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Acanthosis Nigricans in Overt Insulin Resistance: A Non-Invasive Biomarker for Early Stratification of Pre-Dysglycemic Risk

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Disclosure Slide

The authors have **no conflicts of interest**
to disclose.



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Acanthosis Nigricans: A Visible Sign of Metabolic Dysfunction

Acanthosis Nigricans

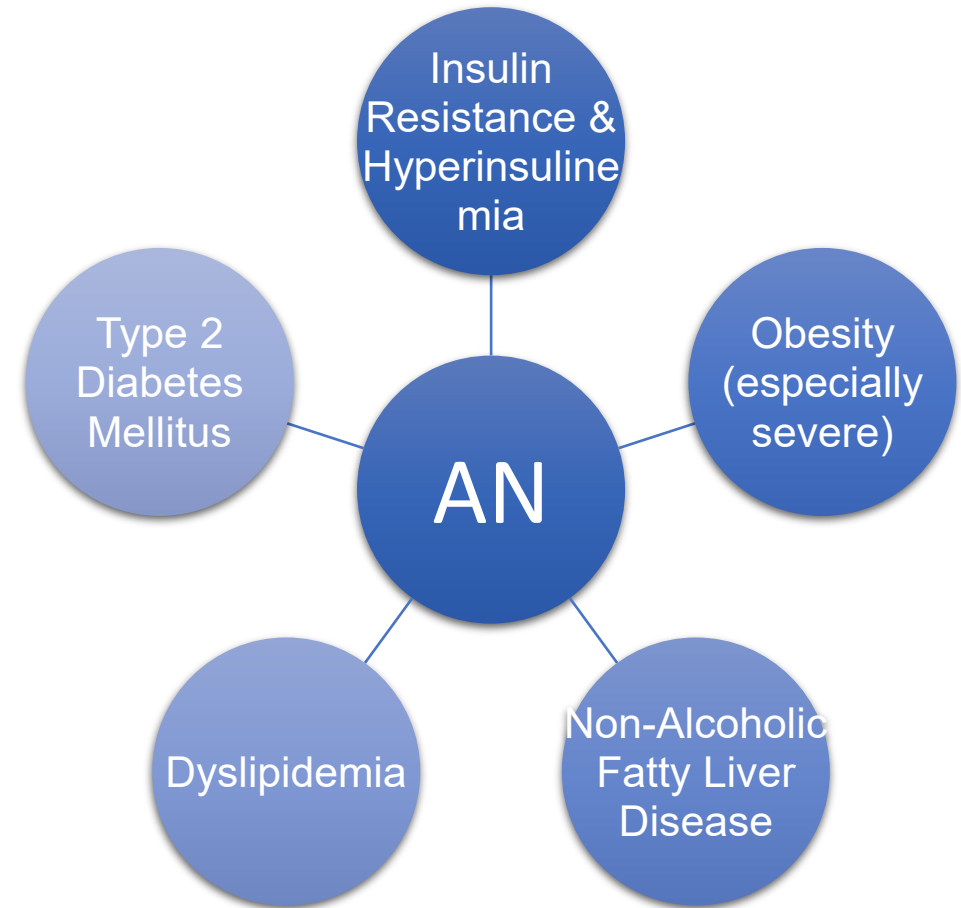


Appearance: Velvety, hyperpigmented, papillose plaques

Distribution: Intertriginous (neck, axillae, groin)

Significance: A cutaneous sentinel of systemic metabolic dysfunction.

