Scaderea ponderala involuntara

Proiect IDEI 2008

C Baicus

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Hernandez, *QJM 2003*

Table 4 Scoring system for malignant neoplasm in the setting of isolated involuntary weight loss

Variable	Points
Age > 80 years	+1
Serum albumin > 3.5 g/dl	−2
White blood count > 12 000/mm^3	+1
Alkaline phosphatase > 300 UI/l	+2
Lactate dehydrogenase > 500 UI/l	+3

Table 5 Distribution of patients according to score level

Score	Non-neoplastic diseases	Malignant neoplasms	LR
<0	115 (68%)	8 (9%)	0.07
0–1	51 (30%)	30 (35%)	1.2
>1	3 (2%)	49 (56%)	28

LR, likelihood ratio. Data show the total number of patients with that score level (percentage in parentheses).

Probabilitatea de a avea cancer (regresie logistică)

VSH>29mm/h	Anemie<10g Hb	Varsta>62a	Risc neo (CI) (%)	Risc non-neo (CI) (%)
NU	NU	NU	9 (0-15)	91 (85-100)
DA	NU	NU	18 (12-27)	82 (73-88)
NU	DA	NU	19 (12-30)	81 (70-88)
NU	NU	DA	23 (15-32)	77 (68-85)
DA	DA	NU	36 (16-63)	64 (37-84)
DA	NU	DA	41 (21-66)	59 (34-79)
NU	DA	DA	43 (21-68)	57 (32-79)
DA	DA	DA	64 (27-90)	36 (10-73)

C.Baicus et al. *Eur J Intern Med, 2006; 17:28-31.*

1. Studiu descriptiv, de evaluare a spectrului etiologic al SPI

2. Studiu diagnostic de evaluare a acuratetei TNF-alfa, IL-1 beta, IL-6, aFL ca markeri ai cancerului ca si cauza a SPI

3. Studiu diagnostic de evaluare a feritinei ca marker al cancerului gastrointestinal, mai sensibil decat anemia

4. Studiu diagnostic de validare a parametrilor clinici si biologici simpli (varsta, VSH, hemoglobina, fosfatazele alcaline, LDH, albumina), care au fost evidentiati in alte studii ca avand valoare predictiva privind existenta cancerului ca si cauza a SPI

5. Studiu diagnostic de evaluare a testului de absorbtie a fierului pentru discriminarea anemiei din bolile cronice de anemia feripriva

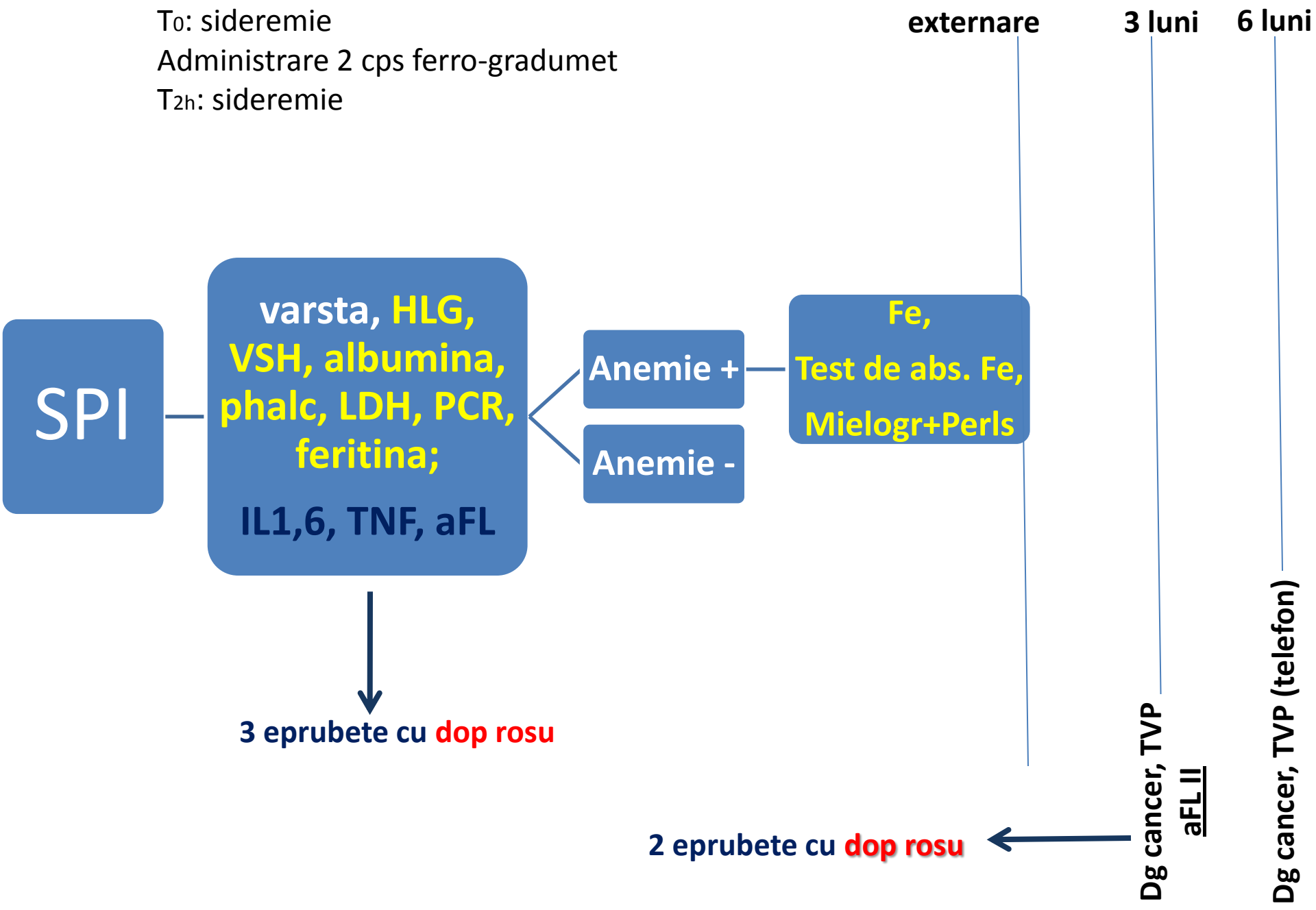
6. Un studiu de evaluare a prevalentei anticorpilor antifosfolipidici la pacientii cu SPI, de comparatie a frecventelor aparitiei lor la pacientii cu si fara cancer drept cauza a SPI si de evaluare a riscului de tromboze la pacientii cu si fara ac. anticardiolipinici.

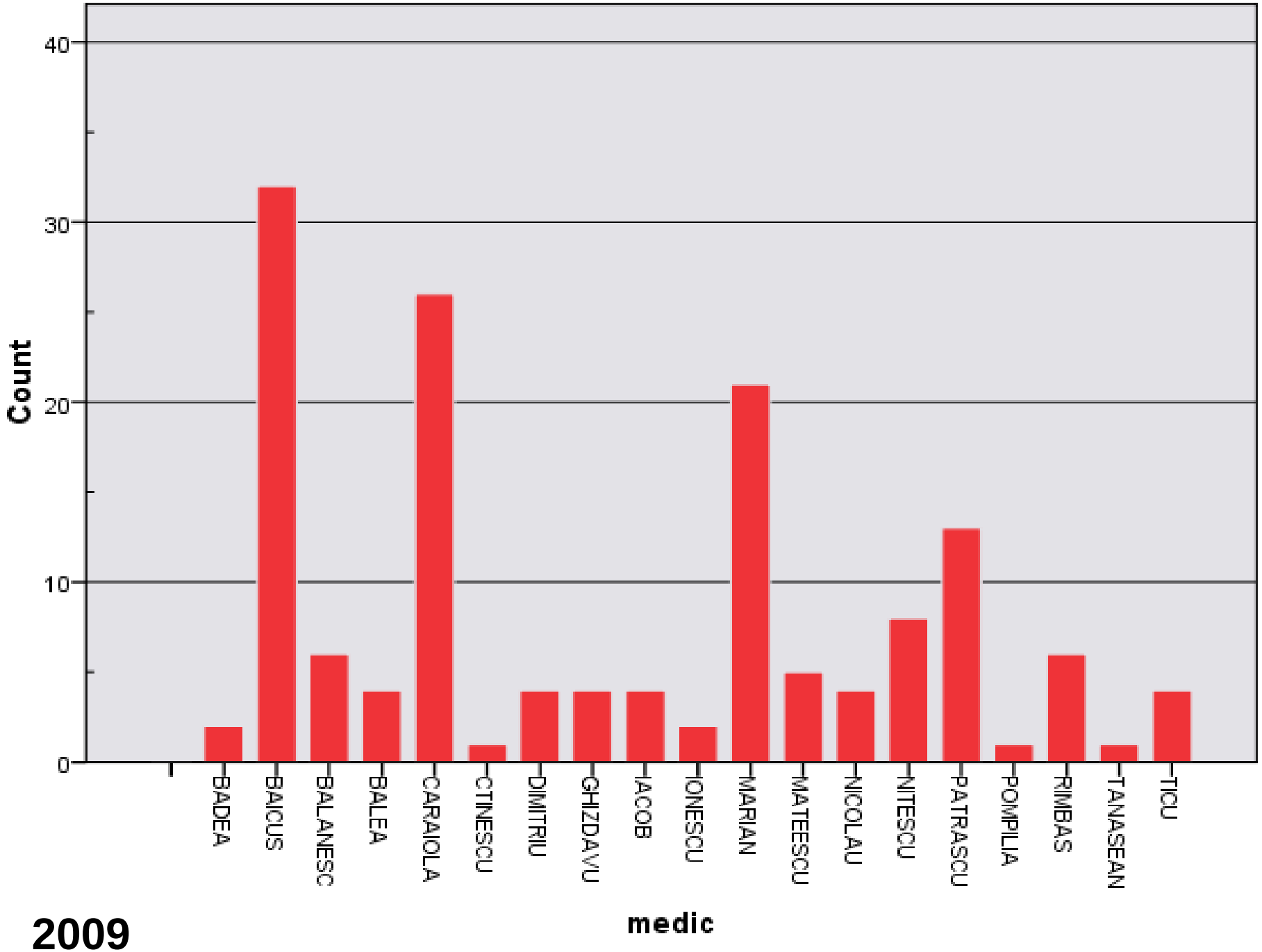
Testul de absorbtie a Fe (pe stomacul gol):

