

EARLY DETECTION OF CARCINOMAS OF THE RIGHT COLON: ROLE OF HEMOGLOBIN AND MEAN CORPUSCULAR VOLUME

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The authors suggest that utilization of the hemoglobin-mean corpuscular volume index (HGB-MCV) can serve as an approach to the early detection of certain colon carcinomas. The results of a study of 50 patients using this index are analyzed.

Cancer of the colon and rectum is the second ranking cause of cancer deaths among adults in the United States. Since there is no known cure for cancer in its advanced stage, it is important that it is detected early and treated as soon as possible.

Carcinomas of the right colon are often silent, but are usually called to clinical attention in the late stages by weakness, malaise, weight loss, and unexplained anemia.¹ This anemia, an iron-deficiency type, is insidious and often severe in the latter stages.¹⁻³

The twofold purpose of this investigation was to determine: (1) whether carcinomas of the right colon are predated by iron-deficiency anemia; and (2) whether an index could be derived from a complete blood count and utilized in the early detection of these carcinomas.

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SELECTION OF CASE STUDIES AND DATA

Charts of patients diagnosed as having carcinoma of the right and descending colon were selected randomly from the tumor registries of local hospitals where one of the authors (R.W.T.) has staff privileges.* The study dealt mainly with cancer of the right colon, but two cases of descending colon cancer were included.

Confidentiality of all patients and medical charts was maintained, being viewed by the senior author only. Patient names were not used, but each was assigned a case number randomly.

From their medical histories, all patients appeared to have been well-fed adults. The charts selected indicated no evidence that the patient had other malignancies, chronic systemic diseases, or disorders that may have resulted in iron-deficiency anemias. Patients on iron therapy or those who had received blood transfusions prior to diagnosis were eliminated. Age and sex of each patient were recorded.

The hemoglobin (HGB) value, the mean corpuscular volume (MCV), and the normal range for each were recorded. Hemoglobin values of pa-

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TABLE 1. HEMOGLOBIN (HGB) AND MEAN CORPUSCULAR VOLUME (MCV) AT THE TIME OF DIAGNOSIS* ACCORDING TO AGE AND SEX

Patient Number	Age	Sex	Date of Diagnosis of Colon Carcinoma	HGB (g/dL) at the Time of Diagnosis	MCV (μ^3) at the Time of Diagnosis
1	77	Female	3/23/84	9.5	103
2	67	Male	9/25/84	7.9	67
3	82	Female	6/13/84	10.9	82
4	77	Male	11/12/84	8.9	85
5	79	Female	2/26/85	8.5	95
6	73	Male	12/30/84	8.6	63
7	72	Female	1/22/85	6.6	66
8	75	Female	6/20/84	10.9	85
9	69	Male	1/18/81	10.6	83
10	63	Female	4/28/84	9.6	73
11	77	Female	3/23/84	9.5	103
12	78	Female	2/18/84	10.0	78
13	57	Male	7/20/82	7.8	69
14	60	Male	10/28/84	10.5	72
15	60	Female	3/09/84	9.2	86
16	86	Female	3/25/84	10.0	88
17	85	Male	9/06/84	10.8	85
**18	55	Male	6/30/84	9.3	85
19	69	Female	9/18/84	10.6	85
20	81	Female	11/10/85	9.3	87
21	48	Female	12/18/80	8.1	71
22	82	Female	7/15/82	8.9	92
23	71	Female	6/29/83	8.7	79
24	66	Male	5/26/83	5.9	57
25	70	Female	11/27/83	9.3	70
26	51	Male	4/07/80	9.2	70
27	83	Female	3/20/84	8.2	64
28	71	Female	1/19/85	10.0	74
29	76	Female	3/21/81	7.0	63
30	52	Female	1/04/81	9.9	76
31	73	Female	12/20/84	9.3	67
32	72	Female	1/31/82	7.6	65
33	72	Female	2/01/82	7.7	65
34	60	Male	10/28/84	10.5	72
35	74	Male	3/04/85	10.9	93
36	71	Female	1/19/85	10.8	73
**37	75	Male	1/19/84	7.0	69
38	69	Female	9/14/78	9.6	82
39	80	Female	11/09/78	9.5	68
40	74	Female	9/22/78	10.3	79
41	84	Female	4/09/78	10.8	83
42	39	Female	8/27/79	8.4	66
43	67	Female	3/24/76	10.2	92
44	53	Female	7/07/73	10.2	73
45	66	Male	12/05/80	9.9	71
46	79	Male	11/05/80	10.7	80
47	78	Male	10/23/80	11.4	78
48	53	Female	12/09/79	11.4	81
49	64	Female	4/13/80	9.5	85
50	61	Female	4/07/82	7.2	73