Associated Comorbidities



The Interplay Between Insulin Resistance and Acanthosis Nigricans

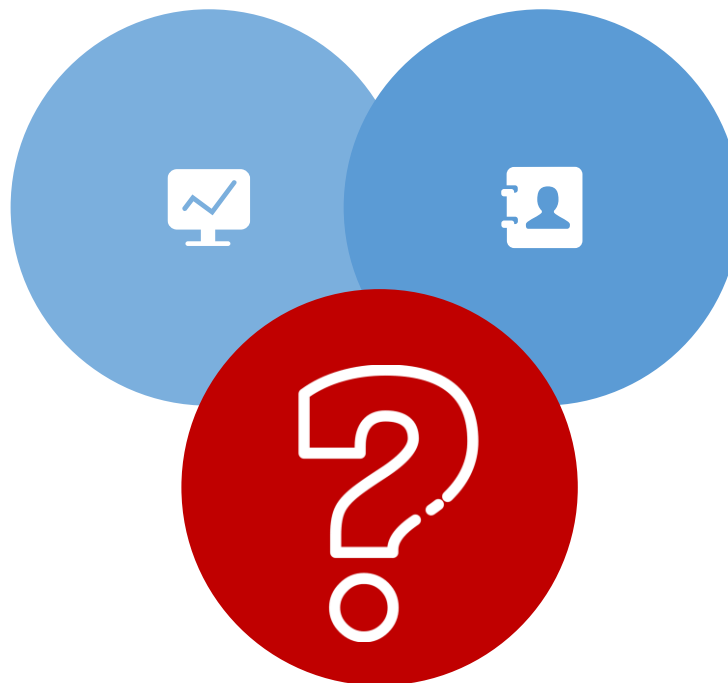


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IR → AN

Chronic hyperinsulinemia mediates the development of AN by activating skin keratinocytes and fibroblasts.



AN → IR

AN serves as a visible physical marker of underlying insulin resistance and more profound metabolic dysregulation.

critical question

Across the entire insulin resistance continuum, when is this association strongest and most clinically meaningful?

Study Design & Population




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Study Design

 **Study Type:** Cross-sectional Study

 **Center:** Single-center (Shanghai Tenth People's Hospital)

 **Clinic:** Endocrinology Clinic

 **Period:** July 2010 - Sept 2021

Participant Selection & Criteria

√ **Inclusion Criteria:**

- Adults undergoing AN screening
- Availability of complete key laboratory data

× **Exclusion Criteria:**

- Missing key data: HbA1c, fasting/2-h glucose, or fasting insulin

Final Analytical Cohort: N = 1,158

Data Collection & Measurements

Anthropometrics: Weight, Height, WC, HC, BP, BMI

Family History: Diabetes, Obesity, Hypertension

Lab Tests: Glucose, Insulin, C-peptide, HbA1c, TC, TG, HDL-C, LDL-C, ALT, AST, Cr, UA, BUN

Insulin Resistance (IR) Continuum Stratification



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Stage	Abbr.	Diagnostic Criteria
Normal Glucose Homeostasis	NINB	Normoglycemia & HOMA-IR < 2.5
Subclinical IR	SIR	Normoglycemia & HOMA-IR \geq 2.5 & Fasting Insulin < 25 μ U/mL
Overt IR	OIR	Normoglycemia & HOMA-IR \geq 2.5 & Fasting Insulin \geq 25 μ U/mL
Prediabetes with IR	PreDM-IR	Prediabetes & HOMA-IR \geq 2.5
Diabetes with IR	DM-IR	Diabetes & HOMA-IR \geq 2.5

Baseline Characteristics by AN Status

Variables	Total (n = 1158)	Non-AN(n = 593)	AN (n = 565)	P value
Sex, n(%)				0.013
Male	521 (45.03)	246 (41.48)	275 (48.76)	
Female	636 (54.97)	347 (58.52)	289 (51.24)	
Age, Mean ± SD	32.60 ± 12.27	37.15 ± 13.12	27.81 ± 9.14	<0.001
BMI, Mean ± SD	35.89 ± 6.58	33.82 ± 5.52	38.01 ± 6.91	<0.001
Waist, Mean ± SD	112.37 ± 16.42	108.22 ± 14.53	116.55 ± 17.16	<0.001
SP, Mean ± SD	135.91 ± 18.58	134.25 ± 18.74	137.63 ± 18.28	0.003
DP, Mean ± SD	83.71 ± 13.20	83.14 ± 12.60	84.31 ± 13.77	0.154
FamiObe, n(%)	218 (22.38)	78 (16.18)	140 (28.46)	<0.001
FamiDM, n(%)	464 (47.64)	219 (45.44)	245 (49.80)	0.173
FamiHBP, n(%)	570 (58.58)	270 (56.02)	300 (61.10)	0.108
BG0, Mean ± SD	6.32 ± 2.46	6.49 ± 2.47	6.15 ± 2.45	0.022
BG120, Mean ± SD	9.35 ± 4.44	9.63 ± 4.74	9.07 ± 4.11	0.038
INS0, Mean ± SD	31.07 ± 28.24	26.51 ± 29.79	35.86 ± 25.67	<0.001
INS120, Mean ± SD	160.63 ± 152.44	129.16 ± 136.69	189.25 ± 160.31	<0.001
CP0, Mean ± SD	4.25 ± 2.00	3.73 ± 1.59	4.75 ± 2.22	<0.001
CP120, Mean ± SD	11.96 ± 5.58	10.84 ± 5.41	12.96 ± 5.55	<0.001
HbA1c, Mean ± SD	6.37 ± 1.50	6.45 ± 1.56	6.28 ± 1.44	0.070
HOMAIR, Mean ± SD	8.90 ± 10.60	7.92 ± 12.08	9.94 ± 8.68	0.001
TC, Mean ± SD	4.73 ± 0.96	4.79 ± 1.01	4.68 ± 0.90	0.056
TG, Mean ± SD	1.98 ± 1.60	2.08 ± 1.83	1.89 ± 1.34	0.065
HDL, Mean ± SD	1.08 ± 0.27	1.10 ± 0.27	1.05 ± 0.27	0.002
LDL, Mean ± SD	2.93 ± 0.84	2.92 ± 0.86	2.93 ± 0.83	0.862
ALT, Mean ± SD	56.97 ± 51.88	51.42 ± 52.08	62.43 ± 51.14	<0.001
AST, Mean ± SD	35.18 ± 27.20	32.67 ± 26.84	37.64 ± 27.35	0.003
AST/ALT, Mean ± SD	0.76 ± 0.44	0.81 ± 0.39	0.71 ± 0.47	<0.001
Cr, Mean ± SD	64.31 ± 16.50	65.27 ± 19.68	63.55 ± 13.37	0.198
UA, Mean ± SD	417.35 ± 106.55	392.81 ± 100.46	440.18 ± 107.08	<0.001
BUN, Mean ± SD	4.69 ± 1.35	4.73 ± 1.43	4.66 ± 1.28	0.504



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Association Between AN and Metabolic Risk Markers

	β (95%CI)	Q1	Q2	Q3	Q4
		OR(95%CI)			
FINS					
Model1	9.35 (6.13 to 12.56)	Ref	1.83(1.29 to 2.60)	4.21(2.96 to 5.98)	6.02(4.20 to 8.63)
Model2	3.93 (0.33 to 7.53)	Ref	1.43(0.90 to 2.28)	2.91(1.82 to 4.65)	2.72(1.67 to 4.43)
Model3	2.50 (-1.28 to 6.29)	Ref	1.28(0.76 to 2.15)	2.51(1.48 to 4.25)	2.35(1.36 to 4.05)
2h-INS					
Model1	60.09 (41.64 to 78.53)	Ref	1.35(0.94 to 1.95)	2.18(1.51 to 3.13)	3.76(2.57 to 5.48)
Model2	53.23 (29.35 to 77.10)	Ref	1.41(0.87 to 2.28)	2.01(1.23 to 3.27)	3.12(1.91 to 5.10)
Model3	43.26 (19.57 to 66.96)	Ref	1.23(0.75 to 2.04)	1.87(1.13 to 3.10)	2.87(1.72 to 4.78)
HOMA-IR					
Model1	2.02 (0.81 to 3.24)	Ref	1.85(1.32 to 2.60)	2.31(1.64 to 3.25)	4.59(3.23 to 6.51)
Model2	0.96 (-0.43 to 2.35)	Ref	1.39(0.92 to 2.08)	1.83(1.16 to 2.89)	2.59(1.62 to 4.13)
Model3	0.35 (-1.13 to 1.82)	Ref	1.26(0.77 to 2.05)	1.59(0.96 to 2.64)	2.11(1.24 to 3.58)
FCP					
Model1	1.02 (0.78 to 1.26)	Ref	2.04(1.42 to 2.94)	2.53(1.76 to 3.63)	7.18(4.85 to 10.63)
Model2	0.59 (0.30 to 0.88)	Ref	2.19(1.35 to 3.54)	2.05(1.26 to 3.3)	4.55(2.69 to 7.69)
Model3	0.43 (0.18 ~ 0.67)	Ref	2.30(1.37 to 3.87)	2.13(1.25 to 3.63)	4.35(2.43 to 7.77)
2h-CP					
Model1	2.12 (1.43 to 2.81)	Ref	1.31(0.91 to 1.88)	1.82(1.26 to 2.61)	3.11(2.14 to 4.52)
Model2	1.80 (0.93 to 2.68)	Ref	1.07(0.70 to 1.70)	1.71(1.07 to 2.75)	2.34(1.46 to 3.75)
Model3	1.59 (0.73 to 2.45)	Ref	0.92(0.56 to 1.51)	1.75(1.06 to 2.88)	2.24(1.36 to 3.68)
FBG					
Model1	-0.33(-0.62 to -0.05)	Ref	0.84(0.61 to 1.16)	0.82(0.59 to 1.13)	0.55(0.40 to 0.75)
Model2	0.11 (-0.25 to 0.46)	Ref	0.89(0.59 to 1.35)	1.10(0.71 to 2.43)	0.96(0.61 to 1.51)
Model3	0.02 (-0.35 to 0.39)	Ref	0.95(0.61 to 1.48)	1.05(0.65 to 1.67)	0.86(0.52 to 1.41)
2h-BG					
Model1	-0.56(-1.08 to -0.03)	Ref	1.22(0.87 to 1.71)	1.05(0.75 to 1.46)	0.87(0.62 to 1.22)
Model2	0.08(-0.56 to 0.71)	Ref	1.23(0.79 to 1.91)	1.25(0.80 to 1.97)	1.34(0.84 to 2.15)
Model3	-0.24(-0.89 to 0.42)	Ref	1.07(0.66 to 1.94)	1.02(0.63 to 1.65)	0.96(0.57 to 1.61)

Model1:unadjusted
Model2:adjusted age, sax,
BMI, FH-obesity, FH-DM, SP
Model3:adjusted age,sax, BMI,
FH-obesity, FH-DM, SP, AST,
TG, HDL-C



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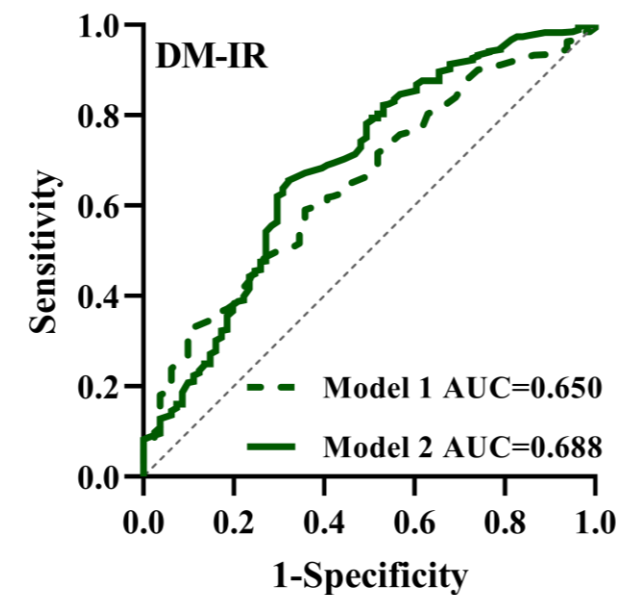
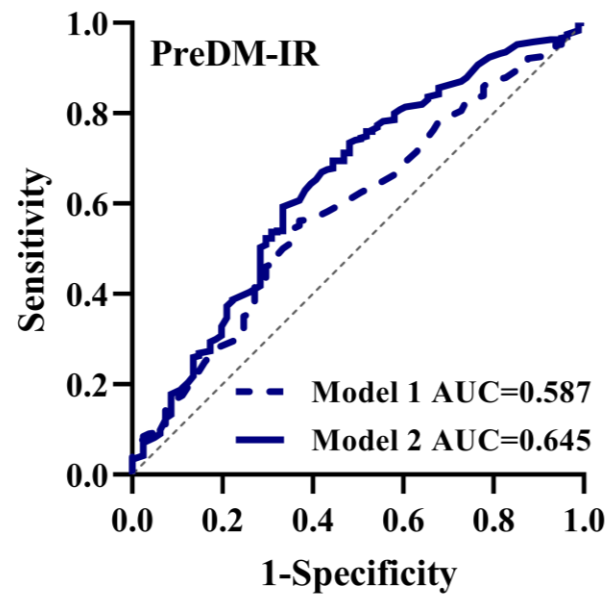
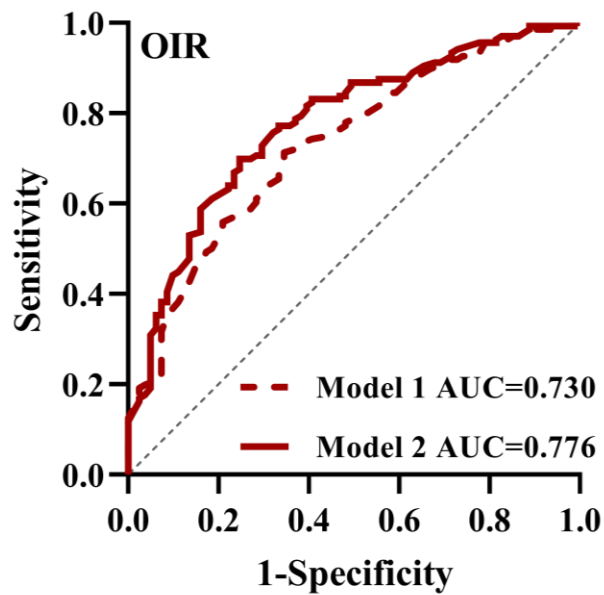
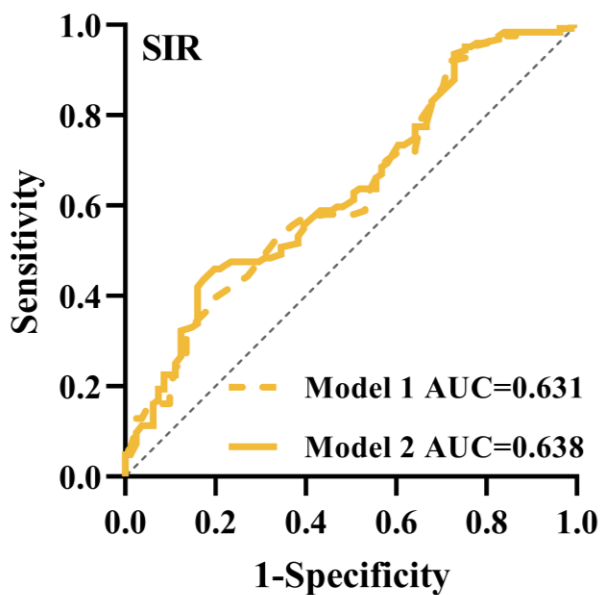
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ROC Curves of Prediction Models



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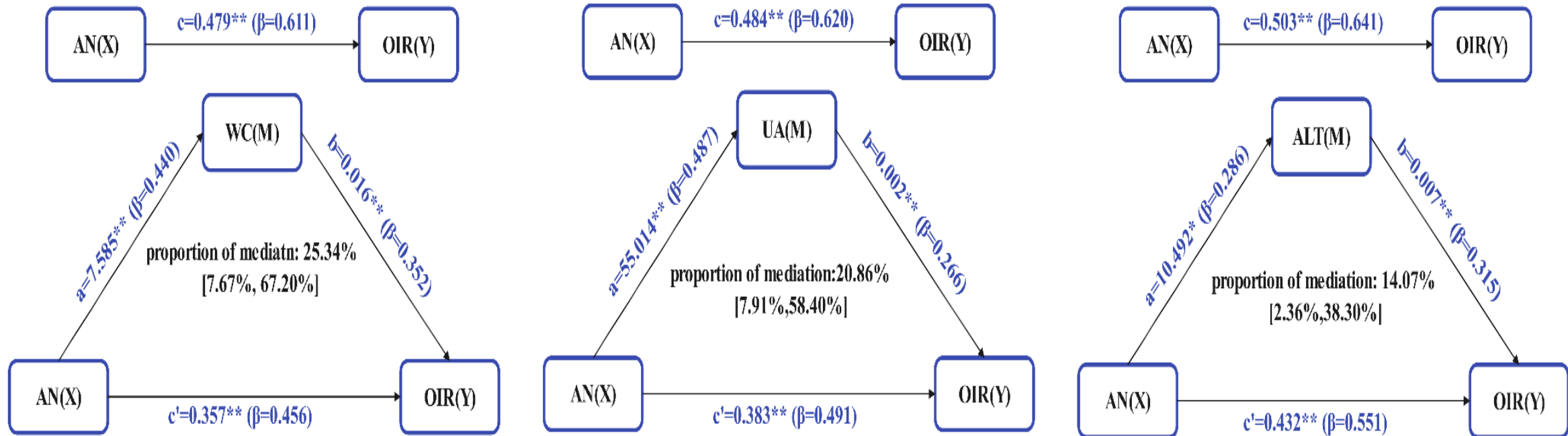
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Model 1: age, sex
Model 2: age, sex, AN



Mediation Analysis of AN's Effect on Overt IR



conclusion

- AN is a strong predictor of overt IR.
- Fasting C-peptide shows the strongest link to AN, suggesting beta-cell hypersecretion as a key mechanism.
- Adding AN to prediction models significantly improves identification of severe metabolic dysfunction.



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