocyte-monocyte indices.

Statistical processing of the obtained quantitative data was carried out using the Attestat program version 9.3.1 (designed by I.P. Gaydyshev, certificate of registration with Rospatent No. 2002611109). The Shapiro-Wilk test was used to check the normality of the distribution of clinical and laboratory parameters. Due to the deviation of the distribution of some samples from the normal law, table data are presented as medians and quartiles. Hypotheses about differences in variables in subgroups were tested using the Mann-Whitney test and Fisher's exact method. Possible relationships between clinical and laboratory parameters were tested using Pearson's test. To assess the diagnostic significance of leukocyte indices, ROC analysis was used with an estimate of the area (AUC) under the specificity and sensitivity curve of the test. Possible differences in distribution functions were checked using the Smirnov test.

RESULTS

The laboratory tests showed that the absolute content of peripheral blood neutrophils was significantly higher in men, both in the subgroups of DC patients ($p < 0.05$) and in healthy individuals ($p < 0.001$). The absolute content of lymphocytes and monocytes was also higher in males, but only in the group of apparently healthy individuals ($p < 0.001$); in DC males and females, the difference in indicators was not statistically confirmed ($p > 0.05$), while in men with CD the absolute the number of lymphocytes decreased compared with the controls ($p = 0.05$), and in DC women, the absolute content of monocytes was significantly increased compared with the controls ($p < 0.001$) (Table 1).

N/L was increased in DC males compared to both healthy controls ($p = 0.05$) and to the subgroup of DC women ($p < 0.05$). L/M in the subgroups of males and females was comparable both in patients with CD and in apparently healthy individuals, while in both male and female DC subgroups, the indicator was significantly reduced compared to the controls ($p < 0.05$).

Table 1

Content of neutrophils, lymphocytes and monocytes in the peripheral blood in patients with Dupuytren's contracture (CD) in comparison with apparently healthy individuals

Group / parameter	Dupuytren's contracture		Healthy subjects	
	1-DC males (n = 122)	2-DC females (n = 40)	3-males (n = 76)	4-females (n = 34)
Age (years)	59.5 (54; 62) $P^{1-3} = 0.34$ $P^{1-2} = 0.22$	62 (54; 66) $P^{2-4} = 0.16$	58 (48.5; 65)	59 (55; 63) $P^{3-4} = 0.60$
Neutrophils (× 10^9/l)	3.97 (3.25; 4.80) $P^{1-3} = 0.76$ $P^{1-2} = 0.01$	3.25 (2.58; 4.22) $P^{2-4} = 0.99$	3.93 (3.47; 4.61)	3.19 (2.67; 3.77) $P^{3-4} = 0.00$*
Lymphocytes (× 10^9/l)	1.95 (1.54; 2.52) $P^{1-3} = 0.05$* $P^{1-2} = 0.67$	2.01 (1.70; 2.49) $P^{2-4} = 0.15$	2.32 (1.71; 2.83)	1.85 (1.62; 2.16) $P^{3-4} = 0.00$*
Monocytes (× 10^9/l)	0.38 (0.26; 0.51) $P^{1-3} = 0.53$ $P^{1-2} = 0.87$	0.39 (0.31; 0.52) $P^{2-4} = 0.00$*	0.35 (0.28; 0.48)	0.25 (0.18; 0.28) $P^{3-4} = 0.00$*
N/L – ratio of neutrophils to lymphocytes	2.02 (1.66; 2.38) $P^{1-3} = 0.05$* $P^{1-2} = 0.01$	1.60 (1.16; 2.24) $P^{2-4} = 0.35$	1.71 (1.37; 2.43)	1.80 (1.31; 2.27) $P^{3-4} = 0.35$
L/M – ratio of lymphocytes to monocytes	5.38 (4.00; 7.50) $P^{1-3} = 0.05$* $P^{1-2} = 0.93$	5.17 (3.75; 6.25) $P^{2-4} = 0.02$*	6.08 (4.56; 9.25)	7 (4.73; 11.25) $P^{3-4} = 0.15$

Note: P1-2, P1-3, P2-4, P3-4 – significance level between the subgroups; * – $p \leq 0.05$

There were no significant correlations of the studied leukocyte indices with the DC severity and the duration of fascial fibromatosis. ROC-analysis of the "N/L – DC stage" model revealed its low sensitivity, 46.7 % in DC males and 55 % in DC females. The model "L/M – DC stage" had high sensitivity and specificity both in the subgroups of men and women, and in the total group of DC patients (sensitivity 90.12; specificity 93.21), the AUC value corresponded to excellent quality (Fig. 1).

