

Bariatric surgery and medicines: from first principles to practice

Teresa Girolamo

General practitioner,
Director and Co-Founder,
Re:You, Adelaide

Rosemary Allin

Clinical pharmacist,
Drug and Therapeutics
Information Service
(DATIS), Adelaide

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SUMMARY

Obesity is a major public health issue with significant health and financial costs. Almost one in three Australian adults are living with obesity.

Bariatric surgery can have a role in the management of obesity. There is evidence for its effectiveness in preventing or reversing chronic health conditions.

The type of bariatric surgery can significantly impact the absorption, distribution, metabolism or elimination of orally administered drugs. Some changes can be predicted from pharmacokinetic and physiological effects, but management should be individualised.

The effect of weight loss itself after bariatric surgery may require drug doses to be altered.

A review of the patient's medicines and ongoing follow-up are important before and after surgery to ensure optimal outcomes.

Introduction

Two-thirds of all Australian adults are either overweight (36%) or obese (31%) and the proportion of adults living with obesity is continuing to rise.¹ In 2019 Australia had the sixth highest proportion of overweight or obese people over 15 years old among 22 member countries of the Organisation for Economic Co-operation and Development.² During 2015, overweight and obesity contributed to 8.4% of the total burden of disease and was the leading risk factor contributing to non-fatal burden.²

Given the high disease burden from obesity, bariatric surgery is now more frequently being considered as an effective option for sustaining weight loss in patients with this progressive chronic health condition.^{2–4} When less invasive methods for weight loss have failed, indications for bariatric surgery according to National Health and Medical Research Council criteria are Class III obesity (body mass index (BMI) ≥ 40 kg/m²) or a BMI of at least 35 kg/m² with obesity-related comorbidities.⁵ From 2005–06 to 2014–15, the total number of weight loss operations more than doubled, from about 9300 to 22,700.¹ It is now estimated that over 97,000 procedures are being undertaken each year in Australia.⁶ Given the lifelong follow-up required, GPs will be managing increasing numbers of patients who have had bariatric surgery. This includes considering the effects of surgery on the drugs the patient is taking.

Bariatric operations

Bariatric surgery is the most effective treatment modality for patients living with obesity. It often

results in a significant and sustainable loss of 20–35% of the starting weight.⁷

To manage the implications of bariatric surgery, it is important to understand the different types of operations (see Fig.). Bariatric surgeries are classified as having restrictive or malabsorptive properties, or a combination of both. Restrictive surgeries reduce the volume of food that can be consumed at one time, leading to a reduced total caloric intake. Malabsorptive procedures create a diversion around substantial portions of the digestive tract causing reduced absorption of food and drugs.

In Australia, sleeve gastrectomy is currently the most common bariatric operation, followed by gastric bypass surgery (encompassing Roux-en-Y gastric bypass and one anastomosis gastric bypass). Sleeve gastrectomy is primarily restrictive while both Roux-en-Y and one anastomosis gastric bypass combine restriction with malabsorption.⁸

Laparoscopic adjustable gastric banding is now being performed much less frequently. It is purely a restrictive procedure and problems with drug therapy generally only occur if the band is too tight or a complication has occurred such as band slippage. In these situations it is crucial that the patient is reviewed at a bariatric clinic.

Effect on pharmacokinetics

Despite the number of bariatric surgeries performed, the effects on drugs remain poorly understood and documented. Bariatric surgery can significantly impact the absorption, distribution, metabolism or elimination of orally administered drugs through changes

