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Effects of Age, Body Mass Index, and Sex on the Performance of Macimorelin for the Diagnosis of Adult Growth Hormone Deficiency: a Post hoc Analysis

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Conflict of interest disclosures:

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Objective

To determine whether the performance of the macimorelin diagnostic test is affected by age, baseline body mass index (BMI), and sex

Introduction

- The diagnostic performance of macimorelin, an orally active ghrelin receptor agonist FDA-approved for the diagnosis of adult growth hormone deficiency (AGHD) in the United States, has previously been demonstrated in a phase 3 study that compared macimorelin with the insulin tolerance test (ITT)[1]
- However, it is not known if the diagnostic performance of macimorelin varies according to patient demographics that are known to influence peak growth hormone release induced by other secretagogues

Methods

- This post hoc analysis included data from a previously published phase 3 study of subjects with a high likelihood of GHD (Group A, considered to have AGHD based on having a low IGF-I level plus either of these: at least 3 other pituitary hormone deficiencies or a structural hypothalamic or pituitary lesion) vs healthy controls (Group D)[1]
- The probability of AGHD was estimated using 4 logistic models fitted to the data: unadjusted, age-adjusted, baseline BMI-adjusted, and sex-adjusted
- Each model considers all subjects as independent observations, not taking matching into account
- The area under the curve (AUC) of the estimated receiver operating characteristic (ROC) curve (0 to 1 range, where 1 is perfect) from each adjusted model was compared with the AUC from the unadjusted model
- The estimated sensitivity and specificity for each model at cutpoint values of 2.8 and 5.1 ng/mL were calculated

Results

- Summary statistics from the macimorelin test are shown in **Table 1**
  - Of the 70 subjects included in the analysis, 41 had a high likelihood of GHD and 29 were healthy controls
  - Mean±SD (range) age was 41.7±13.9 (18-66) years
  - Mean±SD (range) BMI was 27.1±4.0 (20.8-36.6) kg/m^2
  - 56% were male
  - Peak GH concentration was 0.91 for Group A and 16.2 for Group B

Table 1 Summary statistics from the macimorelin test

	Group A n=41	Group D n=29	Total n=70
Age, years			
Mean	42.9	40.0	41.7
(SD)	(14.8)	(12.5)	(13.9)
Baseline BMI (kg/m^2)			
Mean	27.8	26.1	27.1
(SD)	(4.4)	(3.2)	(4.0)
Sex, n (%)			
Female	17 (41.5)	14 (48.3)	31 (44.3)
Male	24 (58.5)	15 (51.7)	39 (55.7)
Peak GH concentration (ng/mL)			
Mean	0.91	16.2	7.2
(SD)	(1.9)	(7.4)	(9.0)

BMI, body mass index; GH: growth hormone; SD, standard deviation.

- The ROC AUC for the unadjusted model was 0.9924 (95% CI: 0.9807, 1), age-adjusted ROC AUC was 0.9924 (95% CI: 0.9807, 1), BMI-adjusted ROC AUC was 0.9916 (95% CI: 0.9786, 1), and sex-adjusted ROC AUC was 0.9950 (95% CI: 0.9861, 1) **(Figure 1 and Table 2)**

Figure 1 ROC curves for unadjusted and adjusted models

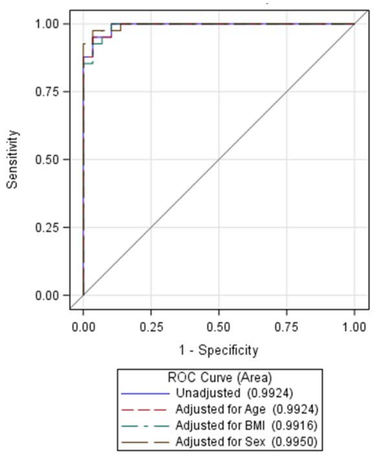

Table 2 ROC AUC for unadjusted and adjusted models

Model	ROC AUC	95% CI	*P*-value for AUC Adjusted vs. Unadjusted
Unadjusted	0.9924	(0.9807, 1)	
Adjusted for Age	0.9924	(0.9807, 1)	1
Adjusted for BMI	0.9916	(0.9786, 1)	0.6861
Adjusted for Sex	0.9950	(0.9861, 1)	0.4207

BMI, body mass index; CI, confidence interval

- For the unadjusted model at cutpoint values of 2.8 and 5.1, estimated sensitivity was 88% and 93%, and specificity was 97% and 97% **(Table 3)**
- These values remained the same for cutpoint 2.8 when adjusting for age and adjusting for mean or median BMI
- At cutpoint 5.1, the values remained the same when adjusting for age and mean BMI **(Table 4)**
- When adjusting for sex, sensitivity for females was 88% and specificity was 93% at cutpoint 2.8, and sensitivity for females was 94% and specificity was 93% at cutpoint 5.1
- Sensitivity for males was 88% and specificity was 100% at cutpoint 2.8, and sensitivity for males was 92% and specificity was 100% at cutpoint 5.1

Table 3 Estimated sensitivity and specificity at the prespecified cut-off of 2.8 ng/mL for the macimorelin test

	Sensitivity (%)	Specificity (%)	Covariate equals
Unadjusted (95% CI)	88 (74, 96)	97 (82, 100)	
Adjusted for Age (95% CI)	88 (74, 96)	97 (82, 100)	
Adjusted for BMI (95% CI)	90 (77, 97)	97 (82, 100)	BMI = minimum = 20.4
Adjusted for BMI (95% CI)	88 (74, 96)	97 (82, 100)	BMI = mean = 27.1
Adjusted for BMI (95% CI)	88 (74, 96)	97 (82, 100)	BMI = median = 26.7
Adjusted for BMI (95% CI)	76 (60, 88)	100 (88, 100)	BMI = maximum = 36.6
Adjusted for Sex (95% CI)	88 (64, 99)	93 (66, 100)	Sex = Female
Adjusted for Sex (95% CI	88 (68, 97)	100 (78, 100)	Sex = Male

BMI, body mass index; CI, confidence interval

Table 4 Estimated sensitivity and specificity at the prespecified cut-off of 5.1 ng/mL for the macimorelin test

	Sensitivity (%)	Specificity (%)	Covariate equals
Unadjusted (95% CI)	93 (80. 99)	97 (82, 100)	
Adjusted for Age (95% CI)	93 (80, 99)	97 (82, 100)	
Adjusted for BMI (95% CI)	95 (84, 99)	93 (77, 99)	BMI = minimum = 20.4
Adjusted for BMI (95% CI)	93 (80, 99)	97 (82, 100)	BMI = mean = 27.1
Adjusted for BMI (95% CI)	93 (80, 99)	93 (77, 99)	BMI = median = 26.7
Adjusted for BMI (95% CI)	90 (77, 97)	97 (82, 100)	BMI = maximum = 36.6
Adjusted for Sex (95% CI)	94 (71, 100)	93 (66, 100)	Sex = Female
Adjusted for Sex (95% CI	92 (73, 99)	100 (78, 100)	Sex = Male

BMI, body mass index; CI, confidence interval

Conclusions

Results of this post hoc analysis show that the diagnostic performance of macimorelin was not meaningfully affected by age, baseline BMI, or sex over the ranges that were studied.

References:
1. Garcia JM, et al. J Clin Endocrinol Metab. 2018;103(8):3083-3093.

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