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REVIEW

Surgical Mouse Models of Vertical Sleeve Gastrectomy and Roux-en Y Gastric Bypass: a Review

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Abstract

Reviewed here are multiple mouse models of vertical sleeve gastrectomy (VSG) and Roux-en Y gastric bypass (RYGB) that have emerged over the past decade. These models use diverse approaches to both operative and perioperative procedures. Scrutinizing the benefits and pitfalls of each surgical model and what to expect in terms of post-operative outcomes will enhance our assessment of studies using mouse models, as well as advance our understanding of their translational potential. Two mouse models of bariatric surgery, VSG-lembert and RYGB-small pouch, demonstrate low mortality and most closely recapitulate the human forms of surgery. The use of liquid diets can be minimized, and in mice, RYGB demonstrates more reliable and longer lasting effects on weight loss compared to that of VSG.

Keywords Bariatric surgery · Technique · RYGB · VSG · Rodent

Introduction

The effectiveness of bariatric surgery may be difficult to ascertain clinically, as confounding factors like diet, physical activity, and behavior may impact results. In mouse models, these factors are much easier to control and measure. However, variations seen in surgical technique [1–15], perioperative diet administration, and weight related outcomes, as well as lack of data on anemia and mortality make data from mouse studies difficult to assess. Admittedly, an equivalent translation of surgical care and technique from humans to mice is challenging, but current conceptions about mouse models of bariatric surgery could be improved upon and made more consistent between laboratories. Other reviews addressing the translational challenges of using mouse models of bariatric surgery exist [9, 16, 17], but here, it seems relevant to evaluate current mouse models of vertical sleeve gastrectomy (VSG) and Roux-en Y gastric bypass (RYGB).

Methods

Seventy-three articles using mouse models of bariatric surgery published between years 2011 and 2018 [1–16, 18–74] were reviewed (Fig. 1). Some of these articles included models of both VSG and RYGB and so have been considered separately, making the total 82 (VSG = 42 and RYGB = 40). Collecting data from each article was performed via manual review as well as partially automated word searches. For the partially automated word searches, specific text-string searches, such as "mort-," "anem-," and "surv-," using the search tools already programmed into applications such as Adobe Reader or web browsers like Chrome or Internet Explorer, were performed to augment the data collected by manual review. Additionally, estimations of certain data (i.e., final body weight, return to preoperative weight, nadir of weight loss) were sometimes extrapolated from graphs when no other

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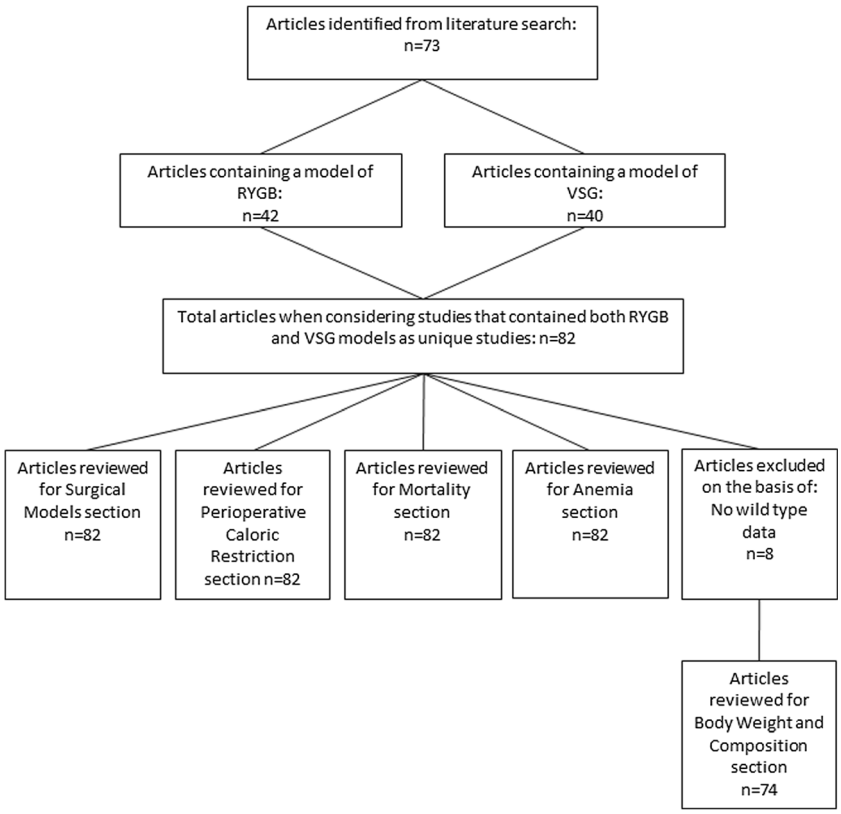