T_0: sideremie

Administrare 2 cps ferro-gradumet

T_{2h}: sideremie

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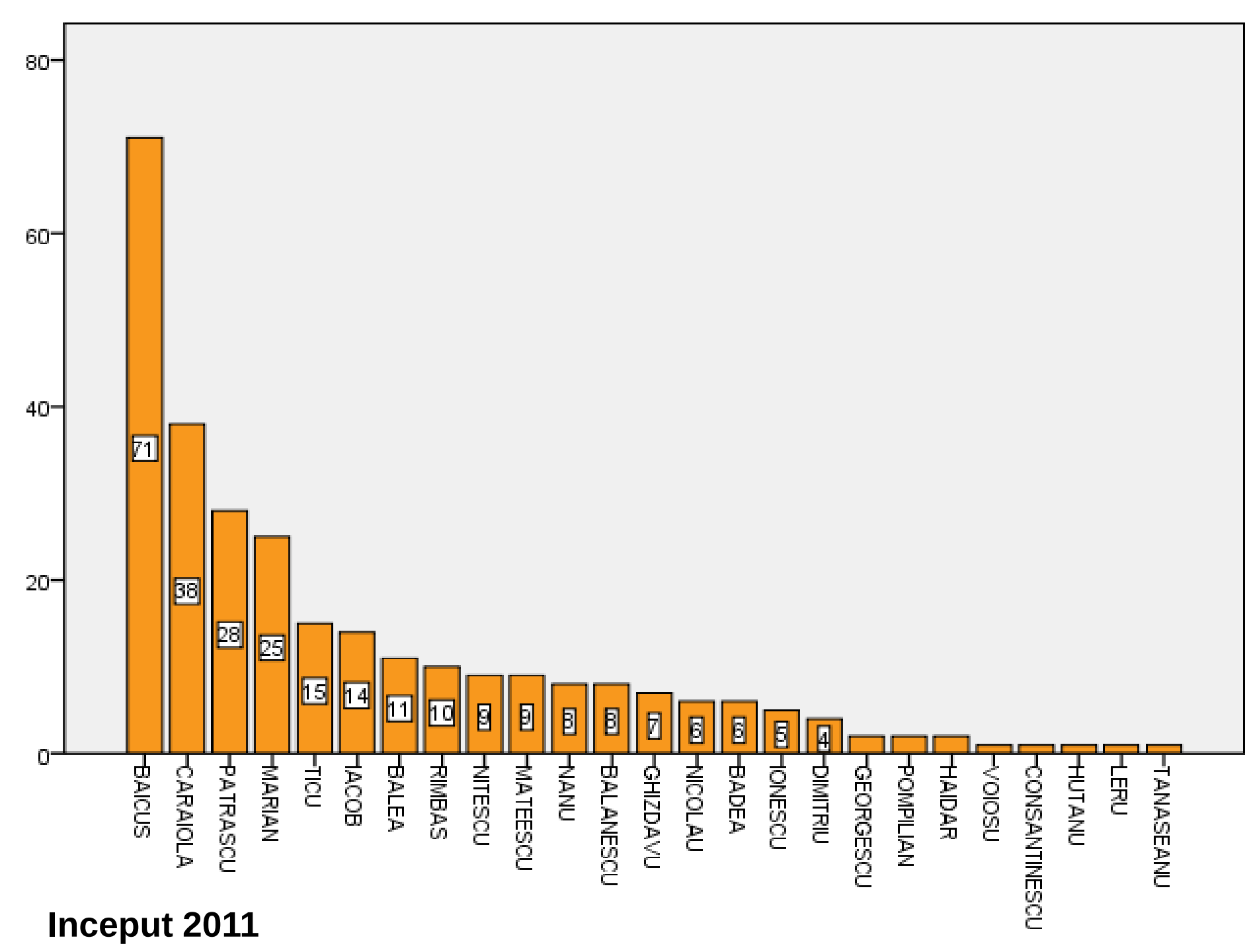

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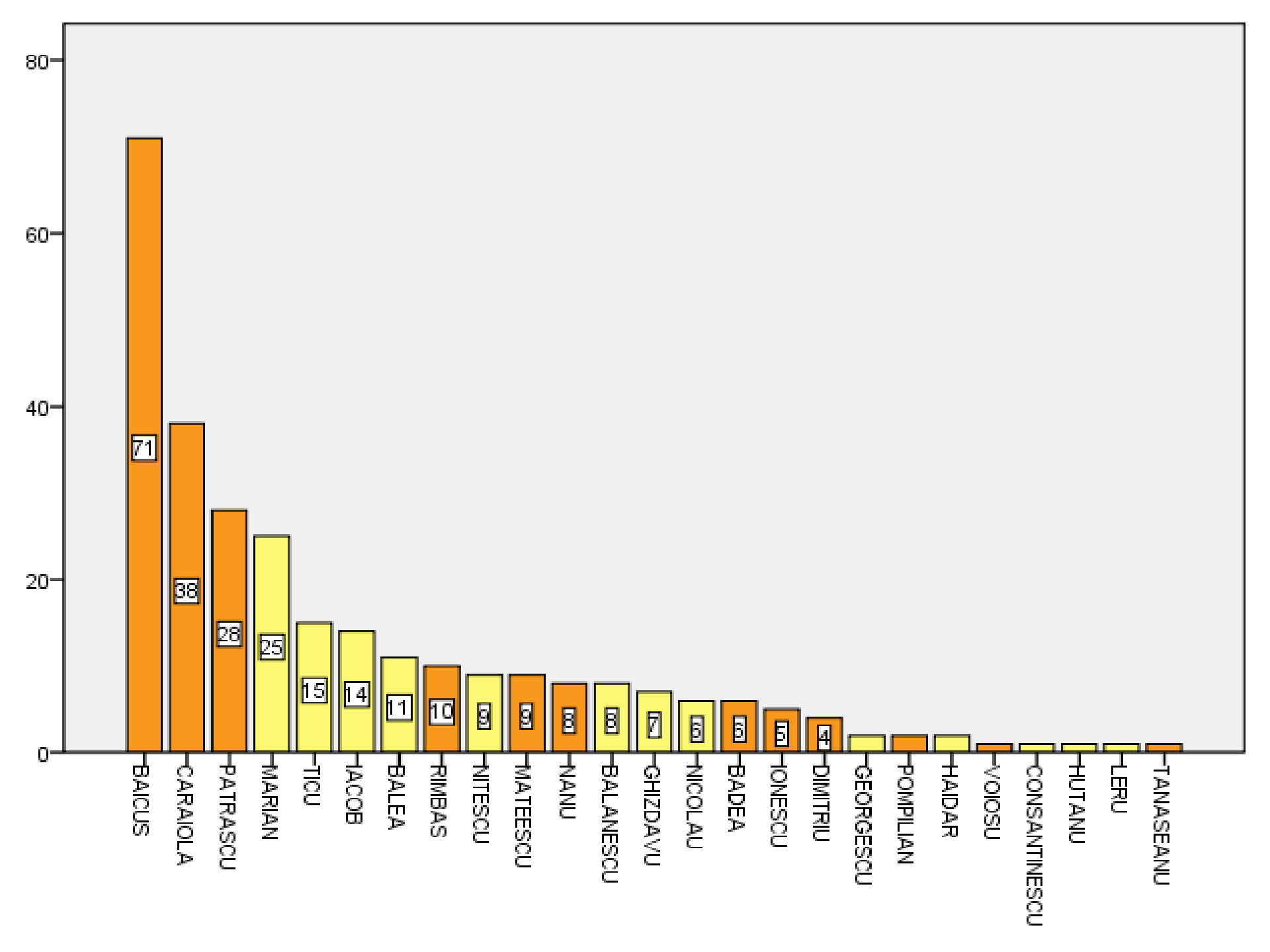
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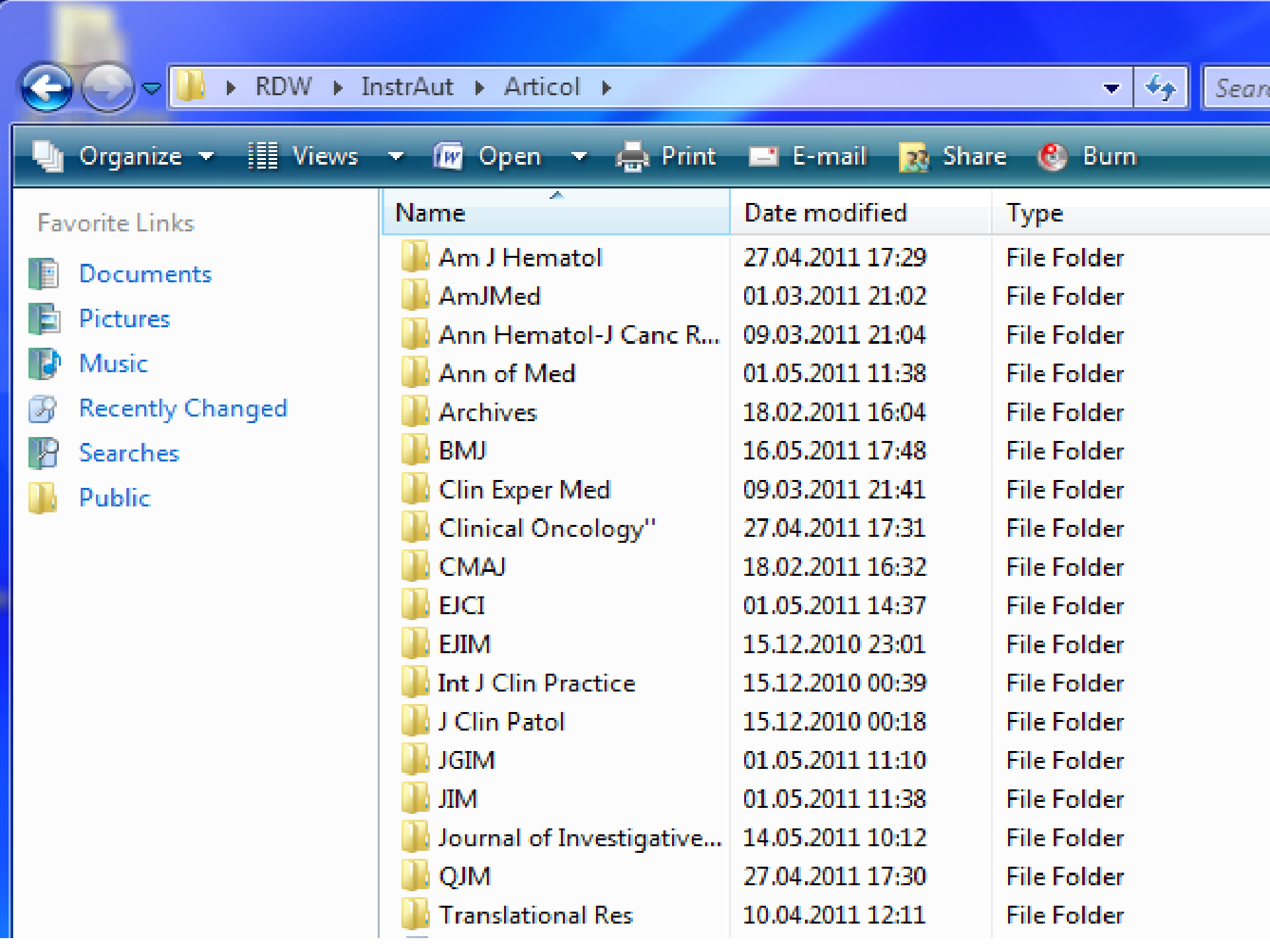
Running head: RDW for diagnosis of cancer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Subject: MS #10186 Invitation to Review