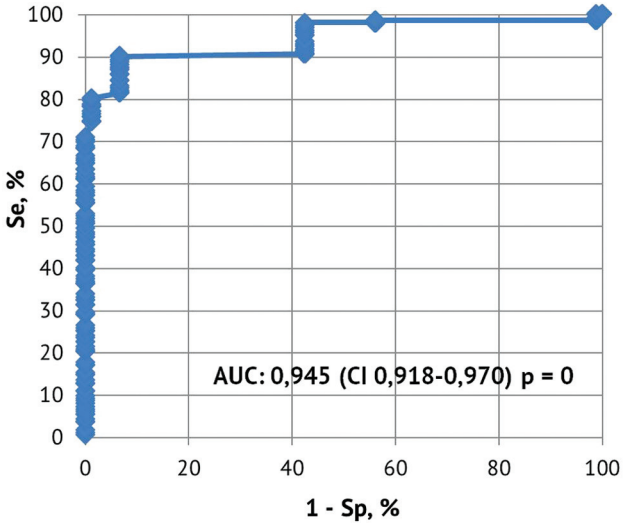

Fig. 1 Diagnostic significance of the lymphocyte-monocyte index in assessing the degree of Dupuytren's contracture: AUC - area under the curve; CI - confidence interval

At the second stage of the study, based on the automatically set optimal threshold of the L/M index = 3.102, patients with CD were divided into subgroups with low L/M (≤ 3.00) and high L/M (> 3.00). The subgroup with low L/M accounted for 10 % of the total sample of DC patients. A similar indicator in the group of apparently healthy people was 7 % (not significantly lower). The histogram of the distribution of patients in terms of L/M in the group of patients with CD compared with apparently healthy individuals had a shift towards lower values, however, the difference in distribution functions was not confirmed statistically (p = 0.21 according to the Smirnov criterion).

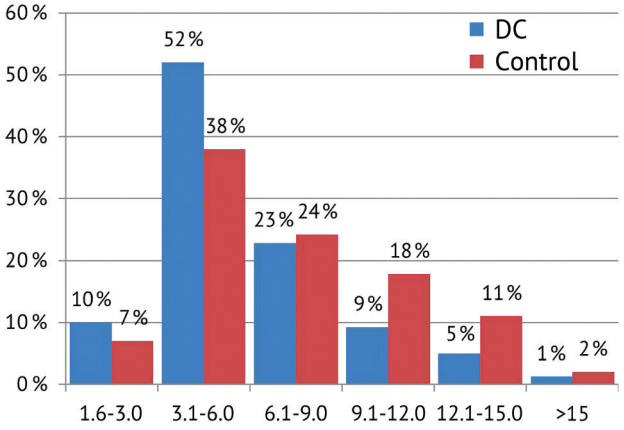

Fig. 2 Distribution of patients according to the value of the lymphocyte-monocyte index L/M in the groups of healthy individuals (control) and with Dupuytren's contracture (DC): abscissa - the value of L/M; ordinates – percentage of patients in samples n = 162 (DC) and n = 110 (control)

Data on L/M dynamics were available in 12 patients with bilateral palmar fascial fibromatosis who were surgically treated first on one hand and several months or years later on the other hand. In 11 out of 12 patients,

L/M did not change and only in one patient changed downwards within four months.

The subgroup of patients with low L/M did not differ significantly from the subgroup with high L/M in terms of age at the onset of the first symptoms of palmar fascial fibromatosis and the ratio of males to females (Table 2). However, in patients with low L/M, the incidence of involvement of both hands and the incidence of severe grades of contracture were 27.75 % and 27.15 %, respectively, ($p < 0.05$), higher than in the high L/M subgroup. The percentage of patients with impaired function of more than two fingers was comparable. The percentage of relapses in the low L/M group was also 7 % higher than in the high L/M group, but the difference was not statistically significant ($p > 0.05$). The reduced L/M value was due to both a decrease in the content of lymphocytes and an increase in the content of monocytes in the peripheral blood ($p < 0.001$).

