Predizione della fibrosi epatica in bambini con steatosi epatica non alcolica

Giorgio Bedogni

www.giorgiobedogni.it

Problema

- È possibile predire in maniera *non invasiva* la presenza di fibrosi epatica in bambini con steatosi epatica non alcolica (NAFLD) seguiti presso un centro di cura terziario (Epatologia pediatrica)?

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The pediatric NAFLD fibrosis index: a predictor of liver fibrosis in children with non-alcoholic fatty liver disease

Valerio Nobili*[1], Anna Alisi[1], Andrea Vania[2], Claudio Tiribelli[3], Andrea Pietrobattista[1] and Giorgio Bedogni[3]

Table 1: Measurements of children with and without fibrosis.

	Fibrosis (*n* = 141)	No fibrosis (*n* = 62)	*p*-value*
Gender (male/female)	96/45	40/22	0.630
Age (years)	12.1 (3.6)	11.6 (3.3)	0.807
Weight (kg)	62.0 (27.6)	58.9 (19.5)	0.378
Weight (SDS)	1.8 (1.1)	1.8 (1.3)	0.430
Height (m)	1.53 (0.23)	1.52 (0.15)	0.983
Height (SDS)	0.2 (1.4)	0.2 (2.1)	0.319
BMI (kg/m^2)	26.4 (6.5)	25.4 (4.2)	0.078
BMI (SDS)	1.9 (0.7)	1.7 (0.6)	0.079
Waist circumference (cm)	94 (11)	87 (12)	< 0.001
ALT (U/L)	67 (82)	66 (27)	0.414
AST (U/L)	47 (32)	42 (16)	0.070
GGT (U/L)	21 (19)	18 (11)	0.031
Albumin (mg/dl)	4.5 (0.4)	4.4 (0.6)	0.175
Prothrombin time (INR)	1.0 (0.2)	1.0 (0.3)	0.756
Glucose (mg/dl)	79 (11)	82 (11)	0.166
Insulin (μU/ml)	13 (10)	9 (7)	0.174
HOMA-IR	2.5 (2.1)	2.1 (1.7)	0.289
ISI	3.5 (3.0)	3.9 (2.6)	0.243
Triglycerides (mg/dl)	94 (58)	67 (39)	< 0.001
Cholesterol (mg/dl)	166 (36)	145 (47)	< 0.001

Continuous variables are given as median (interquartile range) and categorical variables as the number of subjects with the characteristic of interest. Abbreviations: SDS = standard deviation score; BMI = body mass index; ALT = alanine transaminase; AST = aspartate transaminase; GGT = gamma-glutamyl-transferase; INR = international normalized ratio; HOMA-IR = homeostasis model assessment index of insulin resistance; ISI = insulin sensitivity index.* Wilcoxon-Mann-Whitney test for continuous variables and Fisher's exact test for categorical variables.

Table 2: Selection of candidate predictors at bootstrapped stepwise logistic regression.

	Model 1	Model 2	Model 3
Male gender	243	241	253
Log_e age	**1,000**	**1,000**	**1,000**
BMI	617	625	643
Waist	**1,000**	**1,000**	**1,000**
Log_e ALT	378	362	350
Log_e AST	281	325	341
GGT	389	363	357
Albumin	439	423	312
INR	189	226	208
Glucose	229	--	--
Log_e insulin	286	--	--
HOMA-IR	--	218	--
ISI	--	--	300
Log_e triglycerides	**999**	**1,000**	**1,000**
Cholesterol	233	198	161

The bootstrap inclusion fraction, i.e. the number of bootstrap samples out of 1,000 where the candidate predictors were selected, is given. Predictors selected for inclusion in the final model are marked in bold. Abbreviations: log_e = natural logarithm; BMI = body mass index; ALT = alanine transaminase; AST = aspartate transaminase; GGT = gamma-glutamyl-transferase; INR = international normalized ratio; HOMA-IR = homeostasis model assessment index of insulin resistance; ISI = insulin sensitivity index.

