

# Effect of weight loss after gastric bypass surgery on thyroid function in euthyroid people with morbid obesity

A. MacCuish<sup>1</sup>, S. Razvi<sup>2,3</sup> and A. A. Syed<sup>1,4</sup>

<sup>1</sup>The University of Manchester, Manchester, UK; <sup>2</sup>Queen Elizabeth Hospital, Gateshead, UK; <sup>3</sup>Newcastle University, Newcastle upon Tyne, UK; <sup>4</sup>Salford Royal Hospital, Salford, UK

Received 30 November 2011; revised 6 February 2012; accepted 12 February 2012

Address for correspondence: Dr AA Syed, Obesity Medicine & Endocrinology, Salford Royal NHS Foundation Trust & University Teaching Hospital, Stott Lane, Salford, Greater Manchester M6 8HD, UK.  
E-mail: aas@DrSyed.org

## Summary

Obesity is positively associated with serum thyrotropin (TSH) concentrations at the high end of the normal range. The relationship between weight loss and thyroid function is less clear and studies to date have yielded inconsistent results. Our aim was to describe changes in thyroid function in obese people in relation to durable and significant weight loss after Roux-en-Y gastric bypass (RYGB) surgery. We recorded percentage of excess weight loss (% EWL), serum TSH and free thyroxine (fT4) before and median 4.5, 15 and 24 months after RYGB in 55 euthyroid patients with morbid obesity ranging in age from 18 to 64 years in a retrospective cohort analysis in a university hospital in Greater Manchester. Mean  $\pm$  standard error preoperative weight was  $135.13 \pm 4.23$  kg and BMI  $48.08 \pm 1.58$  kg m<sup>-2</sup>. Patients attained nadir %EWL of 68% by median 15 months after RYGB. TSH was  $2.00 \pm 0.14$  mU L<sup>-1</sup> at baseline and  $2.02 \pm 0.22$  mU L<sup>-1</sup> at 24 months after RYGB (non-significant). Baseline fT4 was  $13.46 \pm 0.28$  pmol L<sup>-1</sup>, and increased significantly to  $15.14 \pm 0.55$  pmol L<sup>-1</sup> at 24 months ( $P < 0.004$ ). In conclusion, we report that weight loss after RYGB was accompanied by significant increase in serum fT4 but no change in TSH concentrations. Further study to elucidate the effect of significant weight loss on the thyroid axis is required.

**Keywords:** Bariatric surgery, cohort study, thyroid function tests.

## Introduction

Obesity is one of the major global public health concerns of our times. Clear associations between thyroid function and obesity have been observed in the euthyroid general population, with serum thyrotropin (TSH) correlated to weight gain (1,2). In addition, morbid obesity has been associated with higher TSH concentrations (3,4). The relationship with free thyroid hormones is less clear. Furthermore, studies into the effect of weight loss on thyroid function in people with morbid obesity have yielded inconsistent results (4–9). A recent study has reported changes in thyroid function associated with weight loss induced by gastric banding, a restrictive bariatric procedure (10). As malabsorptive bariatric surgery could have distinctive effects on thyroid metabo-

lism, our aim was to describe changes in thyroid function in relation to significant weight loss after Roux-en-Y gastric bypass (RYGB) surgery in obese people with normal thyroid function.

## Patients and methods

We carried out a retrospective, observational cohort analysis of bariatric surgical patients in the setting of a National Health Service university teaching hospital that serves the population of Greater Manchester in northwest England (11). We identified 55 consecutive patients with no prior history of thyroid disease or treatment with thyroxine who had undergone RYGB for the correction of morbid obesity 24 months or more prior to the date of sampling. All

patients post-RYGB were routinely prescribed a multivitamin and micronutrient supplement that included iodine. Data recorded included body weight, TSH and free thyroxine (fT4) at baseline and postoperatively at a median 4½, 15 and 24 months. TSH (reference range, 0.27 mU L<sup>-1</sup> to 4.2 mU L<sup>-1</sup>) and fT4 (12 pmol L<sup>-1</sup> to 22 pmol L<sup>-1</sup>) were measured by immunoassay on a Roche E170 modular analyser with inter-batch coefficients of variation for three quality control samples in each assay <5%; there were no changes in the reference ranges or assay performance characteristics throughout the period of study. Weight loss outcomes were reported as percentage of excess weight loss (% EWL) based on the degree of excess weight above the reference standard body mass index (BMI) of 25 kg m<sup>-2</sup> (12), computed by the formula [Initial weight (kg) – Current weight (kg)]/[Initial weight (kg) – Ideal weight (kg)] × 100, where Ideal weight (kg) = 25 × [Height (m)]<sup>2</sup>. Permission for the audit was obtained from the Caldicott Guardian of the hospital.