Table 2

Clinical, demographic and paraclinical characteristics of patients with Dupuytren's contracture depending on the value of the lymphocyte-monocyte index (L/M)

Group/parameter	L/M ≤ 3.00 (n = 16)	L/M > 3.00 (n = 146)	$P^{1,2}$
Age at the disease onset	51 (46;57)	53 (47; 59)	0.331
Females	12.5 %	26.4 %	0.362
Patients with both hands affected	81.25 %*	53.5 %	0.022
Patients with DC grades III-IV	81.25 %*	54.1 %	0.032
Patients with affected function in more than two fingers	31.25 %	29.17 %	0.522
Patients with contracture recurrence	12.5 %	5.5 %	0.262
Lymphocytes ($\times 10^9$/l)	1.60 (1.47; 2.29)	2.01 (1.63; 2.53)	0.001
Monocytes ($\times 10^9$/l)	0.70 (0.52; 0.90)	0.36 (0.26; 0.46)	0.001

P^1 – level of significance of differences between the studied groups according to the Mann-Whitney test; P^2 – according to Fisher's exact test; * – significant difference ($p \leq 0.05$)

DISCUSSION

To predict the natural course of palmar fascial fibromatosis in patients without surgical treatment or the time interval from surgery to recurrence of Dupuytren's contracture is a difficult task [21], but its solution is necessary to develop optimal individualized treatment protocols. Therefore, a number of studies have focused on the investigation of Dupuytren's diathesis, a constitutional predisposition to an aggressive course and recurrence of the contracture [22, 23, 24]. The criteria for diathesis (appearance of the first symptoms at the age under 50 years, occurrance of the disease in close relatives, ectopic foci of fibromatosis, affected fingers on the radial side of the hand) are based on anamnesis data, which may be unreliable, as well as on clinical signs that occur infrequently and, therefore, are not applicable for most patients. In this regard, intensive studies were carried out to develop a method for assessing the risk of disease progression and recurrence based on circulating biomarkers, but it has not been developed so far [25].

We hypothesized that leukocyte indices of peripheral blood may be useful for solving such problems. According to recent literature, their diagnostic and prognostic significance has been confirmed by numerous publications, mainly in the field of oncology [26, 27, 28, 29]. Our study revealed the features of the leukocytogram of patients with Dupuytren's contracture in comparison with conditionally healthy people for the first time. A statistically significant decrease in the absolute content of lymphocytes was found in males with Dupuytren's contracture, and a significant increase in the absolute content of monocytes in women. However, the gender-related difference in the content of lymphocytes and monocytes in peripheral blood is lost in patients with Dupuytren's contracture. Multidirectional changes in the content of lymphocytes and monocytes in men and women are consistent with the literature data on dual gender-specific ways of regulating the immune system in healthy people and in patients with various diseases [30] that in some cases determine sex-related differences in the prevalence of the disease. This can probably be attributed to palmar fascial fibromatosis, which is significantly more frequent in men than in women.

Sexual dimorphism of the absolute neutrophil count (the median indicator is significantly higher in men) was expressed both in apparently healthy people and in patients with Dupuytren's contracture, while there was no significant difference between the subgroups of patients and apparently healthy people. It is likely that neutrophils do not play a significant role in the pathogenesis of palmar fascial fibromatosis, although a few mature granulocytes near blood vessels and in proliferating fibromatous nodes were found by detailed immunohistochemical study [14]. In ectopic fibromatosis, Peyronie's disease, the neutrophil-lymphocyte index is estimated as an important indicator that clarifies the stage of the disease and treatment tactics [31, 32], but not all research groups have come to such conclusions [33].