*Normal range values: HGB (g/dL) men, 16 ± 2 , women, 14 ± 2 , MCV (μ^3) men and women, 87 ± 5

**Two cases of descending colon cancer were included in the study

TABLE 2. THE CHANGE IN HEMOGLOBIN (HGB) AND MEAN CORPUSCULAR VOLUME (MCV) VALUES IN THE TIME INTERVAL BETWEEN THE DATE PRIOR TO AND AT THE ACTUAL DATE OF DIAGNOSIS OF COLON CARCINOMA

Patient Number	Age at Diagnosis of Colon Carcinoma	Sex	Date prior to Diagnosis of Colon Carcinoma	HGB (g/dL) and MCV (μ^3) prior to the Diagnosis of Colon Carcinoma		Date of Diagnosis of Colon Carcinoma	HGB (g/dL) and MCV (μ^3) at Time of Diagnosis of Colon Carcinoma	
				HGB (g/dL)	MCV (μ^3)		HGB (g/dL)	MCV (μ^3)
7	72	Female	1/07/84	12.00	86	1/22/85	6.60	66
12	78	Female	1/19/83	12.00	78	2/18/84	10.00	78
13	57	Male	10/28/80	15.60	90	7/20/82	7.80	69
17	85	Male	5/15/82	12.60	94	9/06/84	10.80	85
23	71	Female	1/13/83	11.60	93	6/29/83	8.70	79
33	72	Female	3/17/80	11.10	88	2/01/82	7.65	65
34	60	Male	12/17/82	12.70	82	10/28/84	10.50	72
35	74	Male	3/24/82	13.20	95	3/04/85	10.90	93
36	71	Female	7/31/82	12.70	83	1/19/85	10.80	73
37	75	Male	3/24/83	11.30	89	1/19/84	7.00	69
45	66	Male	12/07/77	14.20	88	12/05/80	9.90	71
46	79	Male	3/03/77	12.00	96	11/05/80	10.70	80

Normal range values: HGB, men, 16 ± 2 , women, 14 ± 2 , men and women, 87 ± 5

tients that were higher than expected due to dehydration were used only after the administration of intravenous fluids. A conscientious effort was made to solicit previous hemoglobin values on patients prior to the diagnosis of colon carcinomas; however, most of them had no previous hospitalizations or medical care prior to diagnosis.

RESULTS

The data from Table 1 show that severe anemias of the iron-deficiency type are found in patients diagnosed to have right colon carcinomas. The average hemoglobin value for all 50 patients in the study was 9.3 ± 1.3 g/dL (Normal, 14 ± 2 female and 16 ± 2 male).

The data also showed that the "classic" findings of an iron-deficiency anemia, low hemoglobin and low mean corpuscular volume values do not always coexist.^{4,5} Of the 50 patients in the study, 31 had low HGB and low MCV values. The other 19 had MCV values within or above the normal laboratory range. The average MCV for the 50 pa-

tients was $77.42 \pm 10.40 \times \mu^3$ (Normal, 87 ± 5 for both men and women).

In Table 2 the data show that the anemia preceded the late clinical manifestations of the disease by as much as three and one-half years prior to the time of definitive diagnosis. A marked reduction in the HGB and MCV values during the time interval between the date prior to the actual date of diagnosis is also noted on Table 2. Of 12 cases, the mean HGB prior to diagnosis for the seven men was 13 ± 1.3 and 9.7 ± 1.5 at the time of diagnosis. The difference between the means is 3.3. A test of the significance between means yielded a *t* value of 4.01, for which the *P* value is less than 0.01. The mean MCV value for the men prior to diagnosis was 90 ± 4.5 and 72.0 ± 8.6 at the time of diagnosis. The difference between the means is 18. A test of the significance between means yielded a *t* value of 5.26, for which the *P* value is less than 0.01.

