

Vertex balding, plasma insulin-like growth factor 1, and insulin-like growth factor binding protein 3

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Background: A recent report suggested that men with vertex balding have higher levels of plasma insulin-like growth factor 1 (IGF-1), but circulating levels of insulin-like growth factor binding protein 3 (IGFBP-3), which, along with IGF-1, is thought to mediate the effects of growth hormone, have not been examined.

Methods: Participants were 431 male members of the Health Professionals Follow-up Study who responded to a question in 1992 on their hair pattern at 45 years of age and who were 47 to 81 years old when they provided a blood specimen in 1993-1994. Odds ratios (ORs) of vertex balding associated with IGF-1 and IGFBP-3 were estimated using logistic regression, controlling for age at blood draw.

Results: Of the 431 men, 128 had vertex balding at age 45. Compared with men who were not balding, for a 1 standard deviation increase in plasma IGF-1 level (72.4 ng/mL), the OR for vertex balding was 1.31 (95% CI, 0.95-1.81). For a 1 standard deviation increase in plasma IGFBP-3 (957 ng/mL), the OR for vertex balding was 0.62 (95% CI, 0.44-0.88).

Conclusion: Older men with vertex balding have lower circulating levels of IGFBP-3 and higher levels of IGF-1 when controlling for IGFBP-3 level.

Male scalp hair pattern in adulthood has long been known to be influenced by androgens.¹ However, other factors have been explored recently for a role in mediating the transition of the hair follicle through its cycle of growth, senescence, and regeneration. Signorello et al² evaluated the relation of serum insulin-like growth factor 1 (IGF-1) and male pattern balding in a case-control

study among 51 Greek men older than 65 years and found that men with vertex balding had higher circulating levels of IGF-1. In a case-control study of balding, IGF-1 levels were higher in men with vertex balding. For a 57 ng/mL increase in IGF-1, the relative risk of vertex balding was 1.6 (95% confidence interval [CI], 0.9-3.2) after adjusting for age and 2.0 (95% CI, 1.0-4.6) after also adjusting for steroid hormone concentrations. Serum insulin-like growth factor binding protein 3 (IGFBP-3), the major carrier protein for IGF-1, was not measured in the Greek study.

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Circulating IGF-1 levels in men with vertex balding are higher than in men without vertex balding. Reduced IGF-1 bioavailability, is associated with a reduced risk of vertex balding among middle-aged and elderly men.

MATERIAL AND METHODS

Participants for this analysis were selected from among members of the Health Professionals Follow-up Study, an ongoing prospective cohort study of health professionals. The study includes 27,000 men aged 40-75 years at enrollment in 1986. The study is designed to investigate the relationship between diet and health outcomes. The study is ongoing and will continue to follow up on the health of these men.

Table I. Plasma concentrations of IGF-1 and IGFBP-3 according to vertex balding* at age 45: Health Professionals Follow-up Study 1994

Blood constituent	Vertex balding	Not vertex balding	P value†
No. of men	128	303	
Age at blood draw in 1994 (y)	64.7 ± 8.3	63.8 ± 8.2	.3
<i>Unadjusted</i>			
IGF-1 (ng/mL)	185.0 ± 71.4	190.2 ± 72.4	.5
IGFBP-3 (ng/mL)	3049 ± 871	3285 ± 957	.02
<i>Mutually adjusted‡</i>			
IGF-1 (ng/mL)	194.4 ± 44.4	186.2 ± 50.3	.11
IGFBP-3 (ng/mL)	3084 ± 536	3270 ± 664	.002

Data are presented as mean ± standard deviation.

*Modest, moderate, or substantial vertex balding as self-reported using pictograms in 1992.

†For comparison using the *t* test.

‡By residuals analysis.

Table II. Relation of vertex balding* with plasma IGF-1 and IGFBP-3: Health Professionals Follow-up Study 1994

	Tertile†			Unit‡	OR§	P value§
	1	2	3			
IGF-1						
Cases/controls	47/102	35/102	46/99			
Median (ng/mL)	123.1	181.9	251.2	72.4		
OR	1.00	1.00	1.86		1.31	.09
95% CI	Referent	0.56-1.78	0.93-3.70		0.95-1.81	
IGFBP-3						
Cases/controls	53/101	43/101	32/101			
Median (ng/mL)	2429	3195	4149	957		
OR	1.00	0.69	0.42		0.62	.008
95% CI	Referent	0.30-1.53	0.21-0.86		0.44-0.89	

*Modest, moderate, or substantial vertex balding as self-reported using pictograms in 1992 versus no or little hair loss or receding hairline only.

†ORs from a logistic regression model with plasma level entered as two indicator variables and adjusted for age at blood draw (continuous). Tertile cut points for plasma levels of each factor were determined from the distribution of levels among the controls.

‡One standard deviation.

§ORs from a logistic regression model with plasma level entered as two indicator variables and adjusted for age at blood draw (continuous).

^{||}Mutually adjusted.

IGF-1, we mutually adjusted for these two plasma levels and controlled for age at blood draw. Compared with men in the bottom tertile of IGF-1, the OR for vertex balding in the top tertile of IGF-1 was 1.86 (95% CI, 0.93-3.70) (Table II). Men in the top tertile of IGFBP-3 had a statistically significantly 58% lower risk of vertex balding than men in the bot-

tom tertile. For a 957 ng/mL increase in IGF-1, the OR for vertex balding was 1.31 (95% CI, 0.95-1.81; *P* = .09). For a 957 ng/mL increase in IGFBP-3, the OR for vertex balding was 0.62 (95% CI, 0.44-0.88; *P* = .008) (Table II). These

increments). The OR for vertex balding modestly increased to 1.02 (95% CI, 0.57-1.84) and 2.00 (95% CI, 0.99-4.04) for the middle and top tertiles of IGF-1 and decreased to 0.66 (95% CI, 0.37-1.18) and 0.40

receding hairline only (IGF-1: OR = 1.26, 95% CI [0.90-1.77]; IGFBP-3: OR = 0.61, 95% CI [0.42-0.89]). There was no evidence that the risk of balding associated with IGF-1 or IGFBP-3 was stronger with increasing extent of vertex balding at age 45 in an analysis limited only to men with vertex balding.

Because smoking may influence the IGF axis, we controlled for smoking (in 10-year increments).

IGF-1 adjusted for IGFBP-3 was not as great as shown for IGF-1 by Signorello et al.² Differences in the two studies that might contribute to the disparity in the strength of the association between IGF-1 and vertex balding include different IGF-1 assays, older average age in the Greek study, interviewer-assessed balding in the Greek study versus self-report in our study, and IGF-1 and balding assessed concurrently in the Greek study versus 2 to 36 years apart in our study.

and sex hormone-binding globulin enhanced the

samples that we included in this analysis, adjustment for sex steroids and sex hormone-binding globulin did not appear to alter our estimates for the relation

these methodologic and population differences between the two studies, both the study in elderly Greek men² and our study indicate that the IGF-1

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REFERENCES

1. Demark-Wahnefried W, Lesko SM, Conaway MR, Robertson CN, *Clin Endocrinol* 1999;51:497-500.
2. Signorello LB, Wu J, Hsieh C-c, Tzonou A, Trichopoulos D, Mantzoros CS. Hormones and hair patterning in men: a role for insulin-like growth factor 1? *J Am Acad Dermatol* 1999;40:200-3.
3. Norwood OT. Male pattern baldness: classification and incidence. *South Med J* 1975;68:1359-65.
4. Olsen EA, Weiner MS, DeLong ER, Pinnell SR. Topical minoxidil in *Acad Dermatol* 1995;42:105-11.
5. Rosner B. *Fundamentals of biostatistics*. Boston: Duxbury Press; 1997.

10. Peus D, Pittelkow MR. Growth factors in hair organ development and the hair growth cycle. *Dermatol Clin* 1996;4:559-72.
11. Itami S, Kurata S, Takayasu S. Androgen induction of follicular epithelial cell growth is mediated via insulin-like growth factors-1 from dermal papilla cells. *Biochem Biophys Res Commun* 1995;212:988.
12. Horton R, Pasupuletti V, Antonipillai I. Androgen induction of steroid 5 alpha-reductase may be mediated via insulin-like growth factor-I. *Endocrinol* 1993;133:447-51.
13. Kaufman KD, Olsen EA, Whiting D, Savin R, DeVillez R, Bergfeld W, et al. Finasteride in the treatment of men with androgenetic

14. Hwang JJ, Cohen DM, Brack CP. Reduction of functional testosterone

Becker K, editor. *Principles and practice of endocrinology and metabolism*. Philadelphia: JB Lippincott; 1995. p. 1451-65.

16. Chan JM, Stampfer MJ, Giovannucci E, Gann PH, Ma J, Wilkinson *Science* 1996;273:905-9.
17. Mantzoros CS, Tzonou A, Signorello LB, Stampfer M, *Br J Cancer* 1999;80:105-11.
18. Wolk A, Mantzoros CS, Andersson SW, Bergstrom R, Signorello LB, Lagiou P, et al. Insulin-like growth factor I and prostate cancer risk: a population-based, case-control study. *J Natl Cancer Inst* 1998;90:911-5.
19. Peyrat JP, Bonnetterre J, Hecquet B, Vennin P, Louchez MM, Fournier C, et al. Plasma insulin-like growth factor-I (IGF-I) concentrations in human breast cancer. *Eur J Cancer* 1993;29A:492-7.
20. *Int J Cancer* 1995;62:266-70.
21. Hankinson SE, Willett WC, Colditz GA, Hunter DJ, Michaud DS, Deroo B, et al. Circulating concentrations of insulin-like growth factor-I and risk of breast cancer. *Lancet* 1998;351:1393-6.
22. Bohlke K, Cramer DW, Trichopoulos D, Mantzoros CS. Insulin-like growth factor-I in relation to premenopausal ductal carcinoma *in situ* of the breast. *Epidemiology* 1998;9:570-3.
23. *Int J Cancer* 1999;85:1577.
24. *Int J Cancer* 1999;85:1577.
25. *Int J Cancer* 1999;85:1577.
26. *Int J Cancer* 1999;85:1577.
27. *Int J Cancer* 1999;85:1577.
28. *Int J Cancer* 1999;85:1577.
29. *Int J Cancer* 1999;85:1577.
30. *Int J Cancer* 1999;85:1577.
31. *Int J Cancer* 1999;85:1577.
32. *Int J Cancer* 1999;85:1577.
33. *Int J Cancer* 1999;85:1577.
34. *Int J Cancer* 1999;85:1577.
35. *Int J Cancer* 1999;85:1577.
36. *Int J Cancer* 1999;85:1577.
37. *Int J Cancer* 1999;85:1577.
38. *Int J Cancer* 1999;85:1577.
39. *Int J Cancer* 1999;85:1577.
40. *Int J Cancer* 1999;85:1577.
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43. *Int J Cancer* 1999;85:1577.
44. *Int J Cancer* 1999;85:1577.
45. *Int J Cancer* 1999;85:1577.
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47. *Int J Cancer* 1999;85:1577.
48. *Int J Cancer* 1999;85:1577.
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50. *Int J Cancer* 1999;85:1577.
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52. *Int J Cancer* 1999;85:1577.
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62. *Int J Cancer* 1999;85:1577.
63. *Int J Cancer* 1999;85:1577.
64. *Int J Cancer* 1999;85:1577.
65. *Int J Cancer* 1999;85:1577.
66. *Int J Cancer* 1999;85:1577.
67. *Int J Cancer* 1999;85:1577.
68. *Int J Cancer* 1999;85:1577.
69. *Int J Cancer* 1999;85:1577.
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72. *Int J Cancer* 1999;85:1577.
73. *Int J Cancer* 1999;85:1577.
74. *Int J Cancer* 1999;85:1577.
75. *Int J Cancer* 1999;85:1577.
76. *Int J Cancer* 1999;85:1577.
77. *Int J Cancer* 1999;85:1577.
78. *Int J Cancer* 1999;85:1577.
79. *Int J Cancer* 1999;85:1577.
80. *Int J Cancer* 1999;85:1577.
81. *Int J Cancer* 1999;85:1577.
82. *Int J Cancer* 1999;85:1577.
83. *Int J Cancer* 1999;85:1577.
84. *Int J Cancer* 1999;85:1577.
85. *Int J Cancer* 1999;85:1577.
86. *Int J Cancer* 1999;85:1577.
87. *Int J Cancer* 1999;85:1577.
88. *Int J Cancer* 1999;85:1577.
89. *Int J Cancer* 1999;85:1577.
90. *Int J Cancer* 1999;85:1577.
91. *Int J Cancer* 1999;85:1577.
92. *Int J Cancer* 1999;85:1577.
93. *Int J Cancer* 1999;85:1577.
94. *Int J Cancer* 1999;85:1577.
95. *Int J Cancer* 1999;85:1577.
96. *Int J Cancer* 1999;85:1577.
97. *Int J Cancer* 1999;85:1577.
98. *Int J Cancer* 1999;85:1577.
99. *Int J Cancer* 1999;85:1577.
100. *Int J Cancer* 1999;85:1577.

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