Dear Dr. Baicus:

In light of your interests and expertise, I invite you to review an article submitted to the Journal of General Internal Medicine (JGIM). The manuscript is entitled 'Red cell distribution width as a diagnostic test for cancer in patients with involuntary weight loss'. The abstract is pasted at the end of this note.

I would greatly value your opinion and hope that you are able to do this review. If you are willing to review this manuscript, please go to http://www.jgimed.org/authors/Reviewers.asp and register to be a reviewer; then please respond to this e-mail to say that you are ready to receive the review documents. Assistant Managing Editor Jenni Clarkson will then send the review materials to you via e-mail. Please return your review within three weeks.

If you are unable to review at this time, we'd appreciate suggestions for potential reviewers (and their email addresses). On behalf of the Journal of General Internal Medicine, thank you very much for considering this invitation.

Regards,
Michael Rothberg, MD
Deputy Editor
Journal of General Internal Medicine

Abstract
Introduction
A quarter of patients with involuntary weight loss (IWL) have cancer. Recent studies showed that red blood cell distribution width (RDW) is a predictor of mortality, including cancer-related death.
Objective
The aim of this study was to assess the ability of RDW to diagnose cancer in patients with IWL.
Design
Cohort study with 6-month follow-up

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Utility of routine hematological and inflammation parameters for the diagnosis of cancer in involuntary weight loss

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Mihai Rimbas, MD[1,2]

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† The Group for the Study of Involuntary Weight Loss (Grupul de Studiu al Scaderii Ponderale Involuntare): C Baicus, C Badea, E Balanescu, M Balea, S Caraiola, G Constantin, I Constantinescu, L Dimitriu, D Georgescu, O Ghizdavu, A Haidar, M Ghita, M Iacob, RA Ionescu, P Leru, A Marian, RB Mateescu, A Nanu, A Nicolau, I Nicolescu, D Nitescu, R Patrascu, V Pompilian, M Rimbas, S Tanaseanu, G Ticu, D Ursica, Th Voiosu, R Voiosu, (Colentina Clinical Hospital), A Baicus ("I Cantacuzino" Institute)

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Table 1. Patients' characteristics.

Characteristic	All patients	Patients with cancer	Patients without cancer	p
Age (years)	68 (33, 94)	70 (44, 82)	68 (33, 94)	p=0.069*
Male sex	126/253 (49%)	31/67 (54%)	90/186 (48%)	p=0.479†
RDW§ (%)	15 (11.5, 26.7)	15.1 (12.3, 19.6)	14.6 (11.5, 26.7)	**p=0.022***
Hemoglobin (g/dl)	11.8 (6.1, 16.4)	11.2 (7.2, 15.5)	12.1 (6.1, 16.4)	**p=0.010***
MCV¥ (femtoliters)	88 (64, 125)	87.2 (64, 102)	88.6 (66, 125)	p=0.145*
Serum iron (mcg/dl)	51 (4, 197)	38 (4, 162)	54.5 (11, 197)	**p=0.001***
ESR¥¥ (mm/h)	43 (2, 140)	58 (10, 140)	35 (2, 140)	**p<0.001***
CRP§§ (mg/L)	7.81 (1, 550)	41 (1, 550)	5.2 (1, 258)	**p<0.001***
Ferritin (mcg/L)	106 (5, 2000)	171 (10, 1105)	94 (5, 2000)	**p=0.019***
Death at 6 months	44/226 (19%)	34/61 (56%)	10/165 (6%)	**p<0.001†**
Cancer	67/253 (26%)			

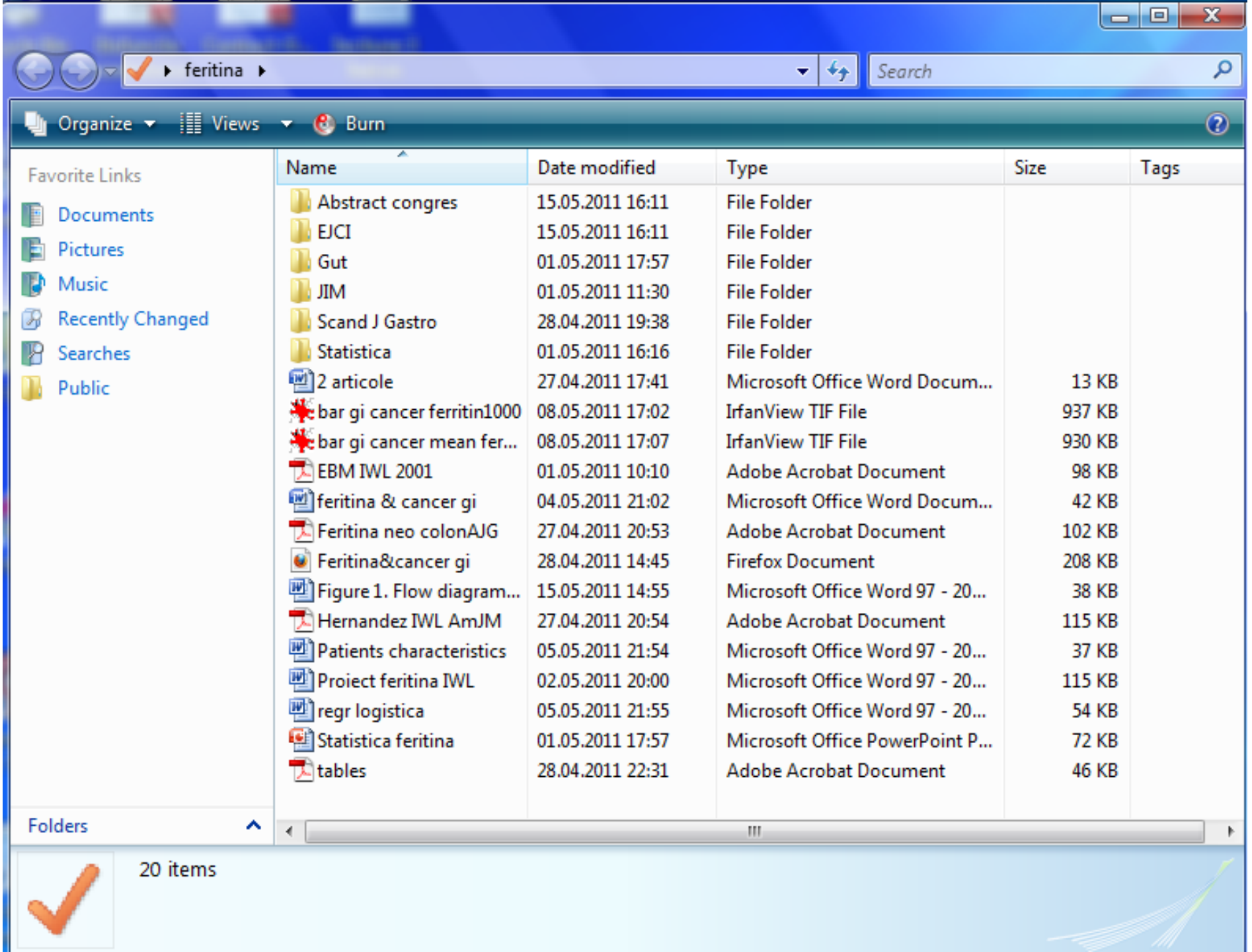
Table 2. Hematological and inflammation parameters as predictors of cancer in patients with involuntary weight loss – logistic regression

Variable	Odds ratio	95% CI	*P* value
RDW[§] (%)	1.01	0.83, 1.24	0.897
Hemoglobin (g/dl)	1.07	0.86, 1.32	0.561
MCV[¥] (femtoliters)	0.97	0.92, 1.02	0.213
Serum iron (mcg/dl)	0.997	0.98, 1.00	0.660
ESR[¥¥] (mm/h)	1.02	1.01, 1.03	**0.011**
CRP[§§] (mg/L)	1.00	0.99, 1.00	0.654
Ferritin (mcg/L)	1.00	0.99, 1.00	0.740

[§] red cell distribution width

Table 3. AUC of hematological and inflammation parameters in the diagnosis of cancer in patients with IWL.