In our study of palmar fascial fibromatosis, the neutrophil-lymphocyte index was elevated in men with Dupuytren's contracture compared with healthy

controls and a subgroup of women with Dupuytren's contracture, probably resulting from a decrease in lymphocyte counts. According to the results of the ROC analysis, the neutrophil-lymphocyte index turned out to be diagnostically useless. However, a high diagnostic significance of the lymphocyte-monocyte index was revealed. This indicator in men and women with Dupuytren's contracture is significantly reduced compared to apparently healthy people, and its lowest values (3.0 or lower) are associated with a significantly increased incidence of severe contractures and an increased incidence of bilateral fibromatosis.

The issue of the key role of lymphocytes and monocytes in the pathogenesis of palmar fascial fibromatosis is based on immunohistochemical studies of surgical material, although it has not been fully elucidated [14, 17]. The mechanism of the relationship between the low lymphocytic-monocytic index and disease severity that we have identified is also not clear enough, since both cell types, lymphocytes and monocytes, are traditionally considered as producers of pro-inflammatory cytokines and growth factors that enhance angiogenesis and the progression of fibromatosis [34]. However, Plander et al [35] found that the advanced stage of Dupuytren's contracture is characterized by a decrease in CD4+ T-lymphocytes and especially natural killer cells, while the number of B-lymphocytes remains unchanged. This suggests an "antifibromatosis" role of T-lymphocytes and is consistent with the reduced number of peripheral blood lymphocytes found in our study in men with Dupuytren's contracture, especially in the group of patients with a low lymphocyte-monocyte index and an increased incidence of involvement of both hands and grade III-IV contractures.

Our study has several limitations. Only the patients who had an indication for surgery were included, and early manifestations of palmar fascial fibromatosis were not studied. The sample size of women is small due to the significantly lower incidence of Dupuytren's contracture in women. In the majority of patients, clinical and laboratory data of only one time-point were available. However, the obtained results allowed us to identify an additional useful available laboratory parameter for assessing the risk of progression of Dupuytren's contracture, which does not require additional costs and can be used in clinical practice along with the criteria for Dupuytren's diathesis. Further studies of the prognostic significance of the lymphocyte-monocyte index in various cohorts of patients with palmar fascial fibromatosis seem promising.

CONCLUSION

In patients with Dupuytren's contracture, there is no sex-related difference in the median content of lymphocytes and monocytes in peripheral blood, characteristic of healthy people.

A significant decrease in the lymphocyte-monocyte index in patients with Dupuytren's contracture compared with conditionally healthy individuals is due to a decrease in the content of peripheral blood lymphocytes (mainly in men) and an increase in the content of monocytes (mainly in women).

Extremely low values of the lymphocyte-monocyte index (≤ 3.0) are associated with an increased rate of bilateral palmar fascial fibromatosis and Dupuytren's contracture grades III-IV. The studied sample of patients shows that the lymphocyte-monocyte index is a useful additional indicator for identifying a risk group of severe fascial fibromatosis.

Conflict of interest *Not declared.*

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Ethical expertise *The study was performed in accordance with the ethical standards of the Declaration of Helsinki (revised in October 2013) and was approved by the ethics committee (protocol No. 4 (68) of 11/11/2020).*

Informed consent *Voluntary informed consent was obtained from all patients to publish the results of the study without disclosing their identity.*

REFERENCES

1. Meyerding HW, Black JR, Broders AC. The etiology and pathology of Dupuytren's contracture. *Surg Gynecol Obstet*. 1941;72(3):582-590.
2. Vi L, Gan BS, O'Gorman DB. The potential roles of cell migration and extra-cellular matrix interactions in Dupuytren's disease progression and recurrence. *Med Hypotheses*. 2010;74(3):510-512. doi: 10.1016/j.mehy.2009.10.009
3. Salari N, Heydari M, Hassanabadi M, et al. The worldwide prevalence of the Dupuytren disease: a comprehensive systematic review and meta-analysis. *J Orthop Surg Res*. 2020;15(1):495. doi: 10.1186/s13018-020-01999-7
4. Murphey MD, Fairbairn KJ, Parman LM, et al. From the archives of the AFIP. Musculoskeletal angiomatous lesions: radiologic-pathologic correlation. *Radiographics*. 1995;15(4):893-917. doi: 10.1148/radiographics
5. Kraus R, Alzen G, Dreyer T, et al. Morbus dupuytren im kindesalter - fallbericht und literaturrecherche [Dupuytren's disease in children - case report and literature review]. *Handchir Mikrochir Plast Chir*. 2012;44(3):175-7. (In German) doi: 10.1055/s-0032-1312655
6. Nordenskjöld J, Englund M, Zhou C, Atroshi I. Prevalence and incidence of doctor-diagnosed Dupuytren's disease: a population-based study. *J Hand Surg Eur Vol*. 2017;42(7):673-677. doi: 10.1177/1753193416687914
7. Diep GK, Agel J, Adams JE. Prevalence of palmar fibromatosis with and without contracture in asymptomatic patients. *J Plast Surg Hand Surg*. 2015;49(4):247-250. doi: 10.3109/2000656X.2015.1034724
8. Ball C, Izadi D, Verjee LS, et al. Systematic review of non-surgical treatments for early dupuytren's disease. *BMC Musculoskelet Disord*. 2016;17(1):345. doi: 10.1186/s12891-016-1200-y