### Statistical analysis

Comparisons between paired measurements were performed by Student's paired-samples *t*-test. Comparisons among groups were done by one-way analysis of variance followed by Tukey's multiple comparison test. We used linear regression to study the relationship between outcome variables. *P* < 0.05 was considered statistically significant. We confirmed significant results by re-analyzing data after imputing missing values by expectation-maximization method. We report results based on original, unimputed data unless specified otherwise. Data were analyzed with Statistical Package for the Social Sciences 16 (SPSS, SPSS Inc., Chicago, IL, USA) and Prism 4 (GraphPad Software Inc., La Jolla, CA, USA).

### Results

We studied 55 patients (13 men), ranging in age from 18 to 64 years, with no history of thyroid disease who had undergone RYGB. Mean ± standard error (SE) age at the time of RYGB was 46.5 ± 1.38 years. Patients had a mean ± SE preoperative weight of 135.13 ± 4.23 kg and BMI of 48.08 ± 1.58 kg m<sup>-2</sup> (Table 1), and achieved significant weight loss following RYGB (Fig. 1). TSH was 2.00 ± 0.14 mU L<sup>-1</sup> at baseline and 2.02 ± 0.22 mU L<sup>-1</sup> at 24 months after bariatric surgery (non-significant). Baseline fT4 was 13.46 ± 0.28 pmol L<sup>-1</sup>, and increased significantly to 15.14 ± 0.55 pmol L<sup>-1</sup> at 24 months following bariatric surgery (*P* < 0.004). Change in fT4 was weakly correlated with change in weight at 24 months (*r*<sup>2</sup> = 0.023). There was no significant change in serum albumin with a mean of 43.4 ± 0.4 g L<sup>-1</sup> at baseline and 43.3 ± 0.7 g L<sup>-1</sup> at 24 months.

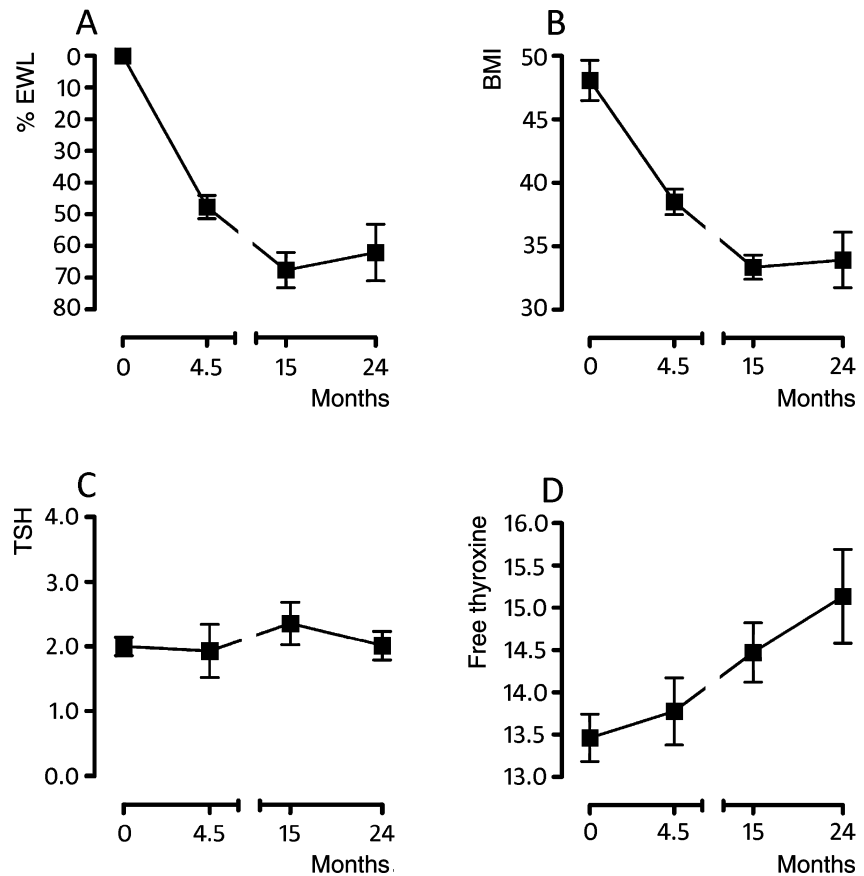
**Table 1** Baseline vs 24-month measurements (mean ± standard error) in participants; analysis by *t*-test

	Baseline	24 months	<i>P</i>
Weight (kg)	135.1 ± 4.2	92.4 ± 4.1	<0.001
Body mass index (kg m <sup>-2</sup> )	48.1 ± 1.6	33.9 ± 2.2	<0.001
Systolic blood pressure (mm Hg)	136.4 ± 4.8	127.6 ± 5.6	0.234
Diastolic blood pressure (mm Hg)	81.0 ± 2.3	76.7 ± 2.4	0.204
Thyrotropin (mU L <sup>-1</sup> )	2.00 ± 0.14	2.02 ± 0.22	0.961
Free thyroxine (pmol L <sup>-1</sup> )	13.46 ± 0.28	15.14 ± 0.55	<0.004
Total cholesterol (mmol L <sup>-1</sup> )	4.81 ± 0.19	4.12 ± 0.19	<0.022
Albumin (g L <sup>-1</sup> )	43.4 ± 0.4	43.3 ± 0.7	0.904

### Discussion

We analyzed TSH and fT4 in euthyroid, morbidly obese people before and after significant weight loss induced by RYGB. While there was no significant change in TSH, fT4 concentrations increased steadily up to 2 years of follow-up. The fT4 immunoassay is unaffected by thyroid-binding proteins. Furthermore, the stability of serum albumin concentrations post-RYGB, as also reported by others previously (13), suggests that there were no substantial changes in carrier proteins. Thus, the regulation of thyroid function is probably a function of changes in body weight and unlikely to be mediated by nutritional status.

Previous studies have reported improvement in thyroid hormone levels following gastric bypass surgery in obese people with subclinical or overt hypothyroidism (6,14). In obese people with normal thyroid function, Dall'Asta and colleagues recently reported an increase in fT4 following gastric banding with no change in TSH (10). They also found reduction in free T3 (fT3) and fT3 : fT4 ratio, and conjectured that these changes were probably due to decreased activity of iodothyronine deiodinase type 1 (D1) and type 2 (D2). A recent *in vivo* study demonstrated that D2 activity and mRNA are present in human preadipocytes in both mesenteric and subcutaneous adipose tissue (15), confirming that human adipose tissue is one of the sites of fT3 production. This lends further credence to the notion that the absolute and relative reductions in the amount of adipose tissue mass, although adipocyte number remains the same even after significant weight loss and reduced adipocyte volume (16), that occurs with significant weight loss as seen after gastric bypass surgery results in decreased conversion of fT4 to fT3 with a consequent rise in fT4 concentrations. Although fT3 is not routinely measured in our clinical practice, the lack of significant change in TSH suggests that the rise in fT4 was probably secondary to changes in deiodinase activity in favour of reduced peripheral conversion to fT3. It is also plausible that changes in thyroid hormone concentrations after significant weight loss may be related to



**Figure 1** Serial changes in outcome measures over 24 months following Roux-en-Y gastric bypass surgery in people with morbid obesity. Panel A, percentage of excess weight loss (% EWL). Panel B, body mass index (BMI) (kg m<sup>-2</sup>). Panel C, thyrotropin (TSH) (mU L<sup>-1</sup>). Panel D, free T4 (pmol L<sup>-1</sup>). Filled squares, mean values. Error bars, standard errors.

alterations in adipokine secretion. For example, leptin has an important effect on the hypothalamic-pituitary-thyroid axis (17,18); more relevantly, it influences deiodinase activity and increases conversion of fT4 to fT3 (19). Leptin is secreted in proportion to body fat mass and decreases after RYGB (20); thus, decline in leptin concentrations with significant weight loss after RYGB may in turn lead to decreased deiodinase activity and reduced conversion of fT4 to fT3. Although nadir weight loss occurred by median 15 months the fT4 concentrations increased progressively during the 24 months of follow-up. Serum leptin levels in a case-control study were reported to be significantly lower in weight-stable RYGB patients 35 months after surgery compared with BMI-matched controls (21). Thus, it is likely that the metabolic effects of RYGB on leptin and thereby thyroid function continue to accrue even after weight loss has plateaued. A longer-term study is needed to ascertain a fuller natural history of changes in thyroid function after bariatric surgery.

It is well recognized that certain medications can sometimes cause interference in thyroid function testing. Anti-hypertensive beta-blockers that only inhibit the peripheral conversion of T4 to T3, however, interfere minimally with thyroid function test results (22). While we do not have data on medication changes in this retrospective study, it is

to be noted that weight loss after RYGB frequently leads to reduction in doses of antihypertensive medications (23), thus further limiting the putative effect of these medications on thyroid function.

In contrast to gastric bypass or banding, it has been reported that biliopancreatic diversion is associated with an increased prevalence of subclinical or even frank hypothyroidism through several integrated mechanisms including iodine malabsorption and increased fT3 losses through changes in the entero-hepatic circulation (24). While we do not have data on iodine status in our retrospective cohort study, we anticipate that patients were iodine-replete as they were routinely prescribed the multivitamin and micro-nutrient supplement, Forceval® (Alliance Pharma plc., Wiltshire, UK) that provides 140 µg of iodine (100% of reference nutrient intake for adults in the UK (25)). As iodine sufficiency is associated with a higher incidence of hypothyroidism and deficiency with hyperthyroidism in population studies (26,27) iodine supplementation may have attenuated the increase in fT4 in our study.

In conclusion, we report a significant rise in free thyroxine concentrations with weight loss following gastric bypass surgery. Further work is required to elucidate the mechanism and natural history of changes in the hypothalamic-pituitary-thyroid axis induced by weight loss.

## Conflicts of Interest Statement

None to declare.

## Authors' contributions

AM performed data extraction and analysis and wrote the first draft. SR participated in study design and interpretation of data and contributed important intellectual content to the paper. AAS participated in study design, supervised data extraction and analysis, and revised the manuscript.

## References

- Knudsen N, Laurberg P, Rasmussen LB *et al.* Small differences in thyroid function may be important for body mass index and the occurrence of obesity in the population. *J Clin Endocrinol Metab* 2005; **90**: 4019–4024.
- Svare A, Nilsen TI, Bjoro T *et al.* Serum TSH related to measures of body mass: longitudinal data from the HUNT study, Norway. *Clin Endocrinol (Oxf)* 2011; **74**: 769–775.
- Michalaki MA, Vagenakis AG, Leonardou AS *et al.* Thyroid function in humans with morbid obesity. *Thyroid* 2006; **16**: 73–78.
- Sari R, Balci MK, Altunbas H *et al.* The effect of body weight and weight loss on thyroid volume and function in obese women. *Clin Endocrinol (Oxf)* 2003; **59**: 258–262.
- Buscemi S, Verga S, Maneri R *et al.* Influences of obesity and weight loss on thyroid hormones. A 3–3.5-year follow-up study on obese subjects with surgical bilio-pancreatic by-pass. *J Endocrinol Invest* 1997; **20**: 276–281.
- Chikunguwo S, Brethauer S, Nirujogi V *et al.* Influence of obesity and surgical weight loss on thyroid hormone levels. *Surg Obes Relat Dis* 2007; **3**: 631–635. discussion 635–636.
- Moulin de Moraes CM, Mancini MC, de Melo ME *et al.* Prevalence of subclinical hypothyroidism in a morbidly obese population and improvement after weight loss induced by Roux-en-Y gastric bypass. *Obes Surg* 2005; **15**: 1287–1291.
- Papavramidis ST, Zisiadis AC, Karamouzis MN *et al.* Alterations in thyroid hormones and thyrotropin (TSH) in morbidly obese patients before and after vertical gastroplasty. *Obes Surg* 1995; **5**: 298–301.
- Yashkov YI, Vinnitsky LI, Poroykova MV *et al.* Some hormonal changes before and after vertical banded gastroplasty for severe obesity. *Obes Surg* 2000; **10**: 48–53.
- Dall'Asta C, Paganelli M, Morabito A *et al.* Weight loss through gastric banding: effects on TSH and thyroid hormones in obese subjects with normal thyroid function. *Obesity (Silver Spring)* 2010; **18**: 854–857.
- Demssie YN, Jawaheer J, Farook S *et al.* Metabolic outcomes 1 year after gastric bypass surgery in obese people with type 2 diabetes. *Med Princ Pract* 2012; **21**: 125–128.
- Bray GA, Bouchard C, Church TS *et al.* Is it time to change the way we report and discuss weight loss? *Obesity (Silver Spring)* 2009; **17**: 619–621.
- Ritz P, Becouarn G, Douay O *et al.* Gastric bypass is not associated with protein malnutrition in morbidly obese patients. *Obes Surg* 2009; **19**: 840–844.
- Fazylov R, Soto E, Cohen S *et al.* Laparoscopic Roux-en-Y gastric bypass surgery on morbidly obese patients with hypothyroidism. *Obes Surg* 2008; **18**: 644–647.
- Nomura E, Toyoda N, Harada A *et al.* Type 2 iodothyronine deiodinase is expressed in human preadipocytes. *Thyroid* 2011; **21**: 305–310.
- Spalding KL, Arner E, Westermark PO *et al.* Dynamics of fat cell turnover in humans. *Nature* 2008; **453**: 783–787.
- Menendez C, Baldelli R, Camina JP *et al.* TSH stimulates leptin secretion by a direct effect on adipocytes. *J Endocrinol* 2003; **176**: 7–12.
- Santini F, Galli G, Maffei M *et al.* Acute exogenous TSH administration stimulates leptin secretion *in vivo*. *Eur J Endocrinol* 2010; **163**: 63–67.
- Zimmermann-Belsing T, Brabant G, Holst JJ *et al.* Circulating leptin and thyroid dysfunction. *Eur J Endocrinol* 2003; **149**: 257–271.
- Beckman LM, Beckman TR, Earthman CP. Changes in gastrointestinal hormones and leptin after Roux-en-Y gastric bypass procedure: a review. *J Am Diet Assoc* 2010; **110**: 571–584.
- Korner J, Bessler M, Cirilo LJ *et al.* Effects of Roux-en-Y gastric bypass surgery on fasting and postprandial concentrations of plasma ghrelin, peptide YY, and insulin. *J Clin Endocrinol Metab* 2005; **90**: 359–365.
- Dong BJ. How medications affect thyroid function. *West J Med* 2000; **172**: 102–106.
- Ghiassi S, Morton J, Bellatorre N *et al.* Short-term medication cost savings for treating hypertension and diabetes after gastric bypass. *Surg Obes Relat Dis* 2011. doi: 10.1016/j.bbcr.2011.03.031 [Epub ahead of print].
- Gniuli D, Leccesi L, Guidone C *et al.* Thyroid function and insulin sensitivity before and after bilio-pancreatic diversion. *Obes Surg* 2010; **20**: 61–68.
- Department of Health. Dietary reference values for food energy and nutrients for the United Kingdom. Report of the panel on dietary reference values of the committee on medical aspects of food policy. *Rep Health Soc Subj (Lond)* 1991; **41**: 1–210.
- Andersen S, Iversen F, Terpling S *et al.* More hypothyroidism and less hyperthyroidism with sufficient iodine nutrition compared to mild iodine deficiency – a comparative population-based study of older people. *Maturitas* 2009; **64**: 126–131.
- Laurberg P, Jorgensen T, Perrild H *et al.* The Danish investigation on iodine intake and thyroid disease, DanThyr: status and perspectives. *Eur J Endocrinol* 2006; **155**: 219–228.