Fig. 1 Literature review flowchart

source was available. As such, report of this information was limited to percentages and ranges and in only a handful of cases resulted in the formulation of a mean.

In order to make the large amount of material extracted from the 82 articles more manageable, the review has been subdivided into the following sections: "Surgical Models," "Perioperative Caloric Restriction," "Mortality," "Anemia," and "Body Weight and Composition." The methods, already having been described above, are not described again in each section.

Lastly, even though studies have looked to identify ideal mouse strains for obesity, there remains no consensus [8, 75]. However, in 88% of the studies reviewed here, diet-induced obese (DIO) models of the C57BL/6 strain were used and so the impact of strain on this review should be nominal.

Surgical Models

Adapting human bariatric surgical techniques to mice is challenging. In humans, the creation of a tubular stomach via a multi-staple approach is commonly utilized for VSG, and for RYGB, intestinal bypass along with the creation of a gastric pouch of reduced volume are the primary gastrointestinal alterations. In mice, similar surgical procedures are more difficult and multiple models have emerged to deal with the mouse microanatomy.

There are four predominant models of mouse vertical sleeve gastrectomy: VSG-stapler [12], VSG-clip [11, 13], VSG-single layer [3, 4], and VSG-lembert [5, 14]. VSG-stapler (Fig. 2b) uses a human surgical stapler to transect 80% of the stomach and to construct the sleeve, a methodology likely adopted from rat bariatric models [12]. For VSG-clip (Fig. 2c), one or two titanium hemostatic clips are applied parallel to the smaller curvature, the stomach distal to the clip excised, and the clip then sutured in place. The final two VSG models, VSG-single layer (Fig. 2d) and VSG-lembert (Fig. 2e), both excise approximately 80% of the stomach, cutting parallel to the smaller curvature and use suturing techniques to construct the sleeve. For VSG-single layer, the sleeve is constructed via continuous or interrupted sutures, and for VSG-lembert, a row of full thickness, interrupted sutures is followed by a row of lembert sutures (performed by invaginating the first sutured layer).

Current RYGB mouse models can be divided into three models: RYGB-small pouch [1, 2], RYGB-fundus [4, 15], and RYGB-esophagus [4]. In all three, either an end-to-end or end-to-side anastomosis for the jejuno-jejunostomy is commonly utilized. The notable difference amongst them is the way in which the new stomach pouch is formed. For RYGB-small pouch (Fig. 3b), a new gastric pouch is created by dividing the stomach approximately 3 mm aboral to the esophageal junction just below the cardia, forming a stomach pouch that is approximately 3–5% of its original volume. In the