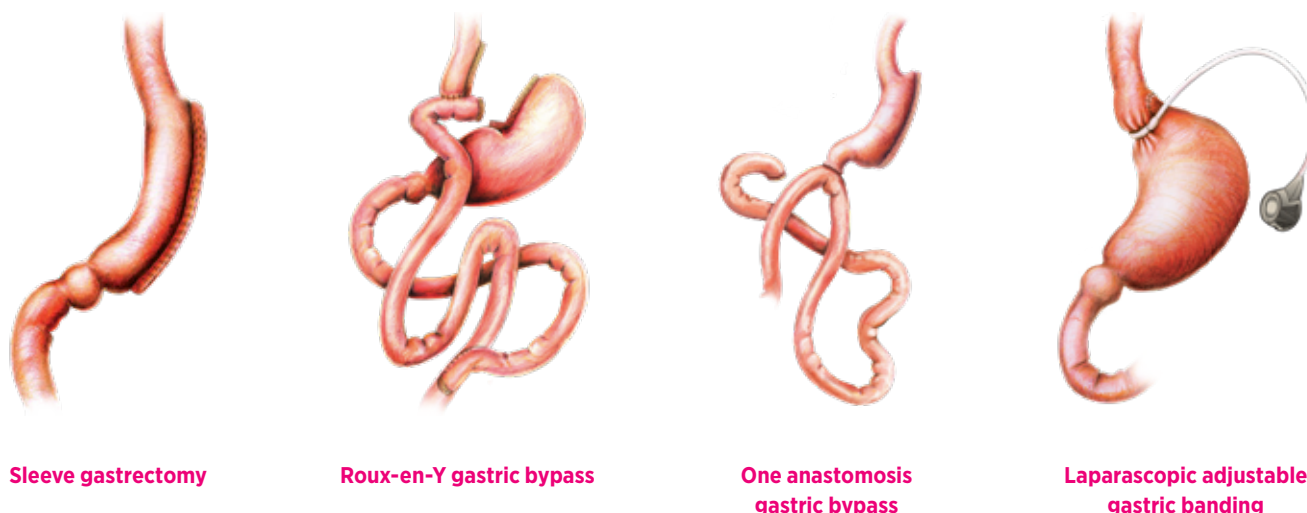
to the anatomy, body weight and adipose tissue composition. Factors that affect the bioavailability of drugs depend on the type of bariatric surgery. These factors include decreased absorptive surface area, reduced exposure to metabolising enzymes and drug transporters in the gut, the rate of gastric emptying and an increased intragastric pH.⁹⁻¹²

Patients undergoing bariatric surgery often have comorbidities requiring multiple drugs. Pharmacotherapy may be complicated not only by physiological or pharmacokinetic changes in absorption and metabolism following surgery, but also by subsequent improvement in weight-related chronic health conditions.

Effect on drug management

By anticipating expected changes to the pharmacokinetics of specific drugs and physiological changes due to the type of surgery, there are general approaches to medicine management that can be implemented (see Box).^{10,13} Strategies to improve drug absorption are not required for all patients and the clinical significance of altered absorption, bioavailability and elimination requires individual assessment, monitoring and close follow-up.^{10,11} There are large inter- and intra-individual variations and the doses of drugs for many chronic conditions may need to be modified as weight loss occurs. Common chronic conditions that may improve with weight

Fig. Common procedures in bariatric surgery



Illustrations supplied by Medtronic

Box General principles for managing drugs after bariatric surgery^{10,13}

- Review the patient's medicines regularly.
- Monitor for decreased efficacy. If efficacy is decreased, consider dose increase, change in formulation or route, or alternative drugs for same indication.
- Monitor for adverse effects and signs of toxicity, which may be a possible result of increased bioavailability.
- Drugs for chronic conditions may need dose reductions, or to be stopped, as obesity-related health conditions improve.
- Be cautious with drugs with a narrow therapeutic index. These will require close monitoring and titration especially following gastric bypass. When possible, monitor serum concentrations and the effects of these drugs e.g. anticoagulants, anticonvulsants, lithium, digoxin.
- Consider staggering the doses of drugs, particularly liquid formulations, due to the reduced capacity of the stomach. Use higher concentration liquid formulations to reduce the volume of each dose.
- Avoid larger tablets (over 10 mm) as they can become stuck and add to the tablet burden. Crush or use alternative formulations.
- Avoid enteric-coated or sustained-release formulations. These products can pass through the altered gastrointestinal tract before absorption is complete and, for some preparations, there is a risk that the inert formulation matrix could accumulate.
- Avoid effervescent formulations.
- Avoid drugs that potentially damage gut mucosa e.g. non-steroidal anti-inflammatory drugs, aspirin and bisphosphonates.
- After gastric bypass, avoid products (including over-the-counter products) that contain a large amount of sucrose, corn syrup, lactose, maltose, fructose, honey or mannitol, as they can result in dumping syndrome.
- Be aware of drugs that may contribute to weight gain.