9. Denkler KA, Park KM, Alser O. Treatment Options for Dupuytren's Disease: Tips and Tricks. *Plast Reconstr Surg Glob Open*. 2022;10(1):e4046. doi: 10.1097/GOX.0000000000004046
10. Müller-Seubert W, Cai A, Arkudas A, et al. A Personalized Approach to Treat Advanced Stage Severely Contracted Joints in Dupuytren's Disease with a Unique Skeletal Distraction Device-Utilizing Modern Imaging Tools to Enhance Safety for the Patient. *J Pers Med*. 2022;12(3):378. doi: 10.3390/jpm12030378
11. Dutta A, Jayasinghe G, Deore S, et al. Dupuytren's Contracture - Current Concepts. *J Clin Orthop Trauma*. 2020;11(4):590-596. doi: 10.1016/j.jcot.2020.03.026
12. Satish L, Gallo PH, Baratz ME, et al. Reversal of TGF-β1 stimulation of α-smooth muscle actin and extracellular matrix components by cyclic AMP in Dupuytren's-derived fibroblasts. *BMC Musculoskelet Disord*. 2011;12:113. doi: 10.1186/1471-2474-12-113
13. van Beuge MM, Ten Dam EJ, Werker PM, Bank RA. Matrix and cell phenotype differences in Dupuytren's disease. *Fibrogenesis Tissue Repair*. 2016;9:9. doi: 10.1186/s13069-016-0046-0
14. Mayerl C, Del Frari B, Parson W, et al. Characterisation of the inflammatory response in Dupuytren's disease. *J Plast Surg Hand Surg*. 2016;50(3):171-9. doi: 10.3109/2000656X.2016.1140054
15. Shchudlo NA, Varsegova TN, Stupina TA, Shchudlo MM. Types and stages of vascular remodeling in Dupuytren's contracture (analysis of 506 arteries in the surgical material of 111 patients). *Genij Ortopedii*. 2020;26(2):179-184. doi: 10.18019/1028-4427-2020-26-2-179-184
16. Shchudlo NA, Kostin VV. Pathogenesis of neuropathy in Dupuytren's contracture. *Genij Ortopedii*. 2019;25(1):58-64. doi: 10.18019/1028-4427-2019-25-1-58-64
17. Andrew JG, Andrew SM, Ash A, Turner B. An investigation into the role of inflammatory cells in Dupuytren's disease. *J Hand Surg Br*. 1991;16(3):267-271. doi: 10.1016/0266-7681(91)90051-o
18. Gudmundsson KG, Arngrímsson R, Arinbjarnarson S, et al. T-and B-lymphocyte subsets in patients with Dupuytren's disease. Correlations with disease severity. *J Hand Surg Br*. 1998;23(6):724-7. doi: 10.1016/s0266-7681(98)80083-1
19. Garcia Rojo E, García Gómez B, Santos-Pérez de la Blanca R, et al. Role of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios in Peyronie's disease: a new diagnostic approach to predict the stage of the disease? *Asian J Androl*. 2021;23(3):325-329. doi: 10.4103/aja.aja_74_20
20. Chen Y, Zhang Y, Zhao G, et al. Difference in Leukocyte Composition between Women before and after Menopausal Age, and Distinct Sexual Dimorphism. *PLoS One*. 2016;11(9):e0162953. doi: 10.1371/journal.pone.0162953
21. Ruettermann M, Hermann RM, Khatib-Chahidi K, Werker PMN. Dupuytren's Disease-Etiology and Treatment. *Dtsch Arztebl Int*. 2021;118(46):781-788. doi: 10.3238/arztebl.m2021.0325
22. Hueston J.T. Dupuytren diathesis. In: McFarlane RM, McGrouther DA, Flint M, eds. *Dupuytren's Disease Biology and Treatment*. Edinburgh: Churchill Livingstone; 1990:246-252.