The mean hemoglobin value for the five women was 11.9 ± 0.5 prior to diagnosis and 8.8 ± 1.5 at the time of diagnosis. The difference between the means is 3.13. A test of the significance between means yielded a *t* value of 4.78, for which the *P*

value is less than 0.01. The mean MCV values for the women prior to the time of diagnosis was 85.6 ± 1.5 and 72.0 ± 5.8 at the time of diagnosis. The difference between the means is 13.6. A test of the significance between means yielded a *t* value of 3.31, for which the P value is less than 0.05. All of the differences are statistically significant.

DISCUSSION

Because of the finding in this study that anemia precedes the late clinical manifestations of right colon carcinomas as early as three and one-half years, the authors were prompted to determine whether an index could be derived from the complete blood count to be employed in the early detection of colonic carcinoma.

It appears from this study that an index of the HGB and MCV values would be applicable to the early detection of carcinomas of the right colon. If evaluated carefully, it can be a useful guide in alerting the clinician to his next course of action in most cases. Merely observing the index figures is not enough, however, especially when the figures yield: (1) HGB and MCV values within the normal range for a given laboratory; (2) low HGB and normal MCV values; or (3) normal HGB and low MCV values (Table 3). These three categories of "non-classic" values for iron-deficiency anemia may present the greatest problem for accurate diagnosis, but a consideration of "masking effects" (described below) often provides a clearer insight.

Sometimes iron-deficiency anemia is overlooked because of its insidious onset and its tendency to be masked by the use of "across-the-counter" hematinics and iron-supplemented vitamins and tonics. Patients using these hematinics usually do not present with the classic findings of an iron-deficiency anemia; they have normal hemoglobin with a low MCV and may be labeled as "normal." It is known that the anemia in iron deficiency may predate any morphologic changes—microcytosis.⁶ Therefore, in an ensuing iron-deficiency anemia, the hemoglobin may be low and the MCV normal. During the time that the anemia is present, the patient may be taking medi-

cations that contain iron, therefore masking the true hemoglobin value. The hemoglobin value may be termed "normal" despite an underlying iron deficiency. From the matrix in Table 3, it can be discerned that if an individual presents with a normal hemoglobin and a low MCV, or a low hemoglobin and a normal MCV, an iron-deficiency anemia is a possibility.

According to the literature, storage iron may be markedly depleted while the serum iron and ferritin levels remain normal.^{7,8} Therefore, one should not rely on serum iron or ferritin levels to rule out an iron-deficiency anemia. A bone marrow biopsy may be of value in identifying an early ensuing iron-deficiency anemia.

Iron-deficiency anemias may also escape early detection due to the masking effects of diuretics, dehydration, and the consumption of alcohol.

Also, an iron-deficiency anemia can be masked by the coexistence of a megaloblastic anemia. A bone marrow biopsy has been shown to be of value in distinguishing iron-deficiency anemia from megaloblastic anemia. If there is a coexistence of an iron-deficiency anemia with a megaloblastic anemia, an index of a low hemoglobin and high MCV could be derived. There would be further masking of these values if the patient consumes across-the-counter preparations of folate or receives parenteral B₁₂ yielding an index of a normal HGB and a high MCV (Table 3).

The individuals within the high range normal present a particularly difficult problem due to numerous variabilities that may be encountered during interval serial monitoring. For example: (1) individuals may consume certain products that may cause hemoconcentration such as alcohol and diuretics, (2) or may be dehydrated due to medical reasons, (3) or may be engaged in vigorous athletic activities on a regular basis, (4) or may have experienced recent changes in altitude, or (5) may be consuming over-the-counter hematinics.