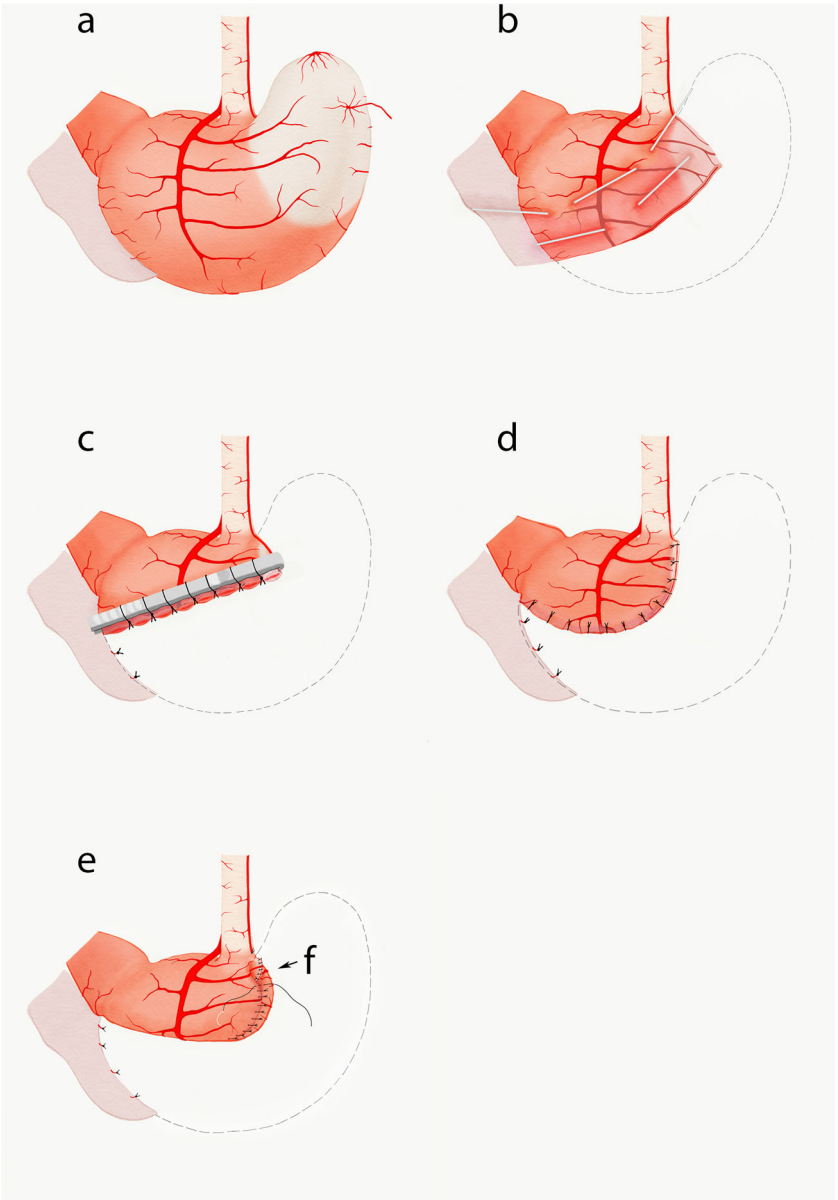

Fig. 2 Illustrations of mouse stomach anatomy and VSG mouse models of surgery. **a** Unmodified stomach. **b** VSG-stapler. **c** VSG-clip. **d** VSG-single layer. **e** VSG-lembert. **f** Unfinished portion of VSG-lembert to illustrate tissue invagination. The dashed line in **b**–**e** represents the portion of stomach that has been excised

RYGB-fundus model (Fig. 3c), the pouch is constructed using a vascular clip or ligation across the white ridge that divides the gastric corpus from the forestomach, resulting in a stomach pouch of 15–30% of its original volume. And in the last model, RYGB-esophagus (Fig. 3d), the stomach is completely excluded and no stomach pouch is constructed. This is accomplished by ligating the stomach above the cardia and then performing an esophago-jejunostomy.

Diagrammatically, the mouse models for VSG and RYGB seem to result in similar constructions: a "sleeve" in the case of VSG, and for RYGB, reduced stomach volume combined with intestinal bypass. However, the applied results of each model may represent diverging paths.

Though the stapler is used on humans, using it on a mouse stomach without altering the instrumentation/staple size is a questionable practice. In VSG-stapler, the application of the stapler on a mouse stomach results in approximately 1–2 rows of staples (2–3 staples per row) to construct *and* close the sleeve. Two factors make the use of the stapler especially problematic: the closed height of the staple (1 mm) and the distance between staples (1 mm). The average thickness of the mouse gastric corpus is 0.4 mm [76], making the closed height of the staple 0.2 mm larger than the two layers of mouse gastric corpus. Likewise, the distance between the rows of staples is enough to provide sufficient spacing for liquids or small food particles to pass between the staples. As such, it is reasonable to expect increased post-operative leakage with comorbid complications of infection, adhesions, abscess, and reduced peristalsis.