Table Effects of bariatric surgery on commonly prescribed drugs

Drugs	Potential effects of bariatric surgery	Comments/management
Antihypertensives	Doses will often need to be reduced or stopped quite soon after surgery, and sometimes even in the preoperative (VLED) phase.	Monitor blood pressure and enquire about symptoms of postural hypotension. Continued surveillance of blood pressure is needed after surgery because of the high risk of recurrence over time. Beware of diuretics and dehydration in the early postoperative phase.
Drugs for diabetes	Requirements for insulin and other antidiabetic drugs change rapidly in the preoperative (VLED) and early postoperative phase.	Monitor blood glucose and adjust doses on a case-by-case basis. Care with insulin or antidiabetic drugs that increase the risk of hypoglycaemia (e.g. sulphonylureas) Metformin to be changed to immediate-release preparation.
Lipid-modifying	Overall, the effects of weight loss on lipids are variable and incomplete.	Monitor lipids and absolute cardiovascular risk. Adjust doses on a case-by-case basis.
Antidepressants (e.g. SSRIs, SNRIs, tricyclics)	Small studies suggest that the bioavailability of antidepressants may be reduced after gastric bypass, particularly in the first six months after surgery. Serum concentrations of SSRIs returned to baseline in 50% of cases after 12 months in one small study, suggesting adaptation to effects may occur over time. In a significant portion of patients, depression may improve as a result of weight loss.	Monitor patients closely for signs of withdrawal or reduced efficacy. Doses may need to be increased or may require a change in formulation (e.g. to immediate release or liquid), particularly in the first six months following bypass surgery.
Antipsychotics/mood stabilisers	There may be impaired absorption of antipsychotics. Lithium concentrations are influenced by the volume of distribution and may become toxic after bariatric surgery.	Monitor for decreased efficacy or signs of toxicity and adjust the dose accordingly.
Thyroxine	Absorption of thyroxine may be reduced after bariatric surgery, however weight loss may result in improvement of hypothyroidism (and hence a decrease in dose). Observational studies suggest most patients will need either no change or a reduction in thyroxine doses. In some patients (particularly those with autoimmune thyroiditis), thyroxine dose requirements may increase.	Periodically monitor thyroid function and adjust doses on a case-by-case basis. There is no need for preventive adjustment of thyroxine doses.
Analgesics	Reduction in absorption of opioids and slow-release analgesic preparations. Less need for analgesia with ongoing weight loss.	Monitor for opioid withdrawal. Monitor for improvement in painful conditions. Immediate-release or non-oral preparations are preferable. Avoid non-steroidal anti-inflammatory drugs.

SNRI serotonin and noradrenaline reuptake inhibitor

SSRI selective serotonin reuptake inhibitor

VLED very low energy diet

Source: adapted with permission from reference 14

loss include hypertension, diabetes and pain from osteoarthritis (see Table).¹⁴

Frequent reviews of medicine management tailored to the individual patient and treatment targets are required. Regular communication between the patient's bariatric clinic, their usual GP and any relevant treating specialists is crucial with regards to any medicine changes. Pharmacists play an important role,^{11,12} contributing as a member of the clinical team through the provision of a range of services including comprehensive medication reviews, which are very useful both in preparation for bariatric surgery and postoperatively.

Alcohol

The effect of alcohol may increase following surgery due to altered alcohol metabolism. Gastric bypass surgery is associated with:

- accelerated alcohol absorption
- higher maximum alcohol concentration
- longer time to eliminate alcohol
- increased risk of alcohol use disorder.

The increased risk of alcohol misuse after surgery could be due to addiction transference. Alcohol (or other substances) may be substituted for food as a coping mechanism.¹⁵⁻¹⁷

Contraception

Oral contraceptives may not be reliable after bariatric surgery. This is due to lower absorption and bioavailability after gastric bypass and concerns about effectiveness following all types of bariatric surgery.^{4,9} Alternative contraceptive methods should be considered, in particular long-acting reversible contraception.

It is important that women avoid pregnancy for at least 12–18 months following bariatric surgery. Fertility can improve dramatically after weight loss, especially in women with polycystic ovary syndrome, therefore effective contraception becomes even more important.^{3,4}

Nutrition

Following bariatric surgery, lifelong vitamin and mineral supplements are required, tailored to each patient's needs. These may include multivitamins, calcium, vitamin D, iron and vitamin B₁₂. Routine supplementation does not ensure an absolute prevention of deficiencies over time, mainly because of individual variations in micronutrient absorption, nutritional requirements, the type of bariatric surgery and adherence to therapy. Periodic laboratory surveillance for nutritional deficiencies is recommended and supplementation should be individualised accordingly.⁴ Given all this, it is crucial that a bariatric-trained dietitian is part of the management team.

