

Screening of Anemia in Patients with Coronary Heart Disease in Outpatient Practice Using a Computer Monitoring System

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Abstract

The aim of this study was to assess the prevalence, structure, and influence of anemic syndrome on the main health indicators of patients with coronary heart disease (CHD), including the main parameters of the quality of life (QOL).

Methods and Results: The study included 1210 patients (309 men and 901 women) with an average age of 67.57±9.35 years who were registered at the dispensary with CHD (angina pectoris CCSA classes II-IV) in 2 Regional Hospitals. With the help of the computer program “Monitoring system for patients with anemia syndrome,” medical records from 2 randomly selected primary care areas were analyzed. The data directly related to anemia, comorbid pathology, and previous treatment formed the main part of the statistical data. The QOL was evaluated using the 36-Item Short Form Survey (SF-36) questionnaire. The FACT-An questionnaire was used to account for the characteristic symptoms, and their severity, accompanying anemia.

Our findings indicate the presence of anemia in 500(41.3%) patients (355/71% women and 145/29% men). The average age of the patients with diagnosed anemia was 65.34±6.37 years in men and 63.49±7.05 years in women. Anemia of mild severity was observed in 410(82%) patients, moderate severity in 75(15%) patients, and severe anemia in 15(3%) patients. IDA was detected in 467(93.4%) cases and B12-deficiency anemia in 33(6.6%) cases. We found a negative correlation between the blood iron level and age ($r=-0.56$, $P<0.05$), which can indirectly indicate the progression of latent iron deficiency with age in CHD patients.

All 500 CHD patients with anemia were included in Group 1. Group 2 included 710 CHD patients without anemia. In Groups 1 and 2, angina severity according to CCSA classification was as follows: CCSA class II - 186(37.2%) and 456(64.2%) cases ($P=0.000$), CCSA class III - 248(49.6%) and 196(27.6%) cases ($P=0.000$), and CCSA class IV - 66(13.2%) and 58(8.2%) cases ($P=0.005$), respectively. Group 1 patients, in contrast to Group 2 patients, had the following characteristic clinical features: palpitation (48.2% vs. 35.0%, $P=0.000$), higher HR (81±9.5 bpm vs. 71.8±8.7 bpm, $P=0.000$) and respiratory rate (18.9±1.1 vs 18.3±1.2 per minute, $P=0.000$).

The assessment of the impact of anemia on QOL by FACT-An revealed a statistically lower Anemia subscale score in Group 1 than in Group 2 (32.0±5.7 vs. 44.0±6.5, $P=0.000$). We found a positive correlation between the Hb level and the FACT-An Anemia subscale score ($r=0.54$, $P<0.05$). Patients in Group 1 demonstrated a low level of QOL in the physical and mental domains, according to SF-36, in comparison with Group 2. Correlation analysis revealed a direct relationship between the Hb level and the average score of the PF (physical functioning) scale ($r=0.52$, $P<0.05$) and PCS (physical component summary) ($r=0.38$, $P<0.05$) of the SF-36 questionnaire.

The observed high incidence of anemic syndrome in CHD patients with angina pectoris (CCSA class II-IV) requires special attention due to the high impact on the QOL of patients and aggravation of the course of the underlying disease. (**International Journal of Biomedicine. 2022;12(3):355-359.**)

Keywords: anemia • coronary heart disease • quality of life

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Abbreviations

BMI, body mass index; **BP**, bodily pain; **CHD**, coronary heart disease; **GH**, general health; **FACT-An**, the Functional Assessment of Cancer Therapy–Anemia; **Hb**, hemoglobin; **HR**, heart rate; **IDA**, iron deficiency anemia; **QOL**, the quality of life; **RBC**, red blood cell; **RBCC**, RBC count, **MCV**, mean corpuscular volume; **MCHC**, mean corpuscular hemoglobin concentration; **MCH**, mean corpuscular hemoglobin; **MCS**, mental component summary; **MH**, mental health; **PF**, physical functioning; **PCS**, physical component summary; **RP**, role-physical functioning; **RE**, role emotional; **SF**, social functioning; **SF-36**, the 36-Item Short-Form Health Survey; **SF**, social functioning; **VT**, vitality.

Introduction

Anemia is a condition in which the number of red blood cells or the hemoglobin concentration within them is lower than the normal range.⁽¹⁾ This condition occurs for various reasons, has different results, and may require specific treatment tactics from a general practitioner or a hematologist.⁽²⁾ Anemia is a quite common pathology.^(3,4) According to statistics, 32.9% of the world's population suffers from anemia, indicating this nosology's widespread prevalence.⁽⁵⁾

The anemic syndrome often accompanies many chronic diseases (cardiovascular diseases, chronic kidney diseases, oncological diseases), worsening the course and progression of these pathologies. Considering that most patients are older people with a sufficient number of concomitant diseases, this problem remains actual.^(6,7)

The aim of this study was to assess the prevalence, structure, and influence of anemic syndrome on the main health indicators of patients with coronary heart disease (CHD), including the main QOL parameters.

Materials and Methods

The study included 1210 patients (309 men and 901 women) with an average age of 67.57 ± 9.35 years who were registered at the dispensary with CHD (*angina pectoris* CCSA classes II-IV) in 2 Regional Hospitals.

With the help of the computer program "Monitoring system for patients with anemia syndrome," medical records from 2 randomly selected primary care areas were analyzed. The information about patients in the registry included personal data, anamnesis data, and laboratory and instrumental test results. The data directly related to anemia, comorbid pathology, and previous treatment formed the main part of the statistical data.⁽⁸⁾ Anthropometric information, ECG archive, and coronary angiography data were also evaluated, as were the blood test parameters, such as hemoglobin (Hb) level, red blood cell count (RBCC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), leukocyte formula, the levels of platelets, serum iron and vitamin B12, and morphological changes in erythrocytes (anisocytosis, poikilocytosis).

The main criteria for anemia were $Hb < 130$ g/L and $RBCC < 4 \times 10^{12}/L$ for men, $Hb < 120$ g/L, and $RBCC < 3.8 \times 10^{12}/L$ for women.⁽⁹⁾ Criteria for iron deficiency anemia (IDA) included $MCV < 80$ fL, $MCH < 26$ pg, $MCHC < 320$ g/L, serum iron < 9 mmol/L, anisocytosis, and poikilocytosis. Criteria for vitamin B12-deficiency anemia included $MCV > 95$ fL, $MCH > 33$ pg, $MCHC$ from 320 g/L to 380 g/L, serum iron level > 9 mmol/L, serum vitamin B12 < 100 pg/mL.

According to the severity, anemia was divided into mild ($Hb \geq 90$ g/L), moderate (Hb from 90 g/L to 70 g/L), and severe ($Hb < 70$ g/L).

All patients underwent the following examinations: 12-lead ECG, Echocardiography, 24-hour Holter monitoring, treadmill test, and coronary angiography.

Stable angina severity was assessed according to the Canadian Cardiovascular Society angina (CCSA) classification.⁽¹⁰⁾ The diagnosis of coronary artery disease included angina pectoris CCSA classes II-IV and documented history of previous myocardial infarction.

The QOL was evaluated using the 36-Item Short Form Survey (SF-36) questionnaire.⁽¹¹⁾ The SF-36 contains eight domains: Physical functioning [PF (10 items)], Role-physical [RP (4 items)], Bodily Pain [BP (2 items)], General Health [GH (5 items)], Vitality [VT (4 items)], Social functioning [SF (2 items)], Role-emotional [RE (3 items)], and Mental Health [MH (5 items)]. These eight scales can be aggregated into two summary measures: the Physical Component Summary (PCS) and Mental Component Summary (MCS). Anemia-related domains such as the Vitality and Physical functioning were previously identified to be of special interest.^(12,13)

The FACT-An questionnaire^(14,15) was used to account for the characteristic symptoms, and their severity, accompanying anemia. The FACT-An includes 13 fatigue-specific items (the Fatigue Subscale) plus an additional 7 items specific to anemia and unrelated to fatigue. Anemia subscales such as FACT-An Total, Fatigue subscale, and Anemia subscale are of special interest. Higher scores indicate better health status.⁽¹⁶⁾

Statistical analysis was performed using Microsoft Excel software package. For descriptive analysis, results are presented as mean \pm standard deviation (SD). Inter-group comparisons were performed using Student's t-test. Pearson's correlation coefficient (r) was used to determine the strength of the relationship between the two continuous variables. A probability value of $P < 0.05$ was considered statistically significant.

