Impaired Sensitivity to Thyroid Hormones is Associated with Elevated Serum Uric Acid Levels in Female Patients with Obesity and is Improved after Laparoscopic Sleeve Gastrectomy

XIN WEN

Department of Endocrinology and Metabolism, Shanghai Tenth People's Hospital, School of Medicine, Tongji University

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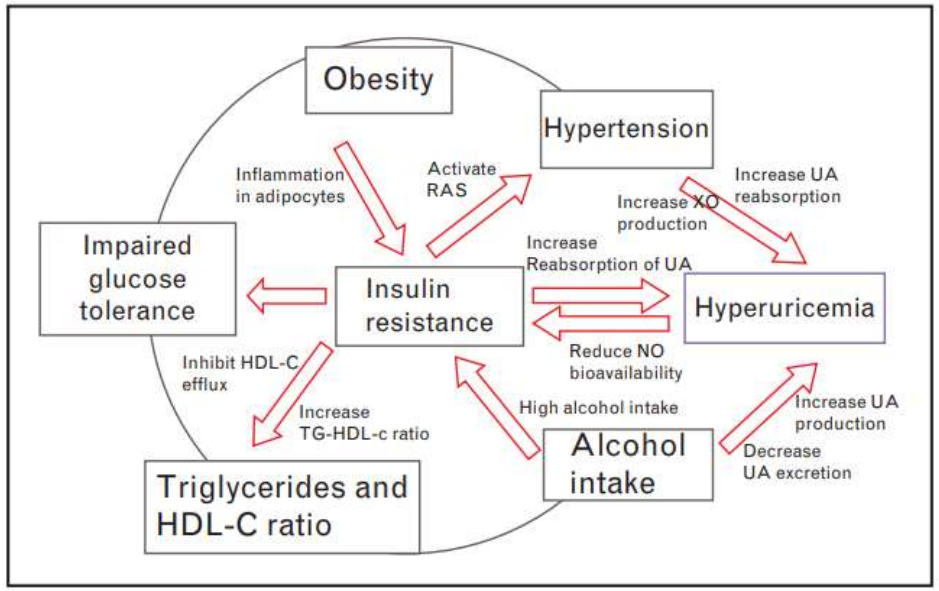
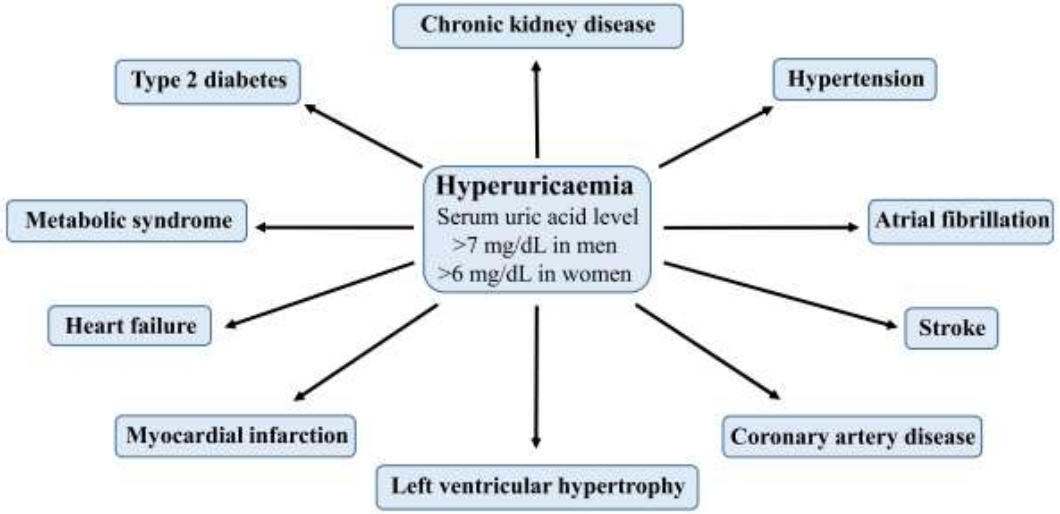
01 Background

Hyperuricemia and obesity share bidirectional causal effects



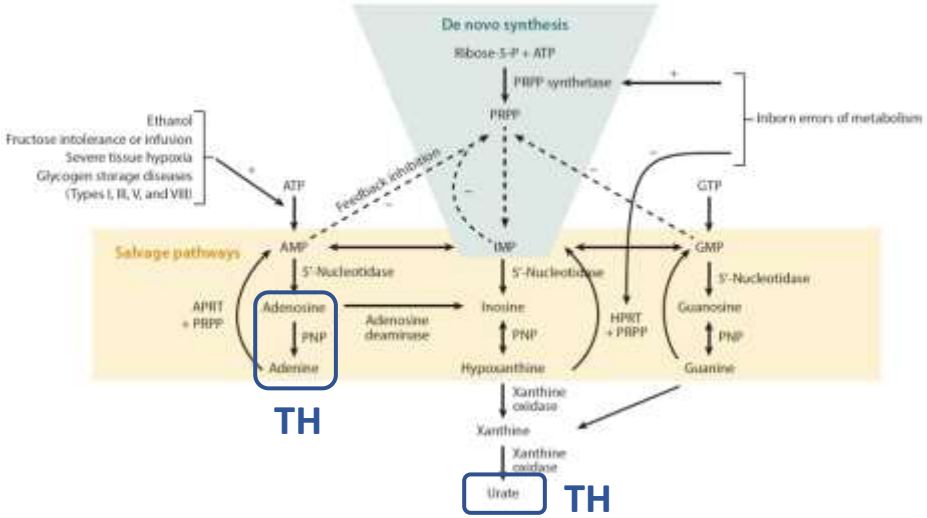


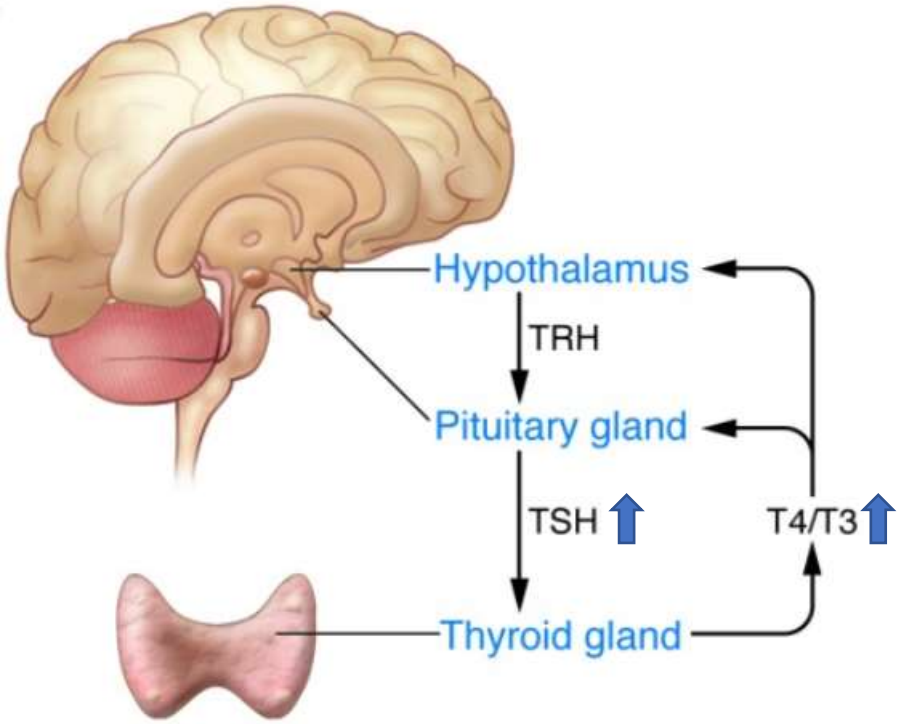
- Obesity induced hyperinsulinemia can increase the reabsorption of uric acid in the proximal tubules, leading to hyperuricemia.
- Hyperuricemia may cause endothelial dysfunction and inhibition of nitric oxide bioavailability leading to subsequent hyperinsulinemia.

Current Opinion in Rheumatology 25(2):p 210-216, March 2013.
Eur J Intern Med. 2020 Oct;80:1-11.

01 Background

Contradiction point





- TH affects uric acid levels by affecting the conversion of purine nucleotides and excretion of uric acid.
- Both hypothyroidism and hyperthyroidism seem to increase the risk for hyperuricemia.

- In morbidly obese patients, thyroid hormone and TSH levels tend to increase, which also seems contradictory

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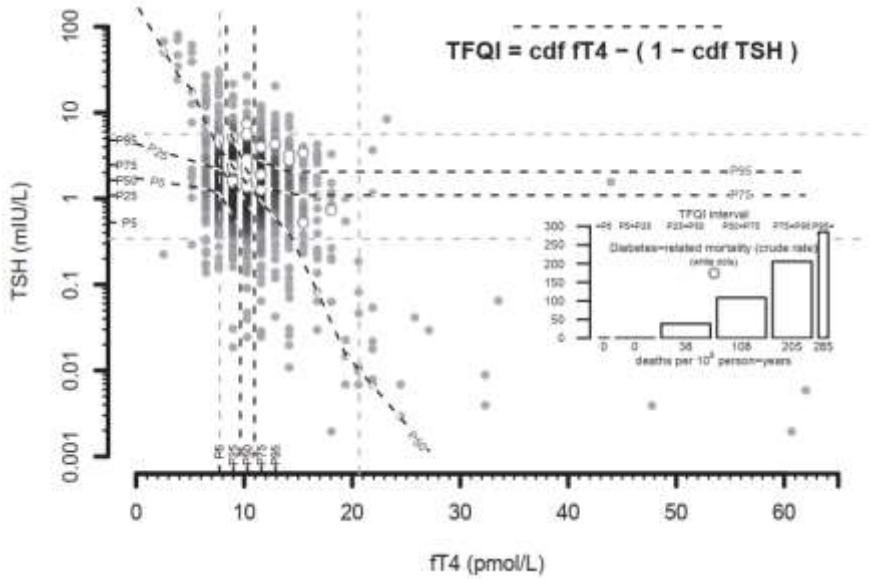
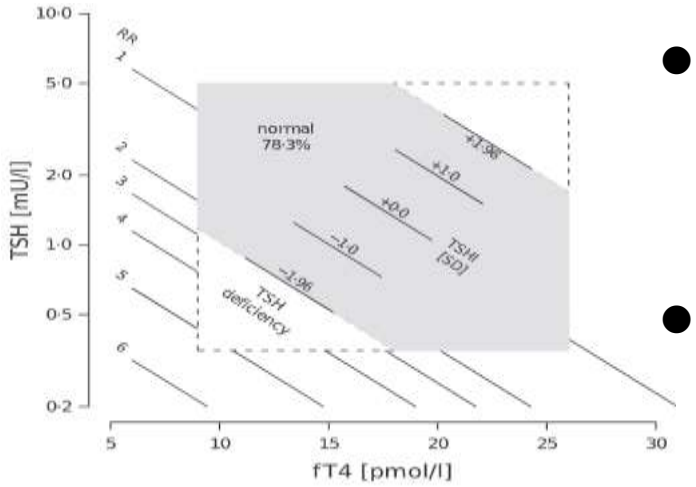
Eur Thyroid J 2012;1:159-67. Clinical Rheumatology. 2016;35(1):143–149.

01 Background

Possible explanation: impaired sensitivity to thyroid hormones





- Thyroid hormone resistance is characterised by the coexistence of high FT4 and TSH levels.
- Impaired sensitivity to thyroid hormones, which is characterised by decreased tissue responsiveness to thyroid hormones

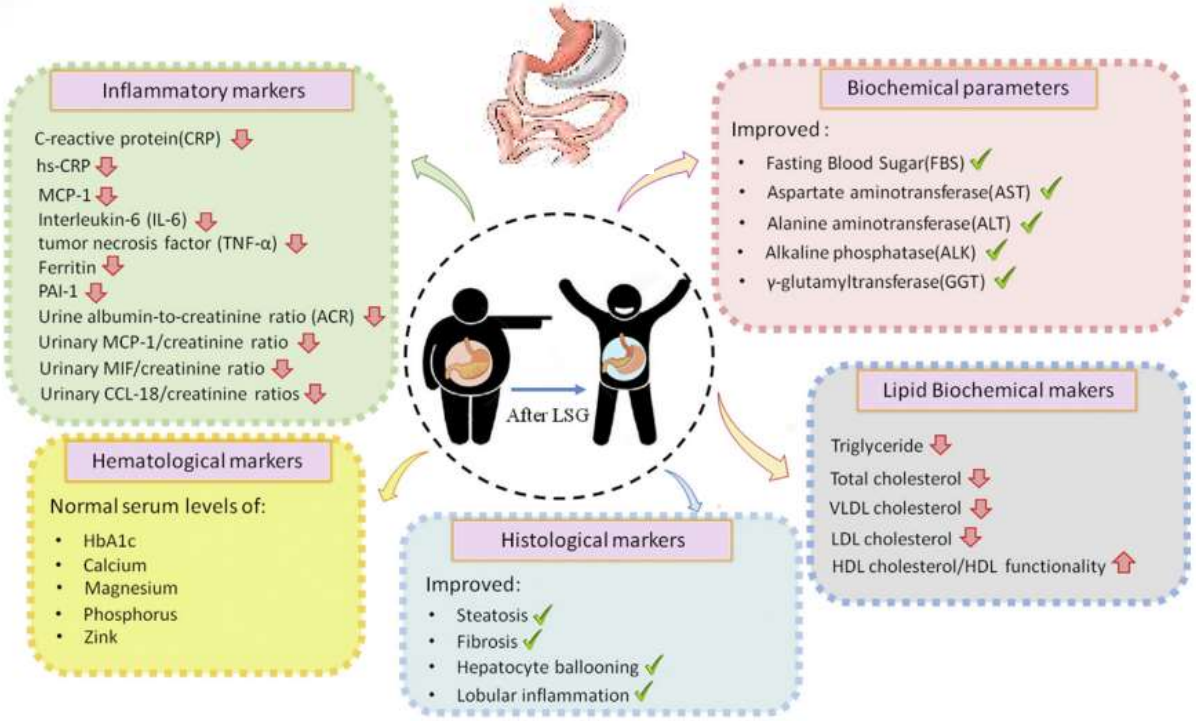
- Thyroid Feedback Quantile-based Index (TFQI)

  a new approach to calculate the central sensitivity index to thyroid hormones
- Thyrotroph T4 Resistance Index (TT4RI) was calculated as fT4(pmol/L) * TSH(mIU/L)
- TSH index (TSHI) was calculated as ln TSH(mIU/L) + 0.1345 * fT4(pmol/L)

Diabetes Care 2019;42:303–310

01 Background

Uncertain issue



BS on changes in thyroid hormone levels after weight loss remains uncertain

- BS has markedly ameliorated obesity and obesity-related diseases, such as hyperuricaemia reduction

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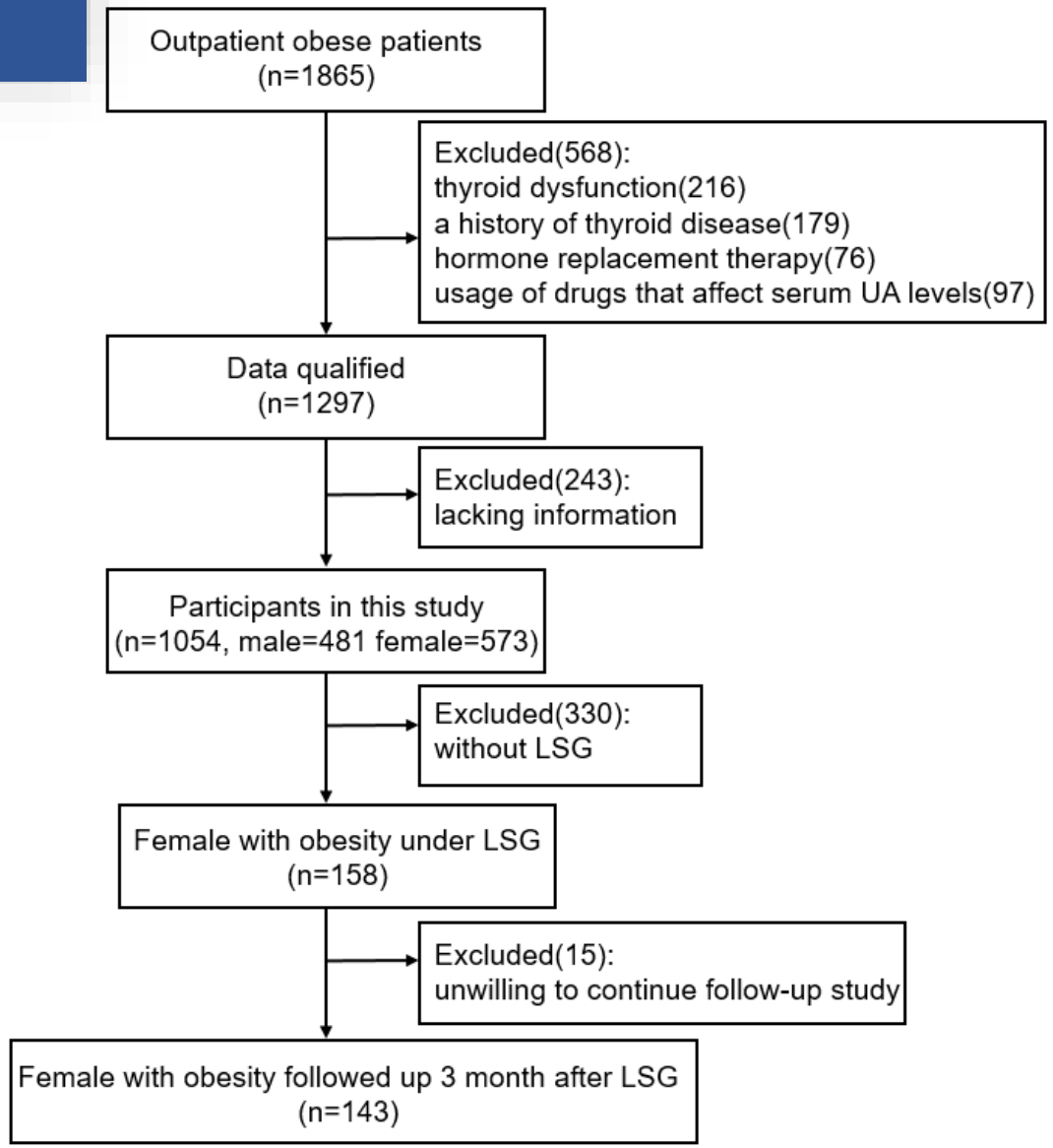
Heliyon. 2020 Feb 29;6(2):e03496.

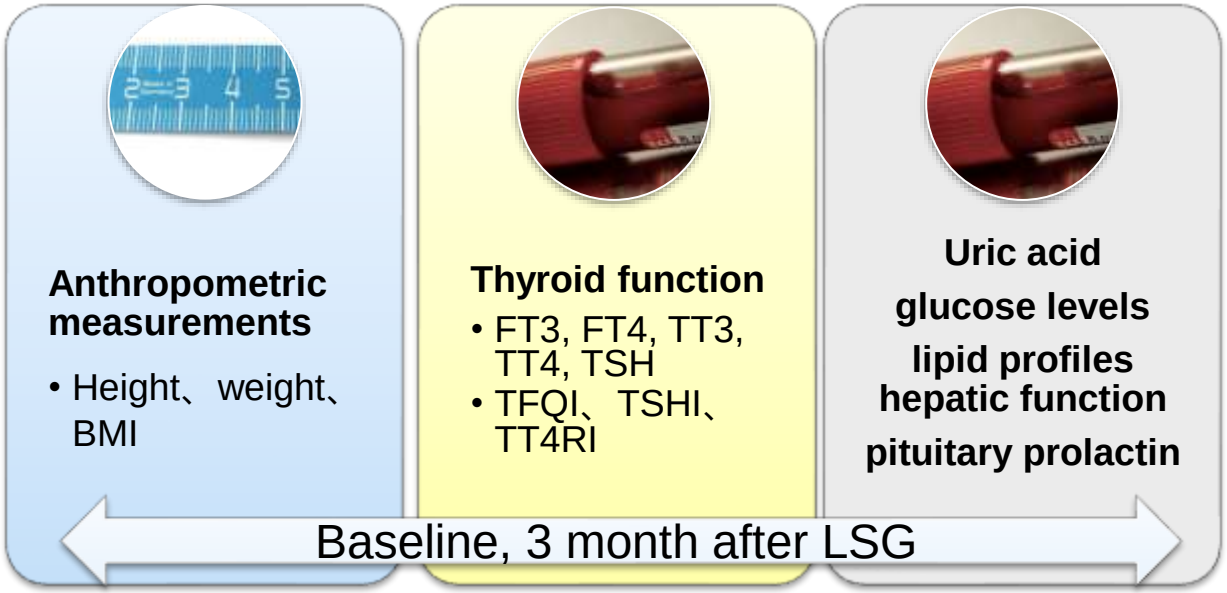
Aim:

- To investigate the relationship between thyroid hormone sensitivity and elevate UA levels in patients with obesity

- To evaluate the change and interrelationships between thyroid hormone sensitivity and UA levels after LSG

02 Methods


Outpatient obese patients
(n=1865)
Excluded(568):
thyroid dysfunction(216)
a history of thyroid disease(179)
hormone replacement therapy(76)
usage of drugs that affect serum UA levels(97)
Data qualified
(n=1297)
Excluded(243):
lacking information
Participants in this study
(n=1054, male=481 female=573)
Excluded(330):
without LSG
Female with obesity under LSG
(n=158)
Excluded(15):
unwilling to continue follow-up study
Female with obesity followed up 3 month after LSG
(n=143)


Anthropometric measurements
• Height、weight、BMI
Thyroid function
• FT3, FT4, TT3, TT4, TSH
• TFQI、TSHI、TT4RI
Uric acid
glucose levels
lipid profiles
hepatic function
pituitary prolactin
Baseline, 3 month after LSG

03 Results

Table 1. Comparison of baseline characteristics between participants with and without HUA

	Male（n=481）			Female(n=573)		
	NUA(n=166)	HUA(n=315)	P value	NUA(n=250)	HUA(n=323)	P value
Age, years	30.00(21.75, 35.00)	29.00(22.00, 35.00)	0.639	29.00(22.00, 37.00)	31.00(24.00, 39.25)	0.036
BMI, kg/m^2	34.34(30.96, 39.45)	36.17(32.80, 40.26)	0.006	31.90(28.00, 35.60)	34.50(30.80, 38.30)	< 0.001
SBP, mmHg	134.50(125.00, 147.50)	138.00(128.00, 150.00)	0.070	130.00(118.00, 139.00)	130.00(121.00, 143.00)	0.091
DBP, mmHg	83.00(75.00, 91.50)	85.00(78.00, 93.00)	0.076	83.00(74.00, 90.00)	83.00(75.50, 91.00)	0.356
HbA1c, %	6.50(5.70, 8.20)	5.80(5.40, 6.30)	< 0.001	5.70(5.40, 6.95)	5.80(5.40, 6.50)	0.432
TC, mmol/L	4.58(3.94, 5.13)	4.78(4.20, 5.48)	0.006	4.61(4.02, 5.31)	4.74(4.24, 5.47)	0.032
TG, mmol/L	1.63(1.22, 2.34)	1.83(1.30, 2.50)	0.063	1.32(0.95, 1.97)	1.56(1.20, 2.19)	< 0.001
HDL, mmol/L	1.03(0.90, 1.18)	0.97(0.84, 1.12)	0.004	1.16(1.00, 1.34)	1.07(0.93, 1.23)	< 0.001
LDL, mmol/L	2.85(2.19, 3.37)	2.98(2.46, 3.63)	0.022	2.76(2.32, 3.40)	2.97(2.48, 3.50)	0.024
ALT, U/L	40.10(25.90, 73.30)	57.90(36.35, 95.30)	< 0.001	22.80(14.95, 37.35)	39.75(23.96, 79.20)	< 0.001
AST, U/L	26.85(20.10, 38.85)	32.05(23.55, 50.58)	< 0.001	20.00(15.45, 27.40)	27.95(19.10, 45.75)	< 0.001
PRL, ng/ml	287.80(210.90, 398.20)	345.30(247.80, 497.15)	0.001	385.75(260.95, 568.33)	396.91(278.70, 566.85)	0.558
Cr, umol/L	66.80(59.50, 76.30)	73.30(63.40, 84.55)	0.003	54.80(50.15, 59.40)	58.65(51.13, 66.43)	0.013
BUN, mmol/L	4.97(3.88, 5.72)	4.90(4.12, 5.73)	0.719	4.50(3.64, 5.40)	4.48(3.85, 5.09)	0.997
UA, umol/L	366.80(324.48, 399.20)	498.00(464.90, 560.00)	< 0.001	305.20(274.00, 339.33)	424.30(393.00, 466.60)	< 0.001
FT3, pmol/L	5.36(4.98, 5.71)	5.49(5.05, 5.88)	0.087	4.94(4.49, 5.31)	5.00(4.60, 5.35)	0.139
FT4, pmol/L	16.64(15.17, 18.51)	16.59(15.11, 18.28)	0.470	15.43(14.29, 17.00)	15.67(14.13, 17.41)	0.215
TSH, mIU/L	1.97(1.36, 2.82)	2.22(1.50, 2.99)	0.077	2.18(1.46, 3.00)	2.55(1.69, 3.59)	< 0.001
TFQI	0.026±0.364	0.048±0.383	0.414	**-0.100±0.362**	**0.019±0.393**	**< 0.001**
TT4RI	32.98(22.70, 45.32)	36.67(24.16, 51.49)	0.100	**33.45(22.79, 46.59)**	**38.75(26.76, 56.45)**	**< 0.001**
TSHI	2.97±0.66	3.01±0.63	0.210	**2.87(2.42, 3.19)**	**3.01(2.64, 3.42)**	**< 0.001**
SH, %	32.53	39.68	0.074	**36.80**	**52.01**	**< 0.001**

03 Results

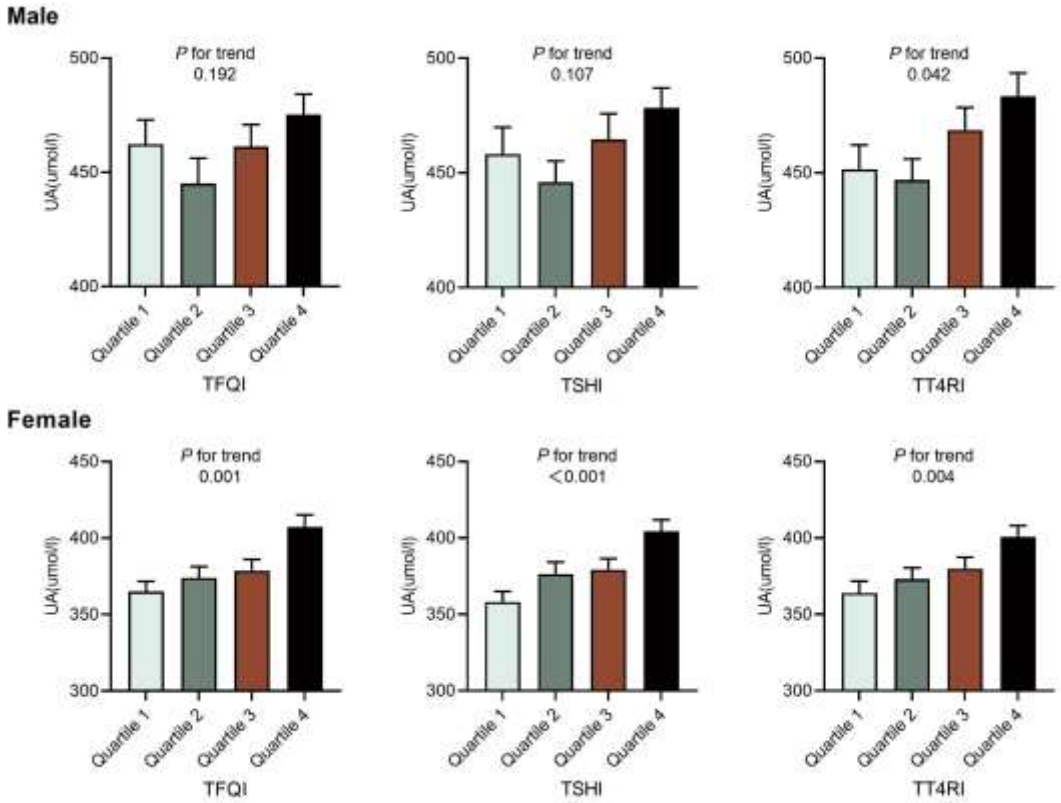


Figure1. Uric acid levels according to the quartiles of TFQI, TSHI, and TT4RI.

Table 2. Linear regression analysis of Thyroid Hormone Sensitivity with UA in obese patients.

		UA		
		β	t	P value
Female	TFQI	0.244	3.335	0.001**
	TT4RI	0.272	3.859	< 0.001***
	TSHI	0.282	3.976	< 0.001***
Male	TFQI	0.024	0.307	0.760
	TT4RI	-0.004	-0.050	0.960
	TSHI	-0.018	-0.219	0.827

P values were adjusted for age, BMI, hypertension, diabetes, dyslipidemia, Cr, BUN, ALT, AST and PRL.

- A significant linear trend in UA levels and increasing quartiles of thyroid hormone sensitivity indices was observed among female patients with obesity;
- multivariate linear regression analysis indicated highly significant positive correlations between UA levels and TFQI , TT4RI and TSHI.

03 Results

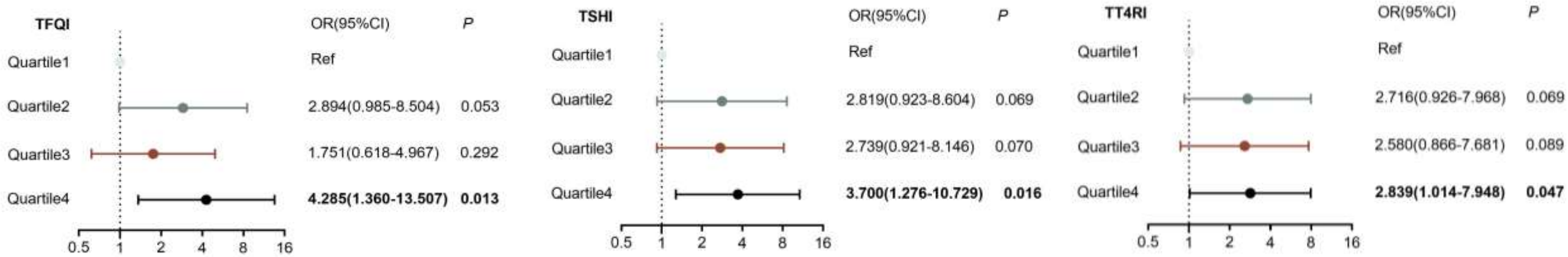


Figure2. Logistic analysis of the association between Hyperuricaemia and TFQI, TSHI, and TT4RI quartiles.
The odds ratios were adjusted for age, BMI, hypertension, diabetes, dyslipidemia, Cr, BUN, ALT, AST and PRL.

The OR (95% CI) for hyperuricaemia for TFQI, TSHI, and TT4RI in the highest quartile were 4.285 (1.360, 13.507), 3.700 (1.276, 10.729), and 2.839 (1.014, 7.948), respectively, all $P < 0.05$.

03 Results

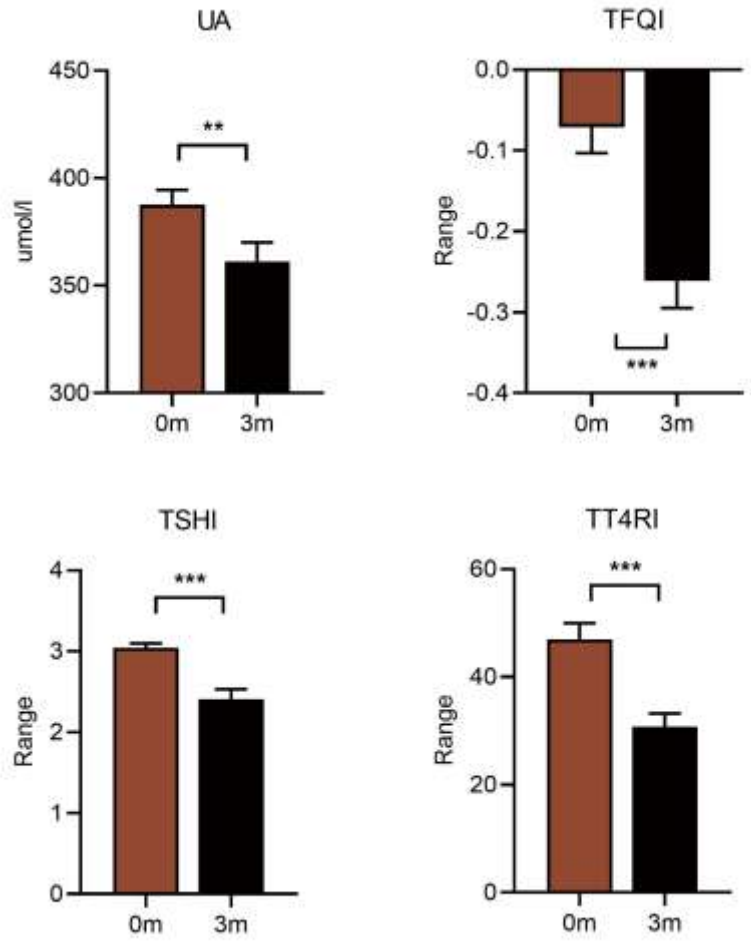


Figure3. Change of UA, TFQI, TT4RI and TSHI in female with obesity 3 months after LSG.
Comparisons of variables, *P<0.05, **P<0.01, ***P<0.001.

- UA levels decreased at 3 months after surgery;
- the changes in TFQI, TT4RI, and TSHI after LSG were significant;
- Impaired Sensitivity to Thyroid Hormones and UA Levels can be Improved in Patients with Obesity after LSG

03 Results

Table 3. Correlation analysis and Multiple regression analysis between the improvement in thyroid hormone sensitivity indices and UA after surgery in females.

	Female（ΔUA）						
	Correlation analysis				Multiple regression analysis		
	Model1		Model2		Model3		
	r	P	r	P	β	t	P value
ΔTFQI	0.207	0.068	0.258	0.062	0.253	1.993	0.052
ΔTT4RI	0.242	0.032*	0.327	0.017*	0.311	2.540	0.014*
ΔTSHI	0.303	0.007**	0.331	0.015*	0.290	2.451	0.019*

Model1, adjusted for age, ΔBMI
Model2, adjust for age, ΔBMI, ΔHbA1c, ΔCr, ΔBUN, ΔRPL
Model3, adjust for age, ΔBMI, ΔHbA1c, ΔCr, ΔBUN, ΔRPL
ΔUA, ΔTFQI, ΔTT4RI and ΔTSHI mean comparison of UA, TFQI, TT4RI and TSHI at 3 months after LSG and baseline.
*P < 0.05; **P < 0.01; ***P < 0.001

- ΔUA levels at 3 months after surgery was positively correlated with Δthyroid hormone sensitivity indices;
- The decrease in UA levels can explain the improvement in thyroid hormone sensitivity after LSG.

04 Conclusion

- Higher values of thyroid hormone resistance indices were related to elevated UA levels in female patients with extreme obesity.
- The improvement in central resistance to thyroid hormones after LSG was significantly and independently related to a decrease in serum UA levels.

05 Limitations

To study the causal relationship between UA levels and sensitivity to thyroid hormones.

thyroid-associated antibodies needs to be further evaluated.

Further optimization of thyroid hormone resistance index.

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I have no potential conflict of interest to report

Acknowledgements

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TONGJI UNIVERSITY

Department of Endocrinology and Metabolism,
Shanghai Tenth People's Hospital,
School of Medicine, Tongji University

Shen Qu's team

Thanks for listening!