Variable	AUROC	95% CI
CRP[§] (mg/L)	0.708	0.627, 0.790
ESR[¥¥] (mm/h)	0.690	0.620, 0.760
Serum iron (mcg/dl)	0.651	0.566, 0.735
Hemoglobin (g/dl)	0.607	0.526, 0.687
Ferritin (mcg/L)	0.598	0.518, 0.679
RDW[§] (%)	0.594	0.517, 0.671
MCV[¥] (femtoliters)	0.561	0.474, 0.649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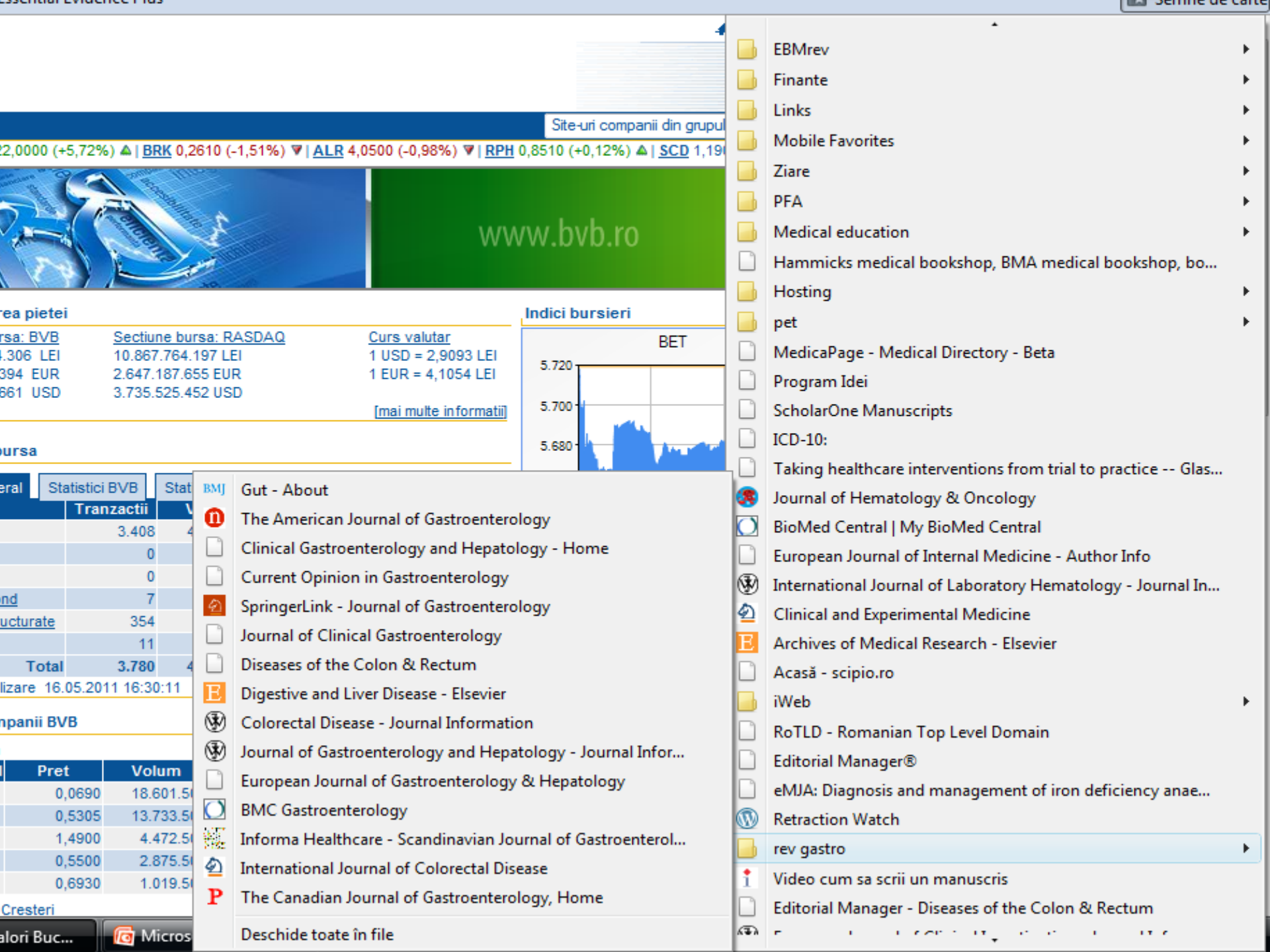
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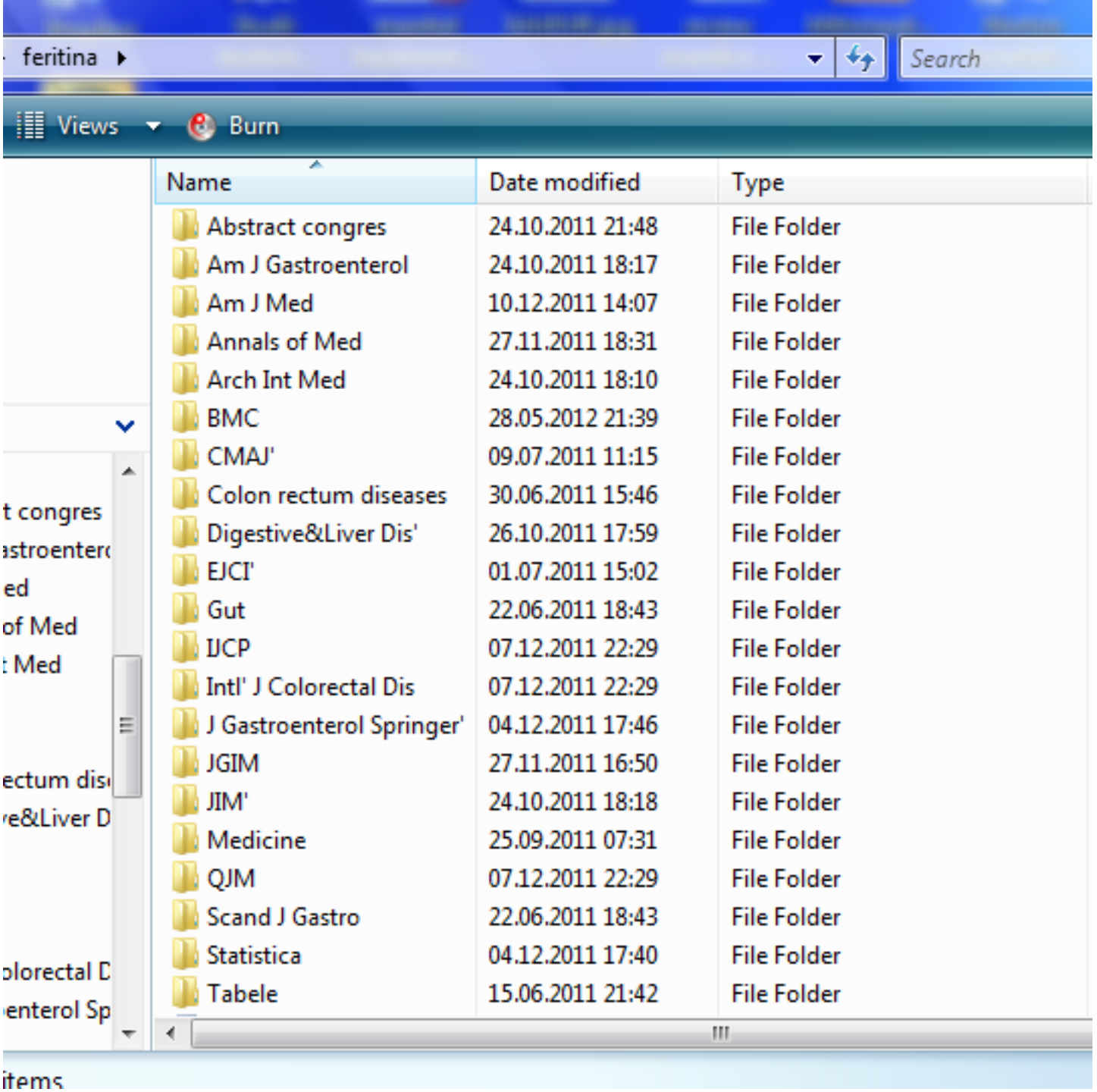
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Ferritin in the diagnosis of gastrointestinal cancer in patients with involuntary weight loss

Introduction

A quarter of patients with involuntary weight loss (IWL) have cancer, and part of them have gastrointestinal cancer, diagnosed by endoscopic studies. Ferritin is the first parameter modifying during the process leading to iron deficiency anemia, so it should be the most sensitive. The aim of this study is to assess the ability of ferritin to rule out gastrointestinal cancer in patients with IWL.