The study was approved by the Ethics Committee of Voronezh State Medical University named after N. N. Burdenko.

Results and Discussion

The results of the study are presented in Tables 1 and 2. Our findings indicate the presence of anemia in 500 (41.3%) patients (355/71% women and 145/29% men). The average age of the patients with diagnosed anemia was 65.34 ± 6.37 years in men and 63.49 ± 7.05 years in women. Anemia of mild severity was observed in 410 (82%) patients, moderate severity in 75 (15%) patients, and severe anemia in 15 (3%)

patients. IDA was detected in 467(93.4%) cases and B12-deficiency anemia in 33(6.6%) cases.

All patients were divided into 2 groups. Group 1 included 500 CHD patients with anemia. Group 2 included 710 CHD patients without anemia.

In Group 1 patients, the average serum iron level (5.6 ± 1.1 mmol/L) was lower than in patients with B12-deficiency anemia (11.1 ± 2.6 mmol/l) on 49.5% ($P < 0.001$), as well as MCV on 19.3% (74.1 ± 1.8 fL vs. 91.8 ± 4.2 fL, $P < 0.01$).

We found that 208(41.6%) cases of anemia were diagnosed as a concomitant disease, and in 292(58.4%) cases, anemia was not included in the diagnosis.

In Groups 1 and 2, angina severity according to CCSA classification was as follows: CCSA class II - 186(37.2%) and 456(64.2%) cases ($P = 0.000$), CCSA class III - 248(49.6%) and 196(27.6%) cases ($P = 0.000$), and CCSA class IV - 66(13.2%) and 58(8.2%) cases ($P = 0.005$), respectively.

Group 1 patients, in contrast to Group 2 patients, had the following characteristic clinical features: palpitation (48.2% vs. 35.0%, $P = 0.000$), higher HR (81 ± 9.5 bpm vs. 71.8 ± 8.7 bpm, $P = 0.000$) and respiratory rate (18.9 ± 1.1 vs. 18.3 ± 1.2 per minute, $P = 0.000$).

The assessment of the impact of anemia on QOL by FACT-An revealed a statistically lower Anemia subscale score in Group 1 than in Group 2 (32.0 ± 5.7 vs. 44.0 ± 6.5 , $P = 0.000$) (Table 1).

Table 1.

The FACT-An Anemia subscale score in patients of the studied groups.

FACT-An	Group 1	Group 2	P-level
Anemia subscale	32.0 ± 5.7	44.0 ± 6.5	0.000

We found a positive correlation between the Hb level and the FACT-An Anemia subscale score ($r = 0.54$, $P < 0.05$) and BMI ($r = 0.21$, $P < 0.05$), and a negative correlation between the Hb level and HR ($r = -0.22$, $P < 0.05$).

Patients in Group 1 demonstrated a low level of QOL in the physical and mental domains, according to SF-36, in comparison with Group 2 (Table 2). In Group 1, about 50% of patients showed PF scores of less than 40 points. In Group 2, 75% of patients had these indicators more than 52 points. In Group 1, the RP score was 0.0, compared to 13 points in Group 2. The differences between the groups before and after treatment were statistically significant. The BP score was 22.0 ± 6.7 in Group 1 versus 32.0 ± 5.1 in Group 2 ($P = 0.000$). The GH score was also lower in Group 1 than in Group 2. The PCS, combining items from the PF, RP, BP, and GH scales with corresponding weighting coefficients, was 31.5 ± 9.1 and 41.5 ± 8.3 in Groups 1 and 2, respectively ($P = 0.000$).

The VT score decreased to 30.0 ± 7.4 points in Group 1, compared to 47.0 ± 9.9 points in Group 2 ($P = 0.000$), indicating a significant decrease in QOL in CHD patients

with anemia. The SF score of 87.0 ± 5.4 points in Group 1, reflecting limitations on social activity due to health problems, indicated a relatively weak effect of anemia on social activity. However, in Group 2, this score was much higher and reached 100. The RE score was 0.0 in Group 1, reflecting a greater effect of anemia on the emotional state of the CHD patients. The MH score, reflecting general mental health (psychological distress and well-being), was below 37 points in 75% of patients in Group 1, which can be interpreted as severe psychological distress on the background of anemia. In Group 2, the MH score was 52.0 ± 6.4 vs. 36.0 ± 7.1 in Group 1 ($P = 0.000$). The MCS, combining items from the VT, SF, RE, and MH scales with corresponding weighting coefficients, was 36.0 ± 7.1 and 41.2 ± 5.1 in Groups 1 and 2, respectively. Differences between groups amounted to 5 points in the median and 5-6 points in the upper and lower quartiles, which was not clinically significant. However, the differences between the groups were statistically significant ($P = 0.000$).

Table 2.

QOL indicators on the SF-36 scales in patients of the studied groups.

SF-36 scale	Group 1	Group 2	P-level
PF	40.0 ± 5.5	53.0 ± 6.1	0.000
RP	0.0	10.0 ± 3.3	-
BP	22.0 ± 6.7	32.0 ± 5.1	0.000
GH	40.0 ± 8.7	50.0 ± 7.1	0.000
PGS	31.5 ± 9.1	41.5 ± 8.3	0.000
VT	30.0 ± 7.4	47.0 ± 9.9	0.000
SF	87.0 ± 5.4	100.0	0.000
RE	0.0	13.3 ± 4.1	-
MH	36.0 ± 7.1	52.0 ± 6.4	0.000
MGS	37.1 ± 3.3	41.2 ± 5.1	0.000

Correlation analysis revealed a direct relationship between the Hb level and the average score of the PF scale ($r = 0.52$, $P < 0.05$) and PCS ($r = 0.38$, $P < 0.05$) of the SF-36 questionnaire. We found a negative correlation between the blood iron level and age ($r = -0.56$, $P < 0.05$), which can indirectly indicate the progression of latent iron deficiency with age in CHD patients.

Anemia, particularly iron deficiency hypochromic microcytic anemia, is a medical-social problem. IDA prevalence and severity are largely determined by the life standard, the nature of nutrition, and cultural traditions. Anemia usually accompanies chronic diseases in therapeutic profile patients, mainly having cardiovascular pathology.⁽¹⁷⁻²⁰⁾ In individuals over 60 years old anemia significantly impaired overall survival and health-related quality of life.⁽²⁰⁻²³⁾ Multiple studies have shown decreased survival in older anemic individuals.⁽²⁴⁻²⁶⁾ In this connection, increased education regarding IDA and a focus

on earlier diagnosis of IDA is very important in order to improve the QOL of patients with anemia.

The medical MIS module «Monitoring system for patients with anemia syndrome» in primary care contributes to the rapid assessment of the results of examinations and therapy of patients with anemia, allowing the correction of IDA. High-quality data entered into the registers of patients with various pathologies contributes to the timely correction of treatment and improvement of the patient's QOL.

Targeting groups of patients who need active detection and treatment of IDA through the use of the computer program «Monitoring system for patients with anemia syndrome» provided an increase in IDA control. Dynamic detection and treatment of anemic syndrome accompanying other chronic diseases (in particular, CHD) were followed by a decrease in the need for primary health care mainly and, to a lesser extent, in inpatient medical care over the year. Improving the effectiveness of IDA treatment through the use of the aforementioned computer program has led to an improvement in all components of the QOL.

Conclusion

The observed high incidence of anemic syndrome in CHD patients with angina pectoris (CCSA class II-IV) requires special attention due to the high impact on the QOL of patients and aggravation of the course of the underlying disease. The severity of anemia syndrome is directly proportional to the age of patients and is more common in women in the form of IDA. In our study, most CHD patients (82%) had mild anemia; IDA was more common (93.4%). CHD patients with reduced Hb levels are more likely to suffer from palpitations and shortness of breath. IDA primarily affects the physical components of the QOL and, to a lesser extent – the mental ones.

Competing Interests

The authors declare that they have no competing interests.

References

- Cascio MJ, DeLoughery TG. Anemia: Evaluation and Diagnostic Tests. *Med Clin North Am.* 2017 Mar;101(2):263-284. doi: 10.1016/j.mcna.2016.09.003. Epub 2016 Dec 8. PMID: 28189170.
- de Las Cuevas Allende R, Díaz de Entresotos L, Conde Díez S. Anaemia of chronic diseases: Pathophysiology, diagnosis and treatment. *Med Clin (Barc).* 2021 Mar 12;156(5):235-242. English, Spanish. doi: 10.1016/j.medcli.2020.07.035. Epub 2020 Dec 24. PMID: 33358297.
- Merlo CM, Wuillemin WA. Diagnostik und Therapie der Anämie in der Praxis [Diagnosis and therapy of anemia in general practice]. *Praxis (Bern 1994).* 2009 Feb 18;98(4):191-9. doi: 10.1024/1661-8157.98.4.191. PMID: 19224487. [Article in German].
- Paul B, Wilfred NC, Woodman R, Depasquale C. Prevalence and correlates of anaemia in essential hypertension. *Clin Exp Pharmacol Physiol.* 2008 Dec;35(12):1461-4. doi: 10.1111/j.1440-1681.2008.05031.x. Epub 2008 Aug 26. PMID: 18759858.
- Pasricha SR. Anemia: a comprehensive global estimate. *Blood.* 2014 Jan 30;123(5):611-2. doi: 10.1182/blood-2013-12-543405. PMID: 24482500.
- Lanier JB, Park JJ, Callahan RC. Anemia in Older Adults. *Am Fam Physician.* 2018 Oct 1;98(7):437-442. PMID: 30252420.
- Budnevsky AV, Simion AY, Shapovalova MM. [Pathophysiology of anemic syndrome in cardiovascular diseases]. *Nauka Molodykh (Eruditio Juvenium).* 2021; 9(2):301-312. [Article in Russian].
- Budnevsky AV, Pronin SS, Voronina EV, Kontsevaya AV, Korotkov IN, Natarov AA, et al. Computer program No. 2019665676 Russian Federation / Monitoring system of the therapeutic and diagnostic process in patients with anemia. Published on 27.11.2019. Application No. 2019664783 dated 21.11.2019. [In Russian]
- WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System. Geneva, World Health Organization, 2013 (WHO/NMH/NHD/MNM/11.1)
- Campeau L. Letter: Grading of angina pectoris. *Circulation.* 1976 Sep;54(3):522-3. PMID: 947585.
- Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992;30(6):473-83.
- Gandra SR, Finkelstein FO, Bennett AV, Lewis EF, Brazg T, Martin ML. Impact of erythropoiesis-stimulating agents on energy and physical function in nondialysis CKD patients with anemia: a systematic review. *Am J Kidney Dis.* 2010 Mar;55(3):519-34. doi: 10.1053/j.ajkd.2009.09.019. Epub 2009 Dec 23. PMID: 20031287.
- Weisbord SD, Fried LF, Mor MK, Resnick AL, Unruh ML, Palevsky PM, Levenson DJ, Cooksey SH, Fine MJ, Kimmel PL, Arnold RM. Renal provider recognition of symptoms in patients on maintenance hemodialysis. *Clin J Am Soc Nephrol.* 2007 Sep;2(5):960-7. doi: 10.2215/CJN.00990207. Epub 2007 Aug 8. PMID: 17702730.
- Cella D. The functional assessment of Cancer therapy-Anemia (FACT-an) scale: a new tool for the assessment of outcomes in cancer anemia and fatigue. *Semin Hematol.* 1997;34(3 Suppl 2):13-9.
- Yellen SB, Cella DF, Webster K, Blendowski C, Kaplan E. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. *J Pain Symptom Manage.* 1997 Feb;13(2):63-74. doi: 10.1016/s0885-3924(96)00274-6. PMID: 9095563.
- Finkelstein FO, van Nooten F, Wiklund I, Trundell D, Cella D. Measurement properties of the Short Form-36 (SF-36) and the Functional Assessment of Cancer Therapy - Anemia (FACT-An) in patients with anemia associated with chronic kidney disease. *Health Qual Life Outcomes.* 2018 May 31;16(1):111. doi: 10.1186/s12955-018-0933-8. PMID: 30000000.

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29855366; PMID: PMC5984470.

17. Farag YM, Keithi-Reddy SR, Mittal BV, Surana SP, Addabbo F, Goligorsky MS, Singh AK. Anemia, inflammation and health-related quality of life in chronic kidney disease patients. *Clin Nephrol.* 2011 Jun;75(6):524-33. doi: 10.5414/cnp75524. PMID: 21612756.

18. Ferrari M, Manea L, Anton K, Bruzzone P, Meneghello M, Zamboni F, Purgato L, Cazzoletti L, Ferrari P, Testi R. Anemia and hemoglobin serum levels are associated with exercise capacity and quality of life in chronic obstructive pulmonary disease. *BMC Pulm Med.* 2015 May 8;15:58. doi: 10.1186/s12890-015-0050-y. PMID: 25952923; PMID: PMC4426177.

19. Wasada I, Eguchi H, Kurita M, Kudo S, Shishida T, Mishima Y, Saito Y, Ushiorozawa N, Seto T, Shimozuma K, Morita S, Saito M, Yokomizo Y, Ishizawa K, Ohashi Y, Eguchi K. Anemia affects the quality of life of Japanese cancer patients. *Tokai J Exp Clin Med.* 2013 Apr 20;38(1):7-11. PMID: 23564569.

20. Kraai IH, Luttik ML, Johansson P, De Jong RM, Van Veldhuisen DJ, Hillege HL, Jaarsma T. Health-related quality of life and anemia in hospitalized patients with heart failure. *Int J Cardiol.* 2012 Nov 29;161(3):151-5. doi: 10.1016/j.ijcard.2012.05.036. Epub 2012 May 28. PMID: 22647414.

21. Dharmarajan TS, Norkus EP. Mild anemia and the risk of falls in older adults from nursing homes and the community. *J Am Med Dir Assoc.* 2004 Nov-Dec;5(6):395-400. doi:

10.1097/01.JAM.0000144734.84172.89. PMID: 15530178.

22. Kamenetz Y, Beloosesky Y, Zeltzer C, Gotlieb D, Magazanik A, Fishman P, Grinblat J. Relationship between routine hematological parameters, serum IL-3, IL-6 and erythropoietin and mild anemia and degree of function in the elderly. *Aging (Milano).* 1998 Feb;10(1):32-8. doi: 10.1007/BF03339631. PMID: 9589749.

23. Wouters HJCM, van der Klauw MM, de Witte T, Stauder R, Swinkels DW, Wolffenbuttel BHR, Huls G. Association of anemia with health-related quality of life and survival: a large population-based cohort study. *Haematologica.* 2019 Mar;104(3):468-476. doi: 10.3324/haematol.2018.195552. Epub 2018 Oct 11. PMID: 30309850; PMID: PMC6395328.

24. Culleton BF, Manns BJ, Zhang J, Tonelli M, Klarenbach S, Hemmelgarn BR. Impact of anemia on hospitalization and mortality in older adults. *Blood.* 2006 May 15;107(10):3841-6. doi: 10.1182/blood-2005-10-4308. Epub 2006 Jan 10. PMID: 16403909.

25. Penninx BW, Pahor M, Woodman RC, Guralnik JM. Anemia in old age is associated with increased mortality and hospitalization. *J Gerontol A Biol Sci Med Sci.* 2006 May;61(5):474-9. doi: 10.1093/gerona/61.5.474. PMID: 16720744.

26. Halawi R, Moukhadder H, Taher A. Anemia in the elderly: a consequence of aging? *Expert Rev Hematol.* 2017 Apr;10(4):327-335. doi: 10.1080/17474086.2017.1285695. Epub 2017 Feb 2. PMID: 28110585.