In the case of the VSG-clip model, a well-functioning stomach in peristaltic terms is uncertain. Not only has the

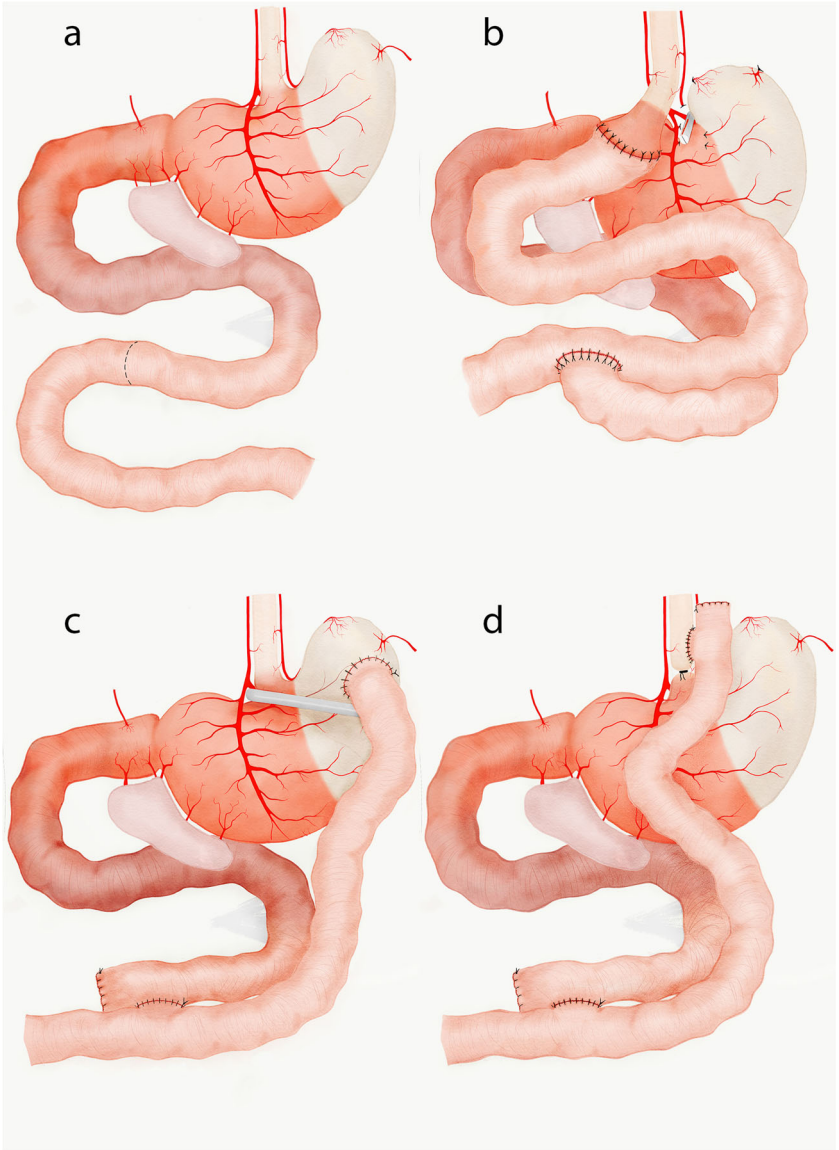

Fig. 3 Illustrations of mouse stomach and intestinal anatomy and RYGB mouse models of surgery. **a** Unmodified stomach, duodenum, and proximal jejunum. **b** RYGB-small pouch. **c** RYGB-fundus. **d** RYGB-esophagus. The dashed line in **a** represents the approximate location for the division of what will become the end of the biliopancreatic limb and the start of the Roux limb

stomach been immobilized along its lengthiest dimension but it also has been permanently distorted in such a fashion that is likely to impede normal peristalsis.

VSG-single layer is closer to the human version of the surgery than the previous two models, but as pointed out above, the gastric corpus has a thickness of approximately 0.4 mm and the difficulty of properly aligning and suturing the stomach layers could be difficult.

Similarly, for the VSG-lembert model, the skill required to invaginate the full thickness of the sutured layers of the stomach (Fig. 2f) as an additional step is difficult at this scale. However, by invaginating the first suture layer, the integrity of the gastric lumen is preserved by enveloping it within the serosa of the stomach (Figure 2f). This should reduce the probability of leakage and the comorbid complications likely seen without this multi-layered approach.

