Supplementary material

Supplementary Table 1 Serum Ferritin in CRC vs. Controls, among participants where ferritin was obtained at/before CRC diagnosis.

	CRC Proportions	Healthy Controls	P-Value
Female: Age 29-39			Fischer's Exact: **p=0.030**
Ferritin ≤ 20 ng/mL	9/13 (69.2%)	10931/34035 (32.1%)	**0.0041**
20.1-45 ng/mL	3/13 (23.1%)	10626/34035 (31.2%)	0.529
45.1-100 ng/mL	0/13 (0%)	8039/34035 (23.6%)	**0.0455**
≥ 100.1 ng/mL	1/13 (7.7%)	4439/34035 (13.0%)	0.569
Male: Age 29-39			Fischer's Exact: **p=0.0002**
Ferritin ≤ 20 ng/mL	4/5 (80%)	423/5892 (7.2%)	**<0.00001**
20.1-45 ng/mL	0/5 (0%)	825/5892 (14.0%)	0.368
45.1-100 ng/mL	0/5 (0%)	1738/5892 (29.5%)	0.147
≥ 100.1 ng/mL	1/5 (20%)	2906/5892 (49.3%)	0.190
Female: Age 40-49			Fischer's Exact: p=0.7881
Ferritin ≤ 20 ng/mL	5/14 (35.7%)	9364/32750 (28.6%)	0.556
20.1-45 ng/mL	5/14 (35.7%)	9947/32750 (30.4%)	0.667
45.1-100 ng/mL	2/14 (14.3%)	8230/32750 (25.1%)	0.347
≥ 100.1 ng/mL	2/14 (14.3%)	5209/32750 (15.9%)	0.865
Male: Age 40-49			Fischer's Exact: **p=0.0001**
Ferritin ≤ 20 ng/mL	7/16 (43.8%)	519/7534 (6.9%)	**<0.0001**
20.1-45 ng/mL	3/16 (18.8%)	920/7534 (12.2%)	0.424
45.1-100 ng/mL	2/16 (12.5%)	2021/7534 (26.8%)	0.197
≥ 100.1 ng/mL	4/16 (25.0%)	4074/7534 (54.1%)	**0.0198**

For the purpose of this analysis, one patient in EO-CRC cohort, age 22 years, was excluded to limit biases. Fisher's exact test was used to compare the proportions of the different ferritin level groups between EO-CRC and HCs. Then post-hoc z-test of proportions were used to compare specific ferritin levels between EO-CRC and HCs. Patients were grouped by age and sex to minimize confounding factors.

Abbreviations: ng/mL= nanogram/milliliter

Supplementary Table 2 Median, IQR Ferritin Levels among participants where ferritin was obtained at/before CRC diagnosis

	Females (n=25)	Males (n=21)	Total (n=46)
AJCC Stage			
I	13 ng/mL **	8.0 ng/mL *	12.5 ng/mL, 19.75 ng/mL
II	10.5 ng/mL **	2.5 ng/mL, 3.75 ng/mL	3 ng/mL, 7.5 ng/mL
III	8.5 ng/mL, 17.5 ng/mL	4.5 ng/mL, 13.75 ng/mL	6.5 ng/mL, 16.5 ng/mL
IV	27 ng/mL, 25 ng/mL	75.5 ng/mL, 164.5 ng/mL	32 ng/mL, 74 ng/mL
Anemia	14 ng/mL, 19.5 ng/mL	10.5 ng/mL, 63.25 ng/mL	12.5 ng/mL, 27.25 ng/mL
No Anemia	34 ng/mL, 100 ng/mL	180 ng/mL **	48 ng/mL, 157.5 ng/mL
Sex	18 ng/mL, 23.5 ng/mL	17 ng/mL, 107.5 ng/mL	-

***3 outliers were removed with ferritin >500 ng/mL (>quartile 3 (75th percentile) plus 5 times IQR)
Abbreviations: IQR, inter-quartile range; AJCC, American Joint Committee on Cancer
*One case included, unable to calculate IQR
**Three cases included, unable to calculate IQR

Supplementary Table 3 Statistical comparisons among participants where ferritin was obtained at/before CRC diagnosis.

	Effect Size	P-Value
Stage		
Kruskal-Wallis	0.421	**<0.001**
Kruskal-Wallis (Females)	0.218	0.099
Kruskal-Wallis (Males)	0.631	**0.004**
I x II	0.371	0.054
I x III	0.112	0.181
I x IV	0.108	0.088
II x III	0.077	0.238
II x IV	0.397	**<0.001**
III x IV	0.338	**<0.001**
Anemia x No Anemia	0.156	**0.007**
Female x Male	0.002	0.749

Standard deviation, ng/mL= nanogram/milliliter
Of note for the purpose of this analysis one patient aged 22 was excluded to limit biases

Supplementary Table 4 Correlation analyses among participants where ferritin was obtained at/before CRC diagnosis.

	r	P-Value
Serum Ferritin x Age *		
Total	0.387	**0.009**
Females	0.459	**0.028**
Males	0.248	0.292
Serum Ferritin x Months From Diagnosis		
Total	-0.075	0.618
Females	-0.324	0.115

Males	0.153	0.508

* Controlled for TNM stage