23. Abe Y, Rokkaku T, Ofuchi S, et al. An objective method to evaluate the risk of recurrence and extension of Dupuytren's disease. *J Hand Surg Br*. 2004;29(5):427-30. doi: 10.1016/j.jhsb.2004.06.004
24. Hindocha S, Stanley JK, Watson S, Bayat A. Dupuytren's diathesis revisited: Evaluation of prognostic indicators for risk of disease recurrence. *J Hand Surg Am*. 2006;31(10):1626-34. doi: 10.1016/j.jhsa.2006.09.006
25. Werker P, Dias J, Eaton C, eds. Dupuytren disease and related diseases - The cutting edge. *Springer*. 2017:450. doi: 10.1007/978-3-319-32199-8
26. Li P, Li H, Ding S, Zhou J. NLR, PLR, LMR and MWR as diagnostic and prognostic markers for laryngeal carcinoma. *Am J Transl Res*. 2022;14(5):3017-3027.
27. Romano A, Laura Parrinello N, Cerchione C, et al. The NLR and LMR ratio in newly diagnosed MM patients treated upfront with novel agents. *Blood Cancer J*. 2017;7(12):649. doi: 10.1038/s41408-017-0019-6
28. Miyahara Y, Takashi S, Shimizu Y, Ohtsuka M. The prognostic impact of neutrophil-to-lymphocyte ratio (NLR) and lymphocyte-to-monocyte ratio (LMR) in patients with distal bile duct cancer. *World J Surg Oncol*. 2020;18(1):78. doi: 10.1186/s12957-020-01847-2
29. Huang Y, Liu Y, Mo G, et al. Inflammation Markers Have Important Value in Predicting Relapse in Patients with papillary thyroid carcinoma: A Long-Term Follow-Up Retrospective Study. *Cancer Control*. 2022;29:10732748221115236. doi: 10.1177/10732748221115236
30. Berghella AM, Contasta I, Del Beato T, Pellegrini P. The discovery of how gender influences age immunological mechanisms in health and disease, and the identification of ageing gender-specific biomarkers, could lead to specifically tailored treatment and ultimately improve therapeutic success rates. *Immun Ageing*. 2012;9(1):24. doi: 10.1186/1742-4933-9-24
31. Garcia Rojo E, García Gómez B, Santos-Pérez de la Blanca R, et al. Role of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios in Peyronie's disease: a new diagnostic approach to predict the stage of the disease? *Asian J Androl*. 2021;23(3):325-329. doi: 10.4103/aja.aja_74_20
32. Özbir S, Değirmentepe RB, Atalay HA, et al. The role of inflammatory parameters (neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and monocyte-to-eosinophil ratio) in patients with Peyronie's disease. *Andrology*. 2020;8(2):348-352. doi: 10.1111/andr.12702
33. Greenberg JW, Kim J, Pincus J, et al. Are neutrophil-lymphocyte and platelet-lymphocyte ratios useful for determining active phase of Peyronie's disease? *Journal of Clinical Urology*. 2022;0(0). doi: 10.1177/20514158221094636
34. Eftimie G, Eftimie R. Quantitative predictive approaches for Dupuytren disease: a brief review and future perspectives. *Math Biosci Eng*. 2022;19(3):2876-2895. doi: 10.3934/mbe.2022132
35. Plander M, Salamon A, Toldy E, et al. Cellular immune response in Dupuytren's disease. *Biochemia Medica*. 2008;18(2):193-200.

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