Table 3: The prediction model of the pediatric non-alcoholic fatty liver disease fibrosis index

	β	95% CI (β)*	*p*-value
Log_e age (years)	-6.539	-9.358 to -4.137	< 0.001
Waist (cm)	0.207	0.135 to 0.286	< 0.001
Log_e triglycerides (mg/dl)	1.957	1.009 to 3.018	< 0.001
Intercept	-10.074	-15.838 to -5.028	< 0.001

Abbreviations: Log_e = natural logarithm; β = regression coefficient; 95%CI (β) = 95% confidence interval for the regression coefficient; *p*-value = value of *p* for the regression coefficient. *Obtained on 1,000 bootstrap samples of 203 subjects with bias-correction.

Table 4: Diagnostic accuracy of the pediatric non-alcoholic fatty liver disease fibrosis index.

Cut-point	*n*	%	TPR	TNR	PLR	NLR	PPV	NPV
≥ 1	198	97.5	99.3 (96.1 to 100.0)	6.4 (1.8 to 15.7)	1.1 (1.0 to 1.1)	0.1 (0.01 to 1.0)	70.7 (63.8 to 76.9)	80.0 (28.4 to 99.5)
≥ 2	190	93.6	97.2 (92.9 to 99.2)	14.5 (6.9 to 25.8)	1.1 (1.0 to 1.3)	0.2 (0.1 to 0.6)	72.1 (65.2 to 78.4)	69.2 (38.6 to 90.9)
≥ 3	179	88.2	95.7 (91.0 to 98.4)	29.0 (18.2 to 41.9)	1.3 (1.1 to 1.6)	0.2 (0.1 to 0.3)	75.4 (68.4 to 81.5)	75.0 (53.3 to 90.2)
≥ 4	167	82.3	93.6 (88.2 to 97.0)	43.5 (31.0 to 56.7)	1.7 (1.3 to 2.1)	0.2 (0.1 to 0.3)	79.0 (72.1 to 84.9)	75.0 (57.8 to 87.9)
≥ 5	154	75.9	88.7 (82.2 to 93.4)	53.2 (40.1 to 66.0)	1.9 (1.4 to 2.5)	0.2 (0.1 to 0.4)	81.2 (74.1 to 87.0)	67.3 (52.5 to 80.1)
≥ 6	138	68.0	81.6 (74.2 to 87.6)	62.9 (49.7 to 74.8)	2.2 (1.6 to 3.1)	0.3 (0.2 to 0.4)	83.3 (76.0 to 89.1)	60.0 (47.1 to 72.0)
≥ 7	118	58.1	76.6 (68.7 to 83.3)	83.9 (72.3 to 92.0)	4.7 (2.7 to 8.4)	0.3 (0.2 to 0.4)	91.5 (85.0 to 95.9)	61.2 (50.0 to 71.6)
≥ 8	94	46.3	62.4 (53.9 to 70.4)	90.3 (80.1 to 96.4)	6.4 (3.0 to 13.9)	0.4 (0.3 to 0.5)	93.6 (86.6 to 97.6)	51.4 (41.6 to 61.1)
≥ 9	66	32.5	46.1 (37.7 to 54.7)	98.4 (91.3 to 100.0)	28.6 (4.0 to 201.0)	0.6 (0.5 to 0.6)	98.5 (91.8 to 100.0)	44.5 (36.0 to 53.3)

95% confidence intervals are given in parentheses. Abbreviations: TPR = true positive rate; TNR = true negative rate; PLR = positive likelihood ratio; NLR = negative likelihood ratio; PPV = positive predictive value; NPV = negative predictive value.

Accuratezza di un test

		Malattia	
		Presente	Assente
Test	Positivo		
	Negativo		

Vero positivo

		Malattia	
		Presente	Assente
Test	Positivo	TP	
	Negativo		

Falso positivo

		Malattia	
		Presente	Assente
Test	Positivo		FP
	Negativo		

Falso negativo

		Malattia	
		Presente	Assente
Test	Positivo		
	Negativo	FN	

Vero negativo

		Malattia	
		Presente	Assente
Test	Positivo		
	Negativo		TN

Accuratezza di un test

		Malattia	
		Presente	Assente
Test	Positivo	TP	FP
	Negativo	FN	TN

Accuratezza di un test

- Sensibilità (SN)
- Specificità (SP)
- Valore predittivo positivo (PPV)
- Valore predittivo positivo (NPV)
- Likelihood ratio positivo (LR+)
- Likelihood ratio negativo (LR-)
- Prevalenza
- Pre-test odds
- Post-test odds
- Post-test probability

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Sensibilità

		Malattia	
		Presente	Assente
Test	Positivo	TP	FP
	Negativo	FN	TN

SN = TP / (TP+FN)

Accuratezza di un test

- Sensibilità (SN)
- Specificità (SP)
- Valore predittivo positivo (PPV)
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Specificità

		Malattia	
		Presente	Assente
Test	Positivo	TP	FP
	Negativo	FN	TN

SP = TN / (FP+TN)

Accuratezza di un test

- Sensibilità (SN)
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- Valore predittivo positivo (PPV)
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- Post-test odds
- Post-test probability

Valore predittivo positivo

		Malattia	
		Presente	Assente
Test	Positivo	TP	FP
	Negativo	FN	TN

PPV = TP / (TP+FP)

Accuratezza di un test

- Sensibilità (SN)
- Specificità (SP)
- Valore predittivo positivo (PPV)
- Valore predittivo positivo (NPV)
- Likelihood ratio positivo (LR+)
- Likelihood ratio negativo (LR-)
- Prevalenza
- Pre-test odds
- Post-test odds
- Post-test probability

Valore predittivo negativo

		Malattia	
		Presente	Assente
Test	Positivo	TP	FP
	Negativo	FN	TN

NPV = TN / (FN + TN)

Accuratezza di un test

- Sensibilità (SN)
- Specificità (SP)
- Valore predittivo positivo (PPV)
- Valore predittivo positivo (NPV)
- Likelihood ratio positivo (LR+)
- Likelihood ratio negativo (LR-)
- Prevalenza
- Pre-test odds
- Post-test odds
- Post-test probability

Likelihood ratio positivo

		Malattia	
		Presente	Assente
Test	Positivo	TP	FP
	Negativo	FN	TN

LR+ = SN / (1-SP)

Accuratezza di un test

Sensibilità (SN)
Specificità (SP)
Valore predittivo positivo (PPV)
Valore predittivo positivo (NPV)
Likelihood ratio positivo (LR+)
Likelihood ratio negativo (LR-)
Prevalenza
Pre-test odds
Post-test odds
Post-test probability

Likelihood ratio negativo

		Malattia	
		Presente	Assente
Test	Positivo	TP	FP
	Negativo	FN	TN

LR- = (1-SN) / SP

Accuratezza di un test

- Sensibilità (SN)
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- Prevalenza
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Prevalenza

		Malattia	
		Presente	Assente
Test	Positivo	TP	FP
	Negativo	FN	TN

Prevalenza = (TP + FN) / (TP + FP + FN + TN)

Accuratezza di un test

- Sensibilità (SN)
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- Likelihood ratio positivo (LR+)
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- Prevalenza
- Pre-test odds
- Post-test odds
- Post-test probability

Pre-test odds

		Malattia	
		Presente	Assente
Test	Positivo	TP	FP
	Negativo	FN	TN

Pre-test odds = prevalenza / (1-prevalenza)

Accuratezza di un test

- Sensibilità (SN)
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- Likelihood ratio positivo (LR+)
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- Prevalenza
- Pre-test odds
- Post-test odds
- Post-test probability

Post-test odds

		Malattia	
		Presente	Assente
Test	Positivo	TP	FP
	Negativo	FN	TN

Post-test odds = pre-test odds * LR

Accuratezza di un test

Sensibilità (SN)
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Prevalenza
Pre-test odds
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Post-test probability

Post-test probability

		Malattia	
		Presente	Assente
Test	Positivo	TP	FP
	Negativo	FN	TN

Post-test probability = post-test odds / (post-test odds + 1)

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Uso del PNFI

			predictors	logits
1				
2				
3	Age (years)		10	-15.057
4	Waist (cm)		84	17.388
5	Tryglicerides		180	10.163
6	Constant		**********	-10.074
7	Sum		**********	2.420
8				
9	The PNFI is		9	
10				
11	Use this table to interpret the PNFI			

Grazie

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