RYGB-small pouch is the most similar to the human version of RYGB, but the surgical skill required is particularly high. Performing a gastro-jejunostomy and jejuno-jejunostomy in a mouse, whose intestinal diameter is approximately 2–3 mm, is especially difficult and time consuming at this small size (16–20 interrupted stitches are recommended for both). Manipulating the new stomach pouch/esophagus while performing the gastro-jejunostomy also presents technical challenges, as special care is required to prevent inadvertent damage to the vagus nerves. Additionally, working with 11-0 sutures also provides challenges to those unfamiliar with microsurgical practices.

RYGB-fundus, like the VSG-clip model, has similar post-operative problems of obstruction related to the immobi lization of the newly formed stomach pouch. Yin et al. noted in 2011, “the forestomach of the mouse lacks sufficient mus cle to push nutrients through the anastomosis in an RYGB [-

fundus] procedure" [16]. Even after the mouse has fully healed from the surgery, there still exists a high risk of obstruction in the new stomach pouch. Furthermore, the newly created stomach pouch, at 15–30% of the original volume, is also much larger than the human version of RYGB.

RYGB-esophagus represents the furthest diversion from the human model as no stomach pouch is formed or created, and the esophageal sphincter is bypassed. Bypassing the esophageal sphincter may have unintended effects such as regurgitation, reflux, or reduced food intake. Additionally, performing an esophago-jejunostomy on the right side of the esophagus increases the risk of right vagus nerve injury. Mortality rates may be lower in this model, but the dissimilarity to the human form of RYGB, increased risk of right vagus nerve injury, and the introduction of a new variable like reflux make it problematic.

A suitable model should be evaluated not by the ease or simplicity of the technique it requires, but by how closely it resembles the human form of the surgery and a demonstrably low incidence of post-operative complication.

VSG-stapler, VSG-clip, VSG-single layer, and RYGB-fundus all have post-operative complications that come in the form of obstructions occurring in the stomach pouch/sleeve, suppressed peristalsis, infection, abscess, and leakage. Even in the context of a well-executed operation (with perhaps the exception of the VSG-single layer model), these same problems still have a strong chance of occurring.

Alternatively, VSG-lembert and especially RYGB-small pouch both seem to fulfill the criteria of a suitable model. These models are likely to have little-to-no long-term adverse effects on mechanical and muscular peristalsis *and* most closely resemble the human forms of VSG and RYGB. Additionally, RYGB-small pouch as devised by Hao et al. is one of the only RYGB models successfully employed for repeated use [1, 14, 24, 25, 27, 29, 30, 36, 37, 39, 47], albeit the majority coming from a single laboratory. And though Hao et al.'s VSG-lembert model has only been used in two studies [10, 14], it should be given serious consideration given their success in developing a robust model of RYGB.

Perioperative Caloric Restriction

Early bariatric rodent surgery protocols emulated the clinical practice of administering a liquid diet in order to ensure the adequate emptying of the gastrointestinal tract pre-operatively and post-operatively, as well as to allow time for tissue healing. As touched upon in the previous section, this trend has continued with current bariatric murine surgical protocols.

Sixty-six percent of all the studies reviewed here used liquid diets (see Table 1 for division by surgical model). Liquid diets are consumed by the mice from 1 to 14 days, with a mean of 7 ± 4 days [2, 3, 5–10, 12–15, 18–23, 28, 32–35, 38, 42–46, 49–60, 62–65, 70–72, 74]. During this same period, when liquid diet is being administered, as much as 48 h of fasting can occur perioperatively. A review of weight related data will be discussed in another section, but when contemplating the impact of perioperative caloric restriction, it is worth noting here that in 91% of RYGB and VSG mouse studies, at least 50% of the total weight loss occurs inside the first 7 days [1–8, 12–14, 18–20, 22, 25, 28, 31, 32, 34, 36–38, 40–44, 47, 49–51, 53–56, 58, 59, 64–67, 69–72, 74], with the remaining studies reaching the 50% weight loss point by 14 days after surgery [18, 21, 24, 27, 29]. Additionally, the nadir of weight loss has a mean of 16 ± 9 days for RYGB and is even shorter for VSG at 10 ± 5 days.