Material and methods

All consecutive patients with IWL admitted in a secondary care university hospital were prospectively studied. Ferritin, hemoglobin with erythrocyte indices and serum iron were recorded for all patients. The reference standard was bidirectional endoscopy and/or 6 months follow-up.

Results

290 patients with IWL were included, a quarter had cancer, of which 24 (7.6%) had gastrointestinal cancer (9 gastric cancer, 1 ileal cancer, 14 colorectal cancer). Ferritin had the best area under the curve (AUC), both for gastrointestinal cancer (0.746, 95% confidence interval [CI]: 0.691-0.794), and colorectal cancer (0.765, CI: 0.713-0.813), compared to the other parameters of iron deficiency anemia. In the diagnosis of colorectal cancer, ferritin with a cut-off value of 100 mcg/L had a sensitivity of 93% (CI: 69-100%), and negative likelihood ratio of 0.13, with a negative predictive value of 99% (96-100%), while for gastrointestinal cancer, the sensitivity was lower (89%, CI: 67-95%), with a negative likelihood ratio of 0.24. There were three false negative patients, two with gastric cancer, and one with rectal cancer.

Conclusions

In patients with involuntary weight loss, a ferritin above 100mcg/L could rule out colon cancer, but not gastric cancer.

AUC

	Colorectal cancer		Gastrointestinal cancer	
	AUC	95% CI	AUC	95% CI
Feritina	0.765	0.713-0.813	0.746	0.691-0.794
Vem	0.669	0.612-0.725	0.627	0.568-0.684
Fe	0.650	0.584-0.710	0.636	0.571-0.697
Hb	0.552	0.491-0.609	0.590	0.530-0.646
Rdw	0.463	0.401-0.528	0.541	0.476-0.602

Feritin100 as dg test

	Gastrointestinal cancer		Colorectal cancer	
		95% CI		95% CI
Sensitivity (%)	86	67-95	93	69-100
Specificity (%)	57	51-62	56	50-62
Positive predictive value (%)	14	9-21	10	6-16
Negative predictive value (%)	98	94-100	99	96-100
Positive likelihood ratio	2		2.1	
Negative likelihood ratio	0.24		0.13	

Feritin50 as dg test

	Gastrointestinal cancer		Colorectal cancer	
		95% CI		95% CI
Sensitivity (%)	59	39-77	64	39-84
Specificity (%)	76	71-81	75	70-80
Positive predictive value (%)	17	10-27	12	6-20
Negative predictive value (%)	96	92-98	98	95-99
Positive likelihood ratio	2.5		2.6	
Negative likelihood ratio	0.54		0.47	

Anemia as dg test

	Gastrointestinal cancer		Colorectal cancer	
		95% CI		95% CI
Sensitivity (%)	68	47-84	64	39-84
Specificity (%)	51	45-57	50	44-56
Positive predictive value (%)	10	6-16	6	3-11
Negative predictive value (%)	95	90-98	97	92-99
Positive likelihood ratio	1.4		1.3	
Negative likelihood ratio	0.63		0.71	

		Colon cancer	Gastrointestinal cancer
Anemia, present	Ferritin (100mcg/L)	P<0.001	P<0.001
	Ferritin (50 mcg/L)	P=0.005	P<0.001
	Ferritin (mcg/L)	P<0.001	P=0.001
Anemia, absent	Ferritin (100mcg/L)	P=0.375	P=0.125
	Ferritin (50 mcg/L)	P=0.154	P=0.196
	Ferritin (mcg/L)	P=1.000	P=0.536

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Submissions with an Editorial Office Decision for Author Cristian Baicus, MD, PhD

Page: 1 of 1 (1 total completed submissions)

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Action	Manuscript Number	Title	Initial Date Submitted	Status Date	Current Status	Date Final Disposition Set	Final Disposition
View Submission View Decision Letter Send E-mail	DLD-11-442	Ferritin for the diagnosis of gastrointestinal cancer in patients with involuntary weight loss	Jun 28, 2011	Sep 27, 2011	Completed - Reject	Sep 27, 2011	Reject

Page: 1 of 1 (1 total completed submissions)

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- Promising results of this study, slightly disagree with data recently published by the same authors. In a series of 253 pts with IWL (Baicus C, Caraiola S, Rimbas M, Patrascu R, Baicus A; for Grupul de Studiu al Scaderii Ponderale Involuntare. Utility of Routine Hematological and Inflammation Parameters for the Diagnosis of Cancer in Involuntary Weight Loss. J Investig Med. 2011 Jun 25), they showed a statistically association with cancer of all hematological and inflammation parameters. Among evaluated parameters, just erythrocyte sedimentation rate remained associated with cancer in the multivariate analysis, being AUC for ferritin levels significantly different from data currently submitted.

- 1) patients were enrolled on an objective evaluation or on a reported or a presumed basis of a weight loss and it coud be a cause of bias in the study group that could explain the low rate of gastrointestinal cancer reported in this study.
  2)the protocol of the study was not standardised and every physician decided on the basis of himself suspicion of a gastrointestinal cancer to suggest a gastrointestinal endoscopic investigation to the patient.
  3) Fecal occult blood test was included in the panel of the lab tests or not?
  4) it would be interesting to know where the colorectal cancers were located in the colon (right vs left colon) and how many patients complaint of other symptoms out of IWL.
  5) the group of patients was not stratified according to the age. It is known that colorectal cancer is increasing in the elderly population. This is probably another cause of the low rate of colorectal cancer observed in this study in which patient with IWL older than 18 were enrolled.

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Scope

BMC Gastroenterology is an open access, peer-reviewed journal that considers article on all aspects of the prevention, diagnosis and management of gastrointestinal and hepatobiliary disorders, as well as related molecular genetics, pathophysiology, and epidemiology.

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From the blog

As an author

Submitted manuscripts

Ferritin above 100 mcg/L could rule out colon cancer, but not gastric or rectal cancer in patients with involuntary weight loss

Revise

Journal:	**BMC Gastroenterology**
Manuscript ID:	3745572546469124
Submitted:	7 December 2011
Last updated:	29 May 2012 View PDF
Peer review status:	Under re-review

Major compulsory revisions

1. The ferritin level is influenced also by inflammation and alcohol. CPR has been measured according to the Methods section, but the results are not presented or discussed in relation to ferritin data. This must be done, particularly in relation to inflammation. How many patients had elevated CRP? What was the situtation in those patients with Ferritin >100? Are the conclusions still valid if the contributions from inflammation and alcohol are included or if patients with active inflammation are excluded?
2. The number of patients that had both upper and lower endoscopy should be clearly stated also in the text - can be concluded from Fig 1.
3. The titel could be more informative. Maybe "Ferritin above 100 mcg/L rule out colon cancer in patients with involuntary weight loss."

Minor essential revisions

1. Explain the meaning of "hospital work-up" Under "Patient inclusion," paragraph 2.
2. Figure 2 may not be needed

Special remarks:

1. Why you used different groups (gastrointestinal or colorectal cancer)? Statistical power may increase if you take them together?
2. It is important to show the differences for mean values of measured parameters (CRV, ERS, HB, MCV) in patents with cancer and without.
3. In results you describe sensitivity and specificity of ferritin and other parameters for diagnosing gastrointestinal- or colorectal cancer. Why in discussion you concluded: ? Ferritin?100 mcg/L could exclude colon cancer, because it had good sensitivity and negative likelihood ratio, and a very high negative predictive value??
4. How do you describe why so many patients with cancer had anemia already?
5. It might be decrease the capacity decreasing doubling the text and figures and some tables.

* * * * * * *

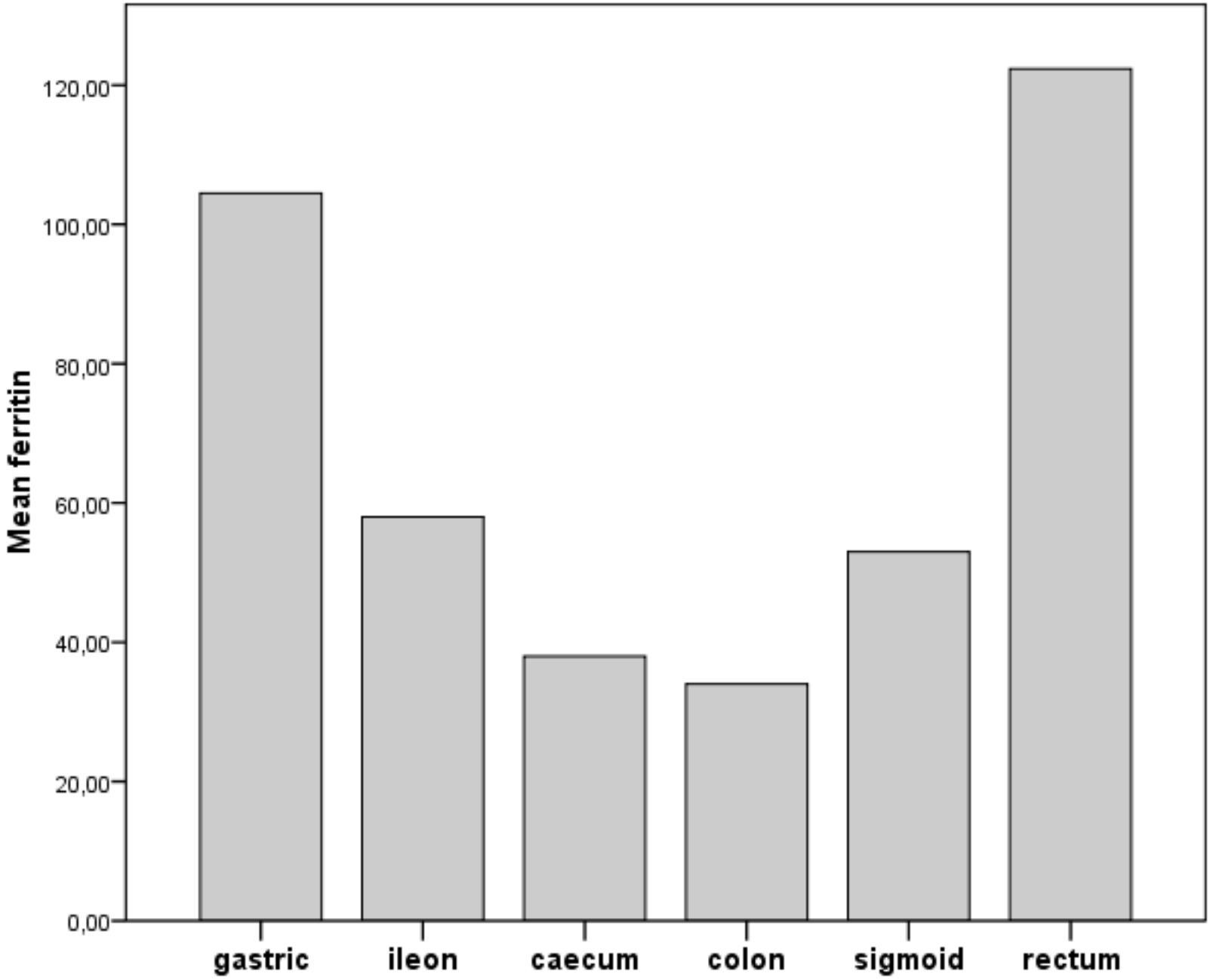
Ferritin above 100 mcg/L could rule out colon cancer, but not gastric or rectal cancer in patients with involuntary weight loss

Table 1. Patients' characteristics

Characteristic	Patients without cancer	Patients with gastrointestinal cancer	Patients with other cancers
Age (yr)	67 (22, 94)	70 (55, 82)	66 (44, 93)
Male sex	104 (48%)	12 (54%)	30 (58%)
RDW (%)	14.5 (10.3, 26.7)	14.8 (12.3, 20.4)	15.1 (11.5, 20.8)
Haemoglobin (g/dL)	12.6 (6.14, 17.4)	11.3 (7.9, 15.1)	11.8 (5.42, 17.7)
MCV (fL)	88 (62, 124)	84.5 (64, 98)	88.2 (72, 102)
Serum iron (mcg/dL)	54 (10, 197)	35.5 (10, 118)	35 (4, 162)
Ferritin (mcg/L)	99.5 (3, 2000)	26.5 (10, 500)	226 (15, 1105)
ESR (mm/h)	28 (2, 140)	44.5 (3, 140)	58 (11, 140)
CRP (mg/L)	5 (0.51, 328)	22 (1.6, 125)	46 (1, 550)
ALAT (u/L)	18 (6, 325)	18 (10, 71)	26 (10, 143)
Total number	216	22	52

Table 6. Ferritin, ESR, CRP, ALAT and alcoholism* in patients with gastrointestinal cancer

localisation of cancer	nr	ferritin	anaemia	ESR	PCR	ALAT	alcoholism
CAECUM	1	38	**NO**	16	5.7	12.7	NO
COLON (ascending, transverse, descending)	1	71	YES	**101**	**77.4**	13	NO
	2	82	YES	**140**	**125**	30	NO
	3	26	YES	**57**	**25.6**	21.7	NO
	4	10	YES	**60**	1.7	12	NO
	5	20	YES	**71**	**53**	12	NO
	6	14	YES	**44**	**29.6**	14.6	NO
	7	17	YES	**45**	**22**	**34**	**YES**
STOMACH	1	16	**NO**	10	1.59	15	NO
	2	87	YES	**53**	**110**	**47**	**YES**
	3	12	YES	**44**	**40**	24	NO
	4	**108**	YES	29	**26.5**	**71**	**YES**
	5	15	YES	24	**18.7**	24	NO
	6	**500**	YES	**90**	**51**	30	NO
	7	86	**NO**	36	**21.7**	18	NO
	8	11	YES	40	**20.7**	10	NO
ILEUM	1	58	YES	**49**	**35**		NO
RECTUM	1	27	**NO**	**51**	**36.5**	13	NO
	2	**322**	**NO**	**56**	**27**	31	NO
	3	18	**NO**	3	7.3	19	NO
SIGMOID	1	23	YES	16	16	10	NO
	2	83	**NO**	18	3	10.4	NO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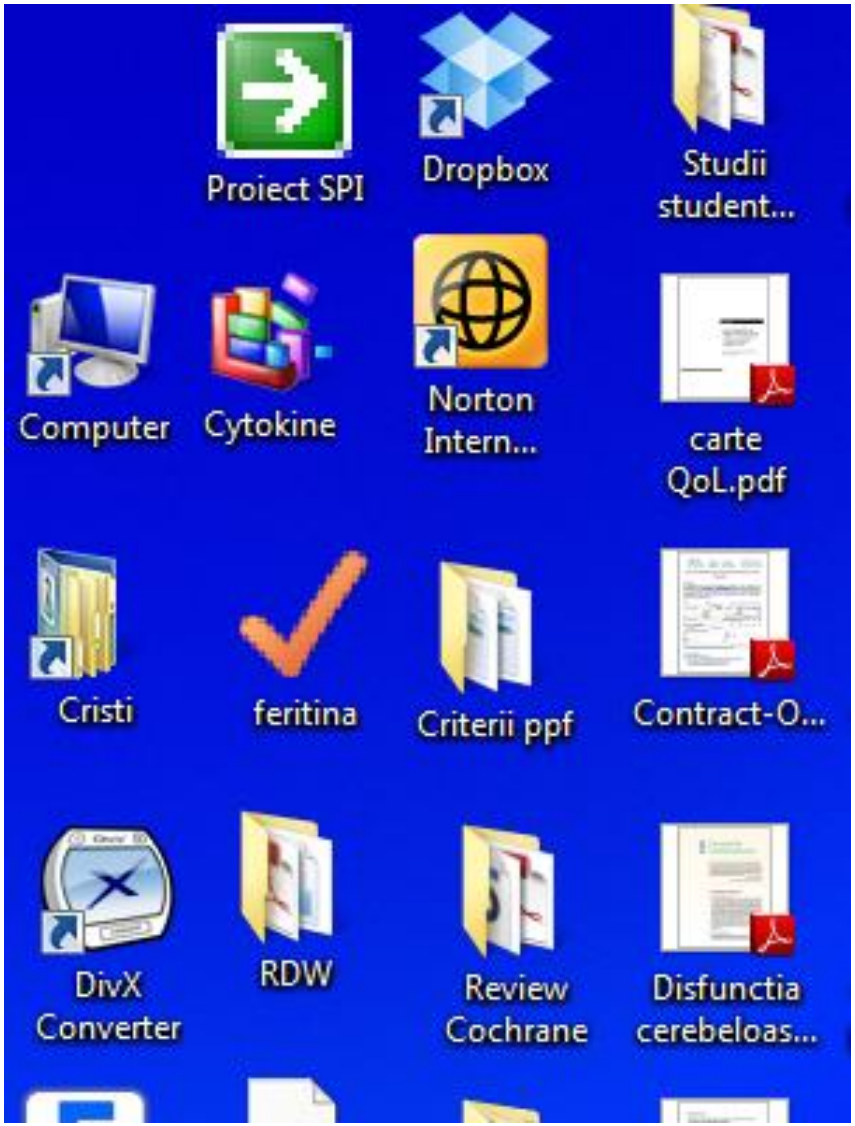
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Table 6. Ferritin, ESR, CRP, ALAT and alcoholism* in patients with gastroin
cancer

localisation of cancer	nr	ferritin	anaemia	ESR	PCR	ALAT
CAECUM	1	38	**NO**	16	5.7	12.7
COLON	1	71	YES	**101**	**77.4**	13
(ascending,	2	82	YES	**140**	**125**	30
transverse,	3	26	YES	**57**	**25.6**	21.7
descending)	4	10	YES	**60**	1.7	12
	5	20	YES	**71**	**53**	12
	6	14	YES	**44**	**29.6**	14.6
	7	17	YES	**45**	**22**	**34**
STOMACH	1	16	**NO**	10	1.59	15
	2	87	YES	**53**	**110**	**47**
	3	12	YES	**44**	**40**	24
	4	**108**	YES	29	**26.5**	**71**
	5	15	YES	24	**18.7**	24
	6	**500**	YES	**90**	**51**	30
	7	86	**NO**	36	**21.7**	18
	8	11	YES	40	**20.7**	10
ILEUM	1	58	YES	**49**	**35**	
RECTUM	1	27	**NO**	**51**	**36.5**	13
	2	**32**				
	3	1				
SIGMOID	1	2				
	2	8				