A detailed medical history may reveal any of the above or other situations that could affect the hemoglobin values during monitoring. Because of the great variability encountered in these high range normal individuals, it is suggested that serial monitoring be extended over an expanded time interval. If during monitoring, one observes a steady decline in the hemoglobin while still within the normal range, such decline would warrant a

TABLE 3. THE HGB-MCV INDEX MATRIX: SUGGESTED EVALUATION OF VARIOUS COMBINATIONS OF HEMOGLOBIN AND MEAN CORPUSCULAR VOLUME VALUES*

	Low MCV	Normal MCV	High MCV
Normal HGB	<p>This could be an iron-deficiency anemia (masked) coexisting with some kind of hemoglobinopathy</p> <p>If proved to be iron-deficiency anemia gastrointestinal evaluation is indicated</p>	<p>High Range Normal: Establish an individual baseline for comparative study through interval serial monitoring over an extended period of time</p> <p>**Low Range Normal, "Suspect Group": Establish an individual baseline for comparative study through close interval serial monitoring over a relatively short period of time</p>	<p>This could be an iron-deficiency anemia (masked) with coexisting megaloblastic anemia or with macrocytosis due to other causes. A bone marrow biopsy would be valuable in distinguishing the iron-deficiency anemia. If proved to be an iron-deficiency anemia, then gastrointestinal evaluation is indicated</p>
Low HGB	<p>The "classic" findings indicative of iron-deficiency anemia</p> <p>Gastrointestinal evaluation indicated immediately</p>	<p>Possible ensuing iron-deficiency anemia because the anemia may precede morphological changes (microcytosis)</p> <p>Consider as an ensuing iron-deficiency anemia. A bone marrow biopsy may be valuable in identification. If proved to be an iron-deficiency anemia, then gastrointestinal evaluation is indicated</p>	<p>This could be an iron-deficiency anemia or with macrocytosis due to other causes. A bone marrow biopsy would be valuable in distinguishing the iron-deficiency anemia. If proved to be an iron-deficiency anemia, then gastrointestinal evaluation is indicated</p>

*Normal range values in most laboratories: HGB (g/dL), men, 16 ± 2 , women, 14 ± 2 ; MCV (μ^3), men and women, 87 ± 5

**HGB (g/dL), men, 14, women, 12; MCV (μ^3), 82

gastrointestinal evaluation.

This study also indicates that if HGB and MCV baseline values are established and if serial monitoring reveals changes in these values, further gastrointestinal workup may be indicated to rule out colon cancer. Even when these values

appear normal on a routine complete blood count, careful evaluation of them (Table 3) may still serve as an early indicator of iron-deficiency anemia, which may predate the late clinical manifestations of colon cancer.

The authors think that two valuable clues in the

early detection of colon cancer are (1) a changing baseline hemoglobin while still within the normal range during close interval serial monitoring or (2) an early ensuing iron-deficiency anemia (low HGB-normal MCV).

SUMMARY

The use of the HGB-MCV values index as an approach to early detection of certain colon cancers (1) emphasizes the recognition of iron-deficiency anemia (even if masked) or ensuing, since it predates the late clinical manifestations of the disease, (2) focuses attention on "normal" individuals not presenting the classic blood values for iron-deficiency anemia and offers a way to sort them out for close serial monitoring, (3) brings attention to the importance of establishing for each patient a baseline HGB-MCV index to which later comparisons can be made, and (4) attempts to show the importance of a changing HGB-MCV index on an individual basis even if they fall within the laboratory established norms.

In addition to the early detection of certain colon carcinomas, the HGB-MCV index would appear to lend itself well to the early detection of other pathologic lesions of the gastrointestinal tract.

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ADDENDUM

The HGB-MCV values index could be an effective, reliable, and acceptable approach to mass screening for early detection of carcinomas of the colon. It could be used in conjunction with the present method of screening for colorectal cancer—the occult blood testing of feces.

If the HGB-MCV index is used in mass screening for various colonic carcinomas, the following advantages would be evident:

1. it need not be performed in privacy;
2. it is cost effective;
3. it requires no specific instructions or restricted diets prior to sample collection;
4. it is reliable, with low probability of false negatives and positives;
5. it yields a quantitative result;
6. it permits the rapid and repeated screening of populations, particularly those at a higher risk of developing colorectal cancer, that is the adult male over age 50 and the postmenopausal female;
7. it enhances better patient acceptance and compliance;
8. it relieves the patient of responsibility in the preparation, collection, and handling of sample material;
9. it affords more aesthetic conditions under which the sample is collected.