Conclusion

Bariatric surgery may alter the pharmacokinetics of orally administered drugs because of physiological and anatomical changes to the gastrointestinal tract, reduced body weight and altered adipose tissue composition. The impact on drugs depends on the type of bariatric surgery. There is limited evidence to guide practice in an area where GPs will be increasingly required to have some knowledge and practical skill. A multidisciplinary approach with regular review of medicines and close monitoring is required. ◀

Conflicts of interest: none declared

REFERENCES

1. Australian Institute of Health and Welfare. Overweight & obesity. Overview. Canberra: AIHW; 2020. <https://www.aihw.gov.au/reports-data/behaviours-risk-factors/overweight-obesity/overview> [cited 2022 Sep 1]
2. Australian Institute of Health and Welfare. Australian burden of disease study 2015: interactive data on risk factor burden. Canberra: AIHW; 2020. <https://www.aihw.gov.au/reports/burden-of-disease/interactive-data-risk-factor-burden/contents/overweight-and-obesity> [cited 2022 Sep 1]
3. Mechanick JI, Apovian C, Brethauer S, Timothy Garvey W, Joffe AM, Kim J, et al. Clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures – 2019 update: cosponsored by American Association of Clinical Endocrinologists/American College of Endocrinology, The Obesity Society, American Society for Metabolic and Bariatric Surgery, Obesity Medicine Association, and American Society of Anesthesiologists. *Obesity (Silver Spring)* 2020;28:1-58. <https://doi.org/10.1002/oby.22719>
4. Busetto L, Dicker D, Azran C, Batterham RL, Farpour-Lambert N, Fried M, et al. Obesity Management Task Force of the European Association for the Study of Obesity released "Practical recommendations for the post-bariatric surgery medical management". *Obes Surg* 2018;28:2117-21. <https://doi.org/10.1007/s11695-018-3283-z>
5. National Health and Medical Research Council. Clinical practice guidelines for the management of overweight and obesity in adults, adolescents and children in Australia. Melbourne: NHMRC; 2013. <https://www.nhmrc.gov.au/about-us/publications/clinical-practice-guidelines-management-overweight-and-obesity> [cited 2022 Sep 1]
6. Bariatric surgery registry. 2019/2020 Annual Report. Melbourne: Monash University; 2021. <https://www.monash.edu/medicine/sphpm/registries/bariatric/reports-publications> [cited 2022 Sep 1]
7. Sjöström L. Review of the key results from the Swedish Obese Subjects (SOS) trial – a prospective controlled intervention study of bariatric surgery. *J Intern Med* 2013;273:219-34. <https://doi.org/10.1111/joim.12012>
8. Australian Institute of Health and Welfare. Weight loss surgery in Australia 2014-2015: Australian hospital statistics. www.aihw.gov.au/reports/overweight-obesity/ahs-2014-15-weight-loss-surgery/contents/table-of-contents [cited 2022 Sep 1]
9. Kingma JS, Burgers DM, Montpellier VM, Wiezer MJ, Blussé van Oud-Alblas HJ, Vaughns JD, et al. Oral drug dosing following bariatric surgery: General concepts and specific dosing advice. *Br J Clin Pharmacol* 2021;87:456-76. <https://doi.org/10.1111/bcp.14913>

10. Lorico S, Colton B. Medication management and pharmacokinetic changes after bariatric surgery. *Can Fam Physician* 2020;66:409-16.
11. Porat D, Dahan A. Medication management after bariatric surgery: providing optimal patient care. *J Clin Med* 2020;9:1511. <https://doi.org/10.3390/jcm9051511>
12. Pollock A, Petrick AT, Gadaleta D. Raising the standard: The role of the clinical pharmacist in the care of the bariatric surgery patient. *Bariatric Times* 2021;18:16-7. <https://bariatrictimes.com/role-pharmacist-care-bariatric-patient> [cited 2022 Sep 1]
13. Bariatric surgery patients and their medicines. *NHS PrescQIPP* 2014;54:1-7. <https://www.prescqipp.info/umbraco/surface/authorisedmediasurface/index?url=%2fmedia%2f1099%2fb54-bariatric-surgery-patients-and-their-medicines-20.pdf> [cited 2022 Sep 1]
14. Rothmore J. Medications after bariatric surgery. In: *DATIS frequently asked questions February 2019*. Adelaide: Drug and Therapeutics Information Service; 2019.
15. Wee CC, Mukamal KJ, Huskey KW, Davis RB, Colten ME, Bolcic-Jankovic D, et al. High-risk alcohol use after weight loss surgery. *Surg Obes Relat Dis* 2014;10:508-13. <https://doi.org/10.1016/j.soard.2013.12.014>
16. Parikh M, Johnson JM, Ballem N; American Society for Metabolic and Bariatric Surgery Clinical Issues Committee. ASMBS position statement on alcohol use before and after bariatric surgery. *Surg Obes Relat Dis* 2016;12:225-30. <https://doi.org/10.1016/j.soard.2015.10.085>
17. Heinberg LJ, Ashton K, Coughlin J. Alcohol and bariatric surgery: review and suggested recommendations for assessment and management. *Surg Obes Relat Dis* 2012;8:357-63. <https://doi.org/10.1016/j.soard.2012.01.016>