* alcoholism as discharge diag

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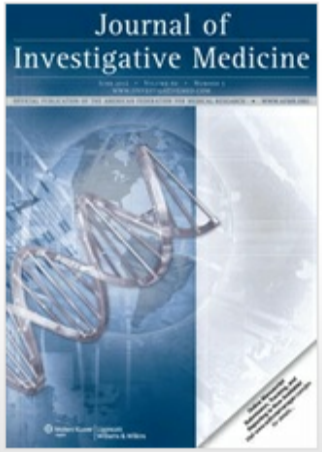

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Submissions with an Editorial Office Decision for Author Cristian Baicus, MD, PhD

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Action	Manuscript Number	Title	Initial Date Submitted	Status Date	Current Status	Date Final Disposition Set	Final Disposition
View Submission R 2 Author Response View Decision Letter Send E-mail	JIM-D-11-00035	Utility of routine hematological and inflammation parameters for the diagnosis of cancer in involuntary weight loss	Mar 09, 2011	May 13, 2011	Completed	May 13, 2011	Accept
View Submission R 1 Author Response View Decision Letter Send E-mail	JIM-D-11-00168	Serum Cytokines and Cancer in Involuntary Weight Loss	Sep 29, 2011	Feb 21, 2012	Completed	Feb 21, 2012	Accept

Page: 1 of 1 (2 total completed submissions)

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Serum Cytokines and Cancer in Involuntary Weight Loss

Cristian Baicus, MD, PhD,† Simona Caraiola, MD,*† Mihai Rimbas, MD,*† Ruxandra Patrascu, MD, PhD,* and Anda Baicus, MD, PhD†‡ for the GSSPI§*

Background: Tumor necrosis factor α (TNF-α), interleukin 1β (IL-1β), and IL-6 may be associated with involuntary weight loss in patients with and without cancer. However, results of previous studies have been conflicting. We evaluated patients who had involuntary weight loss to determine cytokine levels and the correlation of these cytokines with weight loss, the association with inflammation, and the potential for use in cancer diagnosis.

Materials and Methods: In 290 consecutive patients with involuntary weight loss (74 patients [26%] with cancer and 216 patients [74%] without cancer), erythrocyte sedimentation rate (ESR), and serum levels of C-reactive protein, TNF-α, IL-1β, and IL-6 were determined.

Results: Higher ESR and levels of C-reactive protein, TNF-α, IL-1β, and IL-6 were associated with cancer. The levels of TNF-α, IL-1β, and IL-6 did not correlate with the amount of weight loss. In multivariable analysis, only ESR was associated with cancer.

Conclusions: In patients with involuntary weight loss, TNF-α, IL-1β, and IL-6 were associated with cancer but were not weight loss mediators.

Key Words: tumor necrosis factor, interleukin, cachexia

(*J Investig Med* 2012;00: 00–00)

TABLE 1. Clinical Characteristics and Laboratory Studies in Patients with Involuntary Weight Loss*

Characteristic	All Patients	Patients With Cancer	Patients Without Cancer	P†
Number (%) of patients	290 (100)	74 (26)	216 (74)	
Age, yrs	67 (22, 94)	69 (44, 93)	67 (22, 94)	NS
Male sex	146/290 (50%)	42/74 (57%)	104/216 (48%)	NS
Weight loss, kg	10 (3, 36)	10 (4, 36)	10 (3, 32)	NS
Weight loss, %	13 (5, 40)	13 (5, 40)	13.4 (5.12, 35)	NS
ESR, mm/h	40 (2, 140)	50 (3, 140)	28.5 (2, 140)	<0.001
CRP, mg/L	8.76 (0.5, 550)	29.6 (1, 550)	5.1 (0.5, 328)	<0.001
TNF-α, pg/mL	13.6 (2.4, 455)	16.7 (4, 455)	12.05 (2.4, 197)	<0.02
IL-1β, pg/mL	7.4 (0, 863)	15 (0, 435)	6.5 (0, 863)	<0.05
IL-6, pg/mL	25.8 (0, 2364)	59.6 (0, 2085)	15.6 (0, 2364)	<0.001

*Data reported as number (percent) for categorical variables, and median (minimum, maximum) for continuous variables that were not normally distributed.

†NS, not significant ($P \geq 0.05$); sex tested with the Fisher exact test, and all other variables tested with the Mann-Whitney test.

IL-6 than patients without cancer (Table 1). There was no correlation evident between serum cytokine levels and the amount of weight loss, either in the entire group of patients or in the patients with cancer. However, there was a weak correlation be-

When assessed for the diagnosis of cancer in patients with involuntary weight loss, the areas under the receiver operator characteristic curves for TNF-α (0.61; CI, 0.55–0.67), IL-1β (0.57; CI, 0.513–0.633), and IL-6 (0.69; CI, 0.63–0.75) were comparable to those of ESR (0.67; CI, 0.61-0.72) or CRP (0.69; CI, 0.62–0.75). In the logistic regression model using all these variables, only ESR was significantly associated with cancer ($P < 0.001$); TNF-α, IL-1β, and IL-6 were not significantly associated with cancer.

Clinical prediction rules

There are no clinical prediction rules or standardized guidelines that have been externally validated or widely accepted for the clinical evaluation of weight loss. One clinical prediction rule to identify malignancy in patients with unexplained involuntary weight loss was prospectively validated at the same site in a group of 328 patients (in whom malignancy was identified in 35 percent) [47]. The independent predictors of malignancy included elevated levels of alkaline phosphatase and LDH, low albumin, leukocytosis, and advanced age (table 2). This clinical prediction rule requires external validation prior to widespread use.

In a prospective cohort study of 101 patients, 22 of 22 patients with malignancy had an abnormal laboratory test, with C-reactive protein, hemoglobin, lactate dehydrogenase, and albumin having the highest sensitivities [42]. Abnormal abdominal ultrasound and chest radiograph had lower sensitivities, 45 and 18 percent, respectively. However, all of these diagnostic tests were also abnormal, but to a lesser extent, among patients with non-malignant organic disease. Thus, there is no general diagnostic test or group of tests that appears to be specific for malignancy.

MANAGEMENT — The management of weight loss depends on the specific underlying cause.

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Reference:
Hernandez JL, Matorras P, Riancho JA, et al. Involuntary weight loss without specific symptoms: a clinical prediction score for malignant neoplasm. Q J Med 2003; 96: 649-55.

Population:
Patients presenting to a Spanish general medicine clinic with involuntary weight loss and no obvious cause. About 2/3 inpatients, mean age 65 years, 52% male. Final diagnosis established for 308 of 328 patients initially identified.

Type of Validation:
Quality score 2 (1-4): Split-sample with prospective validation

Prevalence of the primary outcome: 35.0%

308 patients were used to develop this rule.

52 patients were used to validate this rule.

IMPORTANT: This clinical calculator simplifies clinical calculations based on information found in the above article. The recommendation made by the software is NOT medical advice, and should be the same as you would get by reading the article and doing the calculations by hand. Your final patient decision should take into account all relevant information about your patient and your best clinical judgment.

Probability of cancer with unwanted weight loss

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In patients w/ involuntary weight loss:

- [ ] Age > 80 years
- [ ] Serum albumin > 3.5 g/dl
- [ ] White blood count > 12,000/mm3
- [ ] Alkaline phosphatase > 300 UI/L
- [ ] Lactate dehydrogenase > 500 UI/L

Mod risk: 30/81 (37%)

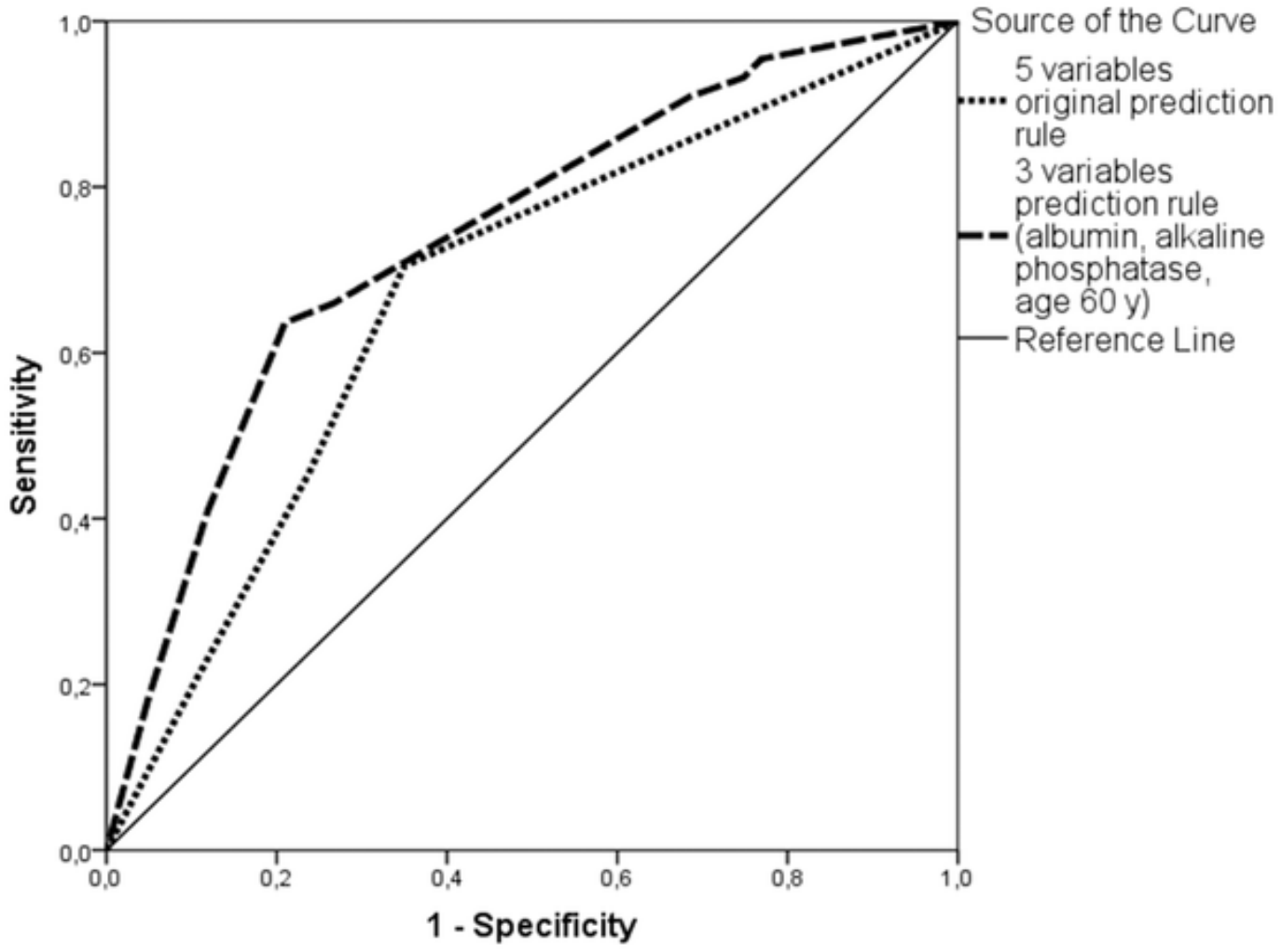
More Info

Table 3. Multivariable Analysis in Patients Who Had Involuntary Weight Loss and Comparison with Hernandez Study*

Variable	All patients (290 patients) AUC: 0.70 (0.61-0.78)			Patients included by the first criterion (known amount of weight loss) (228 patients) AUC: 0.70 (0.61-0.80)			Hernandez study [5] AUC: 0.89 (0.87-0.91)
	Odds Ratio	(95% Confidence Interval)	*P*	Odds Ratio	(95% Confidence Interval)	*P*	Odds Ratio
Age > 80 y	1.2	(0.4-3.7)	.82	0.8	(0.2-3.0)	.69	3.4
High white blood cell count	2.2	(0.9-5.1)	.07	1.8	(0.7-4.7)	.21	3.6
Low serum albumin	2.6	(1.3-5.2)	.02	2.5	(1.1-5.6)	.02	6.7
High serum alkaline phosphatase	2.3	(1.2-4.7)	.01	2.1	(1.0-4.2)	.04	12
High serum lactate dehydrogenase	1.3	(0.6-2.5)	.53	1.3	(0.6-2.8)	.48	12.5
AUC	0.70 (0.61-0.78)			0.70 (0.61-0.80)			0.89 (0.87-0.91)

*Logistic regression. ***Abbreviations:*** AUC, area under the curve.

Figure 2. Receiver Operating Characteristic Curves of the Hernandez and Present Models in Patients Who Had Involuntary Weight Loss.



Baicus C, Rimbas M, Baicus A, Caraiola S, Grupul de Studiu al Scaderii Ponderale Involuntare (2014) Cancer and Involuntary Weight Loss: Failure to Validate a Prediction Score. PLoS ONE 9(4): e95286. doi:10.1371/journal.pone.0095286
http://127.0.0.1:8081/plosone/article?id=info:doi/10.1371/journal.pone.0095286

Table 5. Modified Regression Model For the Relation Between Clinical Variables and Probability of Having Cancer in Patients Who Had Involuntary Weight Loss*.

-----	----Variable---	-----	Probability	of
Age >60 y	Alkaline Phosphatase >104 U/L	Albumin <3.5 g/dL	Having Cancer (%) (95% Confidence Interval)	Not Having Cancer (%) (95 Confidence Interval)
No	No	No	5 (3–8)	95 (92–97)
No	No	Yes	11 (8–14)	89 (86–92)
No	Yes	No	13 (10–17)	87 (83–90)
Yes	No	No	20 (16–24)	80 (76–84)
No	Yes	Yes	25 (21–30)	75 (70–79)
Yes	No	Yes	34 (30–39)	66 (61–70)
Yes	Yes	No	40 (35–45)	60 (56–65)
Yes	Yes	Yes	59 (54–64)	41 (36–46)

*N = 290 patients.

doi:10.1371/journal.pone.0095286.t005

Baicus C, Rimbas M, Baicus A, Caraiola S, Grupul de Studiu al Scaderii Ponderale Involuntare (2014) Cancer and Involuntary Weight Loss: Failure to Validate a Prediction Score. PLoS ONE 9(4): e95286. doi:10.1371/journal.pone.0095286
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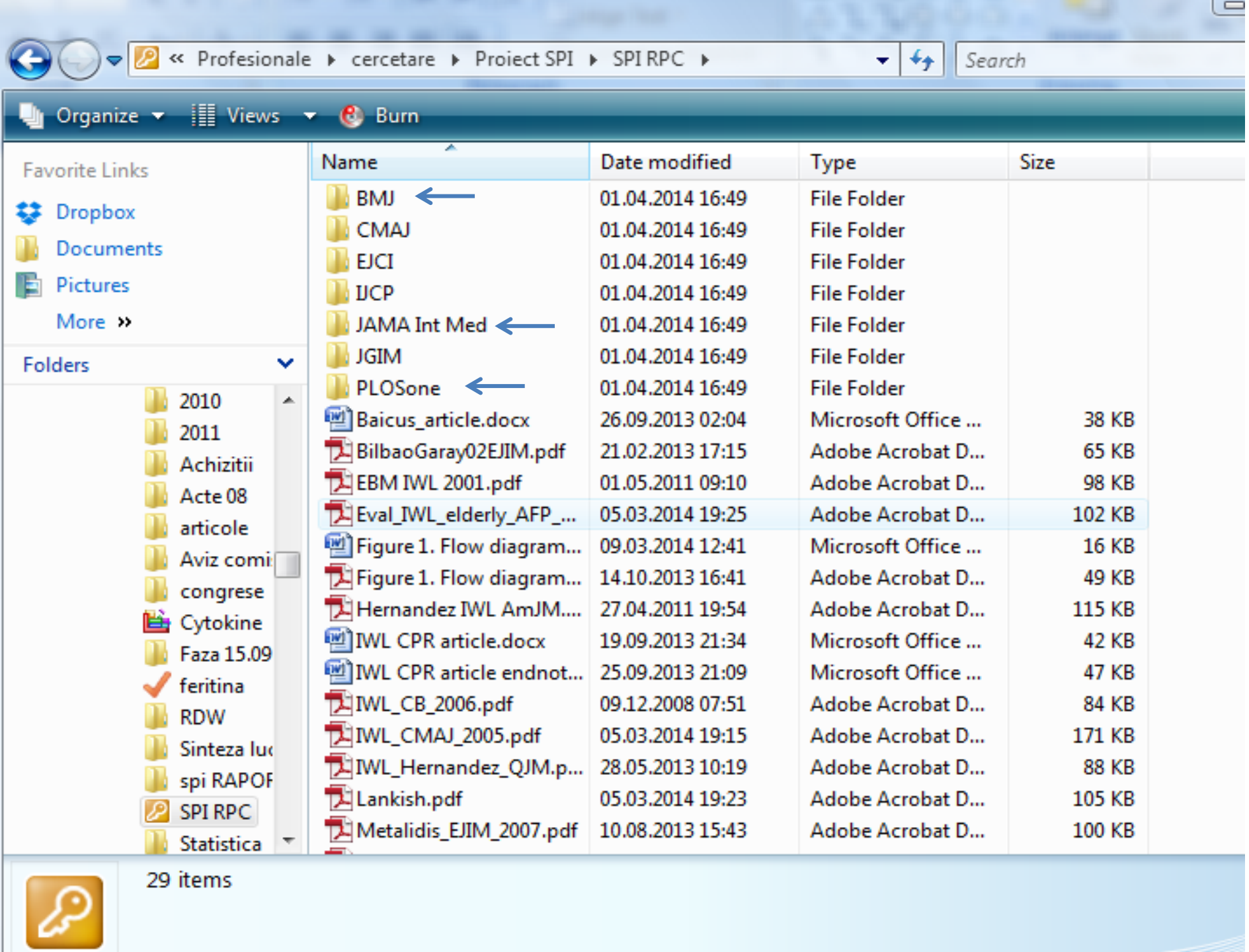
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PLOS ONE

Cancer and Involuntary Weight Loss: Failure to Validate a Prediction Score

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1. Studiu descriptiv, de evaluare a spectrului etiologic al SPI

2. Studiu diagnostic de evaluare a acuratetei TNF-alfa, IL-1 beta, IL-6 ca markeri ai cancerului ca si cauza a SPI

3. Studiu diagnostic de evaluare a feritinei ca marker al cancerului gastrointestinal, mai sensibil decat anemia

4. Studiu diagnostic de validare a parametrilor clinici si biologici simpli (varsta, VSH, hemoglobina, fosfatazele alcaline, LDH, albumina), care au fost evidentiati in alte studii ca avand valoare predictiva privind existenta cancerului ca si cauza a SPI

5. Studiu diagnostic de evaluare a testului de absorbtie a fierului pentru discriminarea anemiei din bolile cronice de anemia feripriva

6. Un studiu de evaluare a prevalentei anticorpilor antifosfolipidici la pacientii cu SPI, de comparatie a frecventelor aparitiei lor la pacientii cu si fara cancer drept cauza a SPI si de evaluare a riscului de tromboze la pacientii cu si fara ac. anticardiolipinici.