Even though a large portion of the studies reviewed here do use liquid diets, in the RYGB-small pouch and VSG-lembert models devised by Hao et al., no liquid diet is required [1, 14]. Both models allow ad libitum access to normal chow 24 h post-operatively, followed by a return to the study diet (i.e., HFD, normal chow, choice diet) on post-operative day 3.

Since the weight loss attributed to the effects of caloric restriction in VSG and RYGB in mice overlaps with other metabolic alterations impacting weight, and because the time course of weight loss in mice is very short, minimizing the length of caloric restriction/liquid diet may be imperative for elucidating early changes after bariatric surgery, especially those linked to energy and weight homeostasis. As highlighted above, both the VSG-lembert and RYGB-small pouch models developed by Hao et al. require no liquid diet, making them ideal in regard to limiting the effects of reduced caloric intake.

Mortality

In mice, defining the underlying cause of mortality is fraught with difficulty as accurate measures of illness in mice are lacking. Furthermore, death may occur at variable times post-operatively, and assessment at the time of death is difficult. Like anemia, discussion of mortality is often omitted in papers, but this is an important area to address as it enables the development of more precise surgical models.

In the 82 studies reviewed here, mortality rates were *reported* 38% of the time for VSG and 50% for RYGB. Amongst those who did report, mortality rates were 17% for VSG and 29% for RYGB. Unfortunately, given the low report rates, as well as an unequal distribution of report between the models, assessments of the superiority of one surgical model over another using information on mortality are difficult (see Table 1).

Nevertheless, VSG-lembert and RYGB-small pouch do demonstrate the lowest mortality. In particular, Hao et al.'s model of RYGB-small pouch has an average mortality of 3% [1, 24–27, 36, 37]. And in general, the RYGB-small pouch

Table 1 Mortality outcomes based upon surgical technique

	No. of studies	% Using liquid diets	No. of studies reporting mortality	% Mortality
VSG-				
Stapler	14	79	2	43
Clip	5	80	3	10
Single layer	14	86	7	9
Lembert	4	75	3	7
Unable to determine VSG model*	5	40	1	78
RYGB-				
Small pouch	19	37	12	17
Fundus	18	89	7	52
Esophagus	2	NA	1	20
Unable to determine RYGB model*	1	NA	0	NA

*In the case of these five VSG models, it was most often that there was insufficient information to determine whether the model was VSG-single layer or VSG-stapler. For the RYGB model, information on surgical model was not provided

model shows both the highest frequency of use and the highest level of report on mortality. However, the technical difficulty of the RYGB-small pouch model is highlighted by He et al. (2018) who, utilizing the RYGB-small pouch model devised by Hao et al., noted that even for an "experienced surgeon" 4 years of practice was required to reduce mortality from 81 to 22% [29].

Mortality is an important measure in animal models, but does not singularly define success. In other words, mortality, high or low, should be considered only in combination with all other factors from a study. Despite both RYGB-small pouch and VSG-lembert models having surgical challenges, low mortality rates (as well as those points highlighted in the previous sections) make these two the most suitable models of bariatric surgery for serious study but are likely to require a considerable investment of time and effort.

Anemia

Proximity of death to surgical intervention often implies an operative or post-operative complication, such as obstruction or infection. Further time from the surgery may imply a physiologic or metabolic alteration that becomes lethally exaggerated. One metabolic complication that has been observed as a common clinical observation after RYGB is anemia [77–81]. Anemia remains an area under-explored but is an important dimension of RYGB that should be examined further as iron homeostasis has emerging links to diabetes [82–85], obesity [86], bone homeostasis [87], brown and white adipose tissue [88–93], adiponectin [94], insulin sensitivity/resistance [95], beta cell function [96], energy homeostasis [97], and non-alcoholic fatty liver disease (NAFLD) [95], all of which overlap well with points of interest regarding bariatric surgery.

Anemia is not well documented in mouse models of bariatric surgery [4, 7, 16, 28, 29, 40], and so, the approaches for addressing anemia amongst those performing mouse RYGB are scarce. Additionally, the information currently available in the sources reviewed here is inconsistent. However, given its evolving connections with bariatric outcomes, it seems useful to cover the current data on anemia in mouse models of bariatric surgery, discuss possible explanations for the inconsistencies, and highlight the importance of report.

Yin et al. [4] measured hematocrit levels in mice 4 weeks post-operatively and found RYGB mice at 22% with comparative lean controls at 50%. In another study, they suggest that "mice undergoing foregut bypass that do not receive iron supplementation will die 8-16 weeks post-operatively due to iron deficient anemia" [16]. More recently, He et al. (2018) conducted a study using RYGB and reported anemia at 30% [29]. Not surprisingly, some studies using mouse RYGB recommend iron supplementation in the form of daily [7] or bi-weekly [16] injections of iron dextran. However, the majority of RYGB studies do not mention anemia or iron supplementation at all [1–3, 9, 14–16, 18–27, 30–47].

The severity of iron deficiency will depend on the length of the biliopancreatic limb and the accuracy of its measurement during surgery as most iron transporters are located in the duodenum and proximal jejunum. The mouse intestines are very elastic, and any minor measurement error of intestinal limbs could make differences in post-RYGB iron absorption. Diet too may impact iron deficiency post-operatively. Mice consume a higher volume of normal chow to that of high fat diet (HFD), approximately 3 to 1. We might expect those researchers using only HFD diet post-operatively to find an

increased incidence of iron deficiency. Other factors, like preoperative blood loss, the number of post-operative tests requiring blood sampling, the length of the study, and surgical expertise could also play a role in the severity of iron deficiency observed.

Like mortality, the lack of information regarding anemia could be explained by lack of report. However, emerging connections to the outcomes of RYGB make anemia and its treatment or lack, thereof, an aspect of mouse research that should be consistently documented when utilizing RYGB in mouse studies.

Body Weight and Composition

There is a twofold purpose in addressing body weight and composition in this review. First, after bariatric surgery, body composition is a reliable, non-invasive measure of change. The effects of surgical model on body weight and composition will likely be subtle, as mortality will already have played a role in eliminating much of the problematic data. However, points already made in the surgical models section concerning model-specific, long-term effects on peristalsis (i.e., infections, adhesions, abscesses, application/position of a clip) should be considered when evaluating body weight and composition as they have the potential to influence the stability, reliability, and range of the data. The second reason for including body weight and composition changes in this review is because there seems to be an ongoing debate about which bariatric surgery achieves superior weight loss, RYGB, or VSG. Clinically, there remains support for the benefit of both [98], but in this review of mouse models of bariatric surgery, the answers to this debate seem clearer.

VSG

Mice receiving VSG surgery return to preoperative weight in nearly 50% of the VSG studies in this review. A post-operative return to preoperative weight occurs anywhere from 3 to 16 weeks [4, 8, 9, 11, 14, 21, 49, 50, 53, 55, 60, 63–67, 70, 71, 74], with an average of 7 weeks to reach preoperative weight. It is important to point out that approximately 25% of the VSG studies reviewed here had limited information on weight change [3, 5, 7, 16, 18, 52, 57, 70, 74]. Of the remaining 25% of the studies, whose results did not indicate a return to preoperative weight, only four were as long as 8 weeks.

One might expect a degree of variability to occur in the return to preoperative weight by the inclusion of diverse surgical models and perioperative protocols. However, even if one reviews the case of VSG weight data within a single laboratory wherein it is more likely the same surgical model and perioperative protocols were used, there are still very different effects on the time it takes for return to preoperative weight. For example, in 9 studies, using the VSG-stapler model [49, 50, 53, 65–67, 70, 71, 74] return to preoperative weight was anywhere between 5 and 16 weeks.

Of the 20 VSG studies documenting changes to body composition, most studies found changes after VSG are the result of reductions to fat mass [12–14, 49, 50, 53, 57, 64–67, 71, 74] with no change to lean mass [4, 12, 49, 65, 66, 74]. Only one study showed no significant change in fat mass [59] and one a reduction to lean mass [14].

RYGB

There have been studies collecting weight data for as long as 39 weeks [27], and a return to preoperative weight has never been observed in any DIO mouse models utