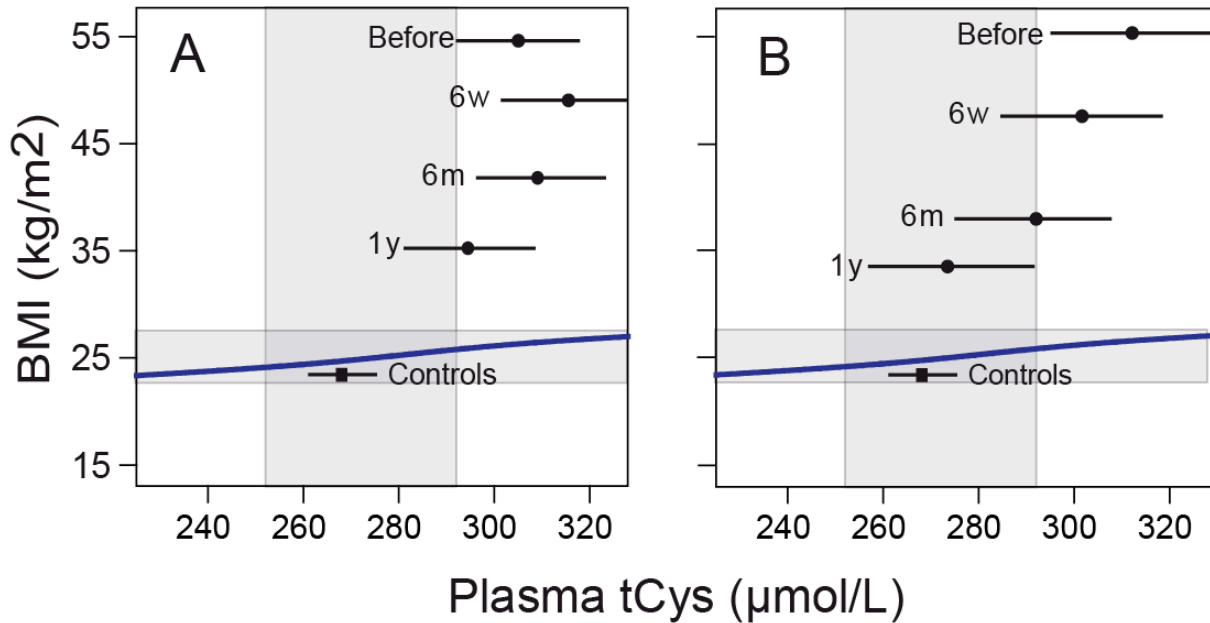


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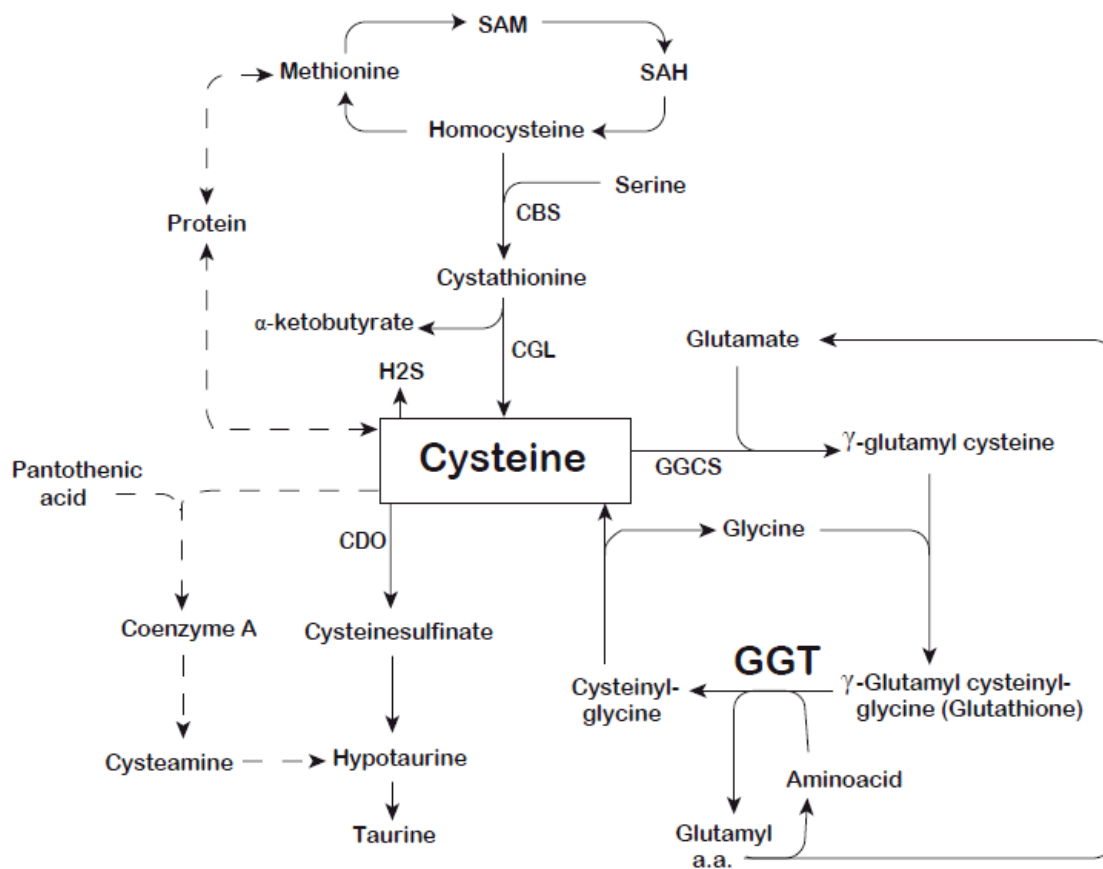
Supplemental Fig. 1



Serum tCys and BMI (age- and gender-adjusted means with 95% CI for tCys) in severely obese patients before and up to one year after gastric bypass surgery (panel A; *n* 31) or duodenal switch (panel B; *n* 29) compared to healthy controls (■; *n* 58) and participants (middle-aged group) in the Hordaland Homocysteine Study (HHS) (solid line; *n* 3721). The shaded areas show the interquartile ranges of tCys and BMI in HHS. The solid line shows the tCys-BMI dose-response relationship in HHS. The length of the X-axis represents the 95% reference interval for tCys in HHS. The 95th percentile of BMI in HHS was 32 kg/m² (not plotted).

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Supplemental Fig. 2



Cysteine metabolic pathways: cysteine can be obtained from food, or from methionine via homocysteine and the transsulfuration pathway. Dotted arrows indicate pathways with omitted intermediates for purposes of clarity.

CBS, cystathionine β -synthase. CDO, cysteine dioxygenase. CGL, cystathionine γ -lyase. GGCS, γ -glutamylcysteine synthase. GGT, γ -glutamyltransferase. H₂S, hydrogen sulfide. Hcy, homocysteine. Met, methionine. SAH, *S*-adenosylhomocysteine. SAM, *S*-adenosylmethionine.

		1 y						0.00
		Methionine	tHcy	Cystathion	tCys	tGSH	Taurine	Glutamate
Creatinine ($\mu\text{mol/L}$)	Controls	0.28	0.43	0.29	0.22	0.33	-0.22	-0.31
	preop	0.14	0.48	0.30	0.27	0.08	-0.18	-0.04
	6 wk	-0.11	0.49	0.46	0.36	-0.11	-0.01	0.26
	6 mo	0.16	0.39	0.34	0.19	-0.08	0.03	0.18
	1 y	0.27	0.01	0.36	0.24	0.18	0.09	0.04
ALT (U/L)	Controls	0.11	0.15	0.07	0.23	0.06	-0.09	0.34
	preop	0.48	0.11	0.18	0.12	-0.33	0.35	0.54
	6 wk	0.32	0.09	-0.13	-0.04	-0.35	0.26	0.14
	6 mo	-0.23	-0.03	0.28	-0.14	-0.26	-0.03	0.07
	1 y	-0.04	-0.13	0.23	-0.28	-0.40	0.21	0.27
GGT (U/L)	Controls	-0.02	0.27	0.25	0.43	-0.11	0.03	0.61
	preop	0.18	-0.07	0.23	0.18	-0.76	0.01	0.84
	6 wk	-0.06	0.17	0.26	0.11	-0.41	0.19	0.79
	6 mo	0.02	-0.15	0.48	0.11	-0.63	0.22	0.79
	1 y	0.10	-0.03	0.21	-0.19	-0.64	0.23	0.82
Total cholesterol (mmol/L)	Controls	-0.17	0.07	0.10	0.30	-0.24	-0.06	0.39
	preop	-0.30	-0.10	-0.09	0.15	-0.13	-0.13	0.09
	6 wk	-0.17	0.10	0.02	0.31	0.02	-0.02	0.11
	6 mo	-0.12	-0.16	0.13	0.05	-0.22	-0.47	0.12
	1 y	0.24	-0.15	0.08	0.21	0.01	-0.18	0.11
Triacylglycerols (mmol/L)	Controls	-0.14	0.07	0.27	0.10	-0.18	-0.08	0.43
	preop	0.10	-0.08	0.16	0.08	-0.41	-0.23	0.30
	6 wk	0.08	0.15	0.26	0.32	-0.16	-0.24	0.16
	6 mo	-0.01	0.04	0.29	0.00	-0.12	-0.35	0.22
	1 y	-0.17	-0.06	0.18	0.04	-0.31	-0.45	0.48
FAD (nmol/L)	Controls	0.22	0.18	-0.08	0.17	0.35	-0.35	0.49
	preop	0.09	0.00	-0.12	0.06	-0.14	0.05	0.18
	6 wk	0.04	-0.19	0.04	-0.09	0.09	-0.13	-0.00
	6 mo	-0.02	-0.06	0.09	0.21	-0.12	-0.24	0.15
	1 y	-0.02	-0.12	0.13	0.30	-0.04	-0.00	0.38

		Methionine	tHcy	Cystathion	tCys	tGSH	Taurine	Glutamate
FMN (nmol/L)	Controls	0.02	-0.15	0.05	-0.03	0.27	-0.03	0.04
	preop	0.06	0.07	0.11	0.22	-0.31	-0.15	0.18
	6 wk	0.18	-0.01	0.11	0.10	-0.12	-0.10	-0.02
	6 mo	0.03	-0.03	0.11	0.15	-0.13	0.00	0.26
	1 y	0.15	0.20	0.34	0.16	-0.45	-0.15	0.48
PLP (nmol/L)	Controls	0.38	0.06	0.00	0.32	0.02	-0.18	0.16
	preop	0.08	-0.01	-0.07	0.12	0.12	0.32	-0.06
	6 wk	0.21	-0.02	-0.10	0.15	0.18	0.14	-0.29
	6 mo	0.20	0.18	-0.09	0.15	-0.08	0.20	-0.03
	1 y	0.46	0.09	-0.07	0.25	0.16	0.44	0.07
Folate (nmol/L)	Controls	0.03	-0.42	0.21	0.13	-0.23	-0.04	0.06
	preop	-0.03	-0.60	-0.18	0.21	-0.33	0.05	0.22
	6 wk	-0.34	-0.27	-0.22	0.15	-0.17	-0.34	-0.33
	6 mo	0.04	-0.69	-0.18	0.16	-0.45	0.22	0.26
	1 y	0.11	-0.44	-0.08	0.16	-0.24	0.34	0.22
Cobalamin (pmol/L)	Controls	0.05	-0.11	-0.21	0.30	0.09	0.01	0.20
	preop	0.12	-0.10	-0.05	0.23	-0.28	-0.09	0.16
	6 wk	-0.29	-0.21	-0.11	-0.12	-0.50	-0.16	0.31
	6 mo	0.05	-0.25	0.08	0.19	-0.30	-0.14	0.50
	1 y	-0.15	-0.45	-0.20	0.06	0.15	-0.06	-0.01
Albumin (g/L)	Controls	0.24	0.12	0.07	0.21	0.17	-0.09	-0.07
	Preop	-0.12	-0.13	-0.06	0.23	-0.29	0.23	0.22
	6 wk	-0.09	0.39	0.02	0.50	0.24	0.12	-0.31
	6 mo	0.16	-0.10	-0.40	0.14	0.07	0.36	-0.33
	1 y	0.16	0.02	0.06	0.44	0.27	0.52	-0.19
BMI (kg/m ²)	Controls	0.10	0.19	0.38	0.14	-0.15	-0.10	0.19
	preop	-0.09	0.20	0.11	0.17	0.13	-0.09	0.06
	6 wk	0.05	-0.00	0.12	-0.11	0.10	-0.34	-0.21
	6 mo	-0.02	-0.26	0.05	-0.03	0.06	-0.11	0.22
	1 y	0.10	-0.24	0.07	0.28	0.51	-0.18	-0.03

GGT, γ -glutamyltransferase. FAD, flavin adenine dinucleotide. FMN, flavin mononucleotide. PLP, pyridoxal-5'-phosphate. tCys, totalcysteine. tGSH, total glutathione. tHcy, total homocysteine.

^a For each variable, the top row shows correlations in controls (n 58) and the other rows show correlations in patients for each visit. Patients, n 60 except for methionine, tGSH, taurine, glutamate, ALT, GGT, and folate (n 30). Bold figures, $P < 0.05$; bold and underlined figures, $P < 0.01$.

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Supplemental Table 2 Amino acids and related variables before and after surgery^{a,b}

	Baseline	6 wk	6 mo	1 y	<i>P</i>
<i>N</i> ^b	57	56	58	52	
Women [<i>n</i> (%)]	40 (70)	40 (71)	41 (71)	37 (71)	
Age (years)	36 ± 6	35 ± 6	36 ± 6	36 ± 6	
BMI (kg/m ²)	55.0 (54.1, 55.9) ^c	47.5 (46.6, 48.4)	40.0 (39.0, 40.9)	35.6 (34.7, 36.6)	0.001 ^e
Gastric bypass	54.8 (53.6, 56.1)	48.2 (46.9, 49.4)	41.7 (40.5, 43.0)	38.5 (37.3, 39.8)	<0.001 ^d
Duodenal switch	55.2 (54.0, 56.4)	46.7 (45.6, 47.9)	38.0 (36.9, 39.2)	32.4 (31.2, 33.6)	<0.001 ^d
Methionine ^f (μmol/L)	21.8 (20.7, 22.8)	18.0 (16.9, 19.1)	17.2 (16.1, 18.2)	18.7 (17.6, 19.8)	<0.001 ^d
tHcy (μmol/L)	11.5 (10.5, 12.6)	13.8 (12.6, 15.2)	15.5 (14.1, 17.0)	12.7 (11.6, 14.0)	<0.001 ^e
Gastric bypass	12.2 (10.7, 13.9)	13.3 (11.7, 15.1)	13.9 (12.2, 15.8)	11.5 (10.0, 13.1)	0.63 ^d
Duodenal switch	10.8 (9.4, 12.3)	14.5 (12.6, 16.6)	17.3 (15.1, 19.8)	14.1 (12.3, 16.1)	<0.001 ^d
Cystathionine (μmol/L)	0.22 (0.19, 0.25)	0.14 (0.12, 0.15)	0.14 (0.12, 0.16)	0.13 (0.12, 0.15)	<0.001 ^d
tCys ^g (μmol/L)	308 (297, 319)	308 (297, 319)	301 (290, 311)	285 (274, 296)	0.02 ^e
Gastric bypass	305 (291, 318)	315 (301, 328)	309 (296, 323)	295 (281, 309)	0.22 ^d
Duodenal switch	312 (295, 329)	301 (284, 319)	292 (275, 308)	274 (257, 291)	<0.001 ^d
Glutamate ^f (μmol/L)	206 (182, 234)	165 (145, 187)	147 (130, 167)	138 (122, 157)	0.09 ^d
Taurine ^f (μmol/L)	82 (76, 88)	89 (83, 95)	83 (77, 89)	81 (76, 87)	0.51 ^d
GGT ^{f,g} (U/L)	38 (30, 48)	25 (19, 32)	22 (17, 27)	23 (18, 29)	0.03 ^e
Gastric bypass	36 (30, 45)	20 (16, 25)	18 (14, 22)	16 (13, 19)	<0.001 ^d
Duodenal switch	40 (28, 56)	33 (24, 48)	26 (19, 37)	28 (20, 40)	0.009 ^d
tGSH ^f (μmol/L)	5.1 (4.6, 5.5)	5.2 (4.7, 5.6)	5.1 (4.6, 5.5)	5.1 (4.6, 5.5)	0.98 ^d
FAD (nmol/L)	309 (296, 321)	289 (277, 301)	314 (302, 328)	317 (304, 330)	0.05 ^d
Vitamin B-12 (pmol/L)	308 (272, 349)	388 (342, 440)	321 (283, 363)	325 (286, 370)	0.03 ^e
Gastric bypass	312 (264, 369)	338 (287, 399)	335 (283, 395)	381 (319, 454)	0.08 ^d
Duodenal switch	304 (253, 364)	456 (379, 550)	307 (256, 368)	282 (235, 339)	0.11 ^d
Creatinine (μmol/L)	63 (60, 67)	64 (61, 67)	59 (56, 62)	57 (55, 60)	<0.001 ^d
ALT ^f (U/L)	26 (22, 31)	32 (27, 38)	23 (19, 27)	23 (19, 27)	0.005 ^d

ALT, alanine aminotransferase. FAD, flavin adenine dinucleotide. GGT, γ -glutamyltransferase. tCys, totalcysteine. tGSH, total glutathione. tHcy, total homocysteine.

^a The biomarker values shown are illustrated in figures 1, 2, and 3 in the manuscript.

^b Total *n* 60 patients (42 women and 18 men). The bariatric procedures were gastric bypass (*n* 31 patients; 23 women) and duodenal switch (*n* 29 patients; 19 women).

^c Predicted means (95% CI) (all such values). The means were estimated in linear mixed-effects models and were adjusted for age, sex, and (where applicable) type of surgery.

^d Time effect.

^e Significant ($P < 0.05$) time \times procedure interaction. *P* values for time \times procedure interaction are only shown when significant, and time effects are then reported by procedure.

^f *n* 30 patients (15 in each surgical group).

^g One duodenal switch patient (outlier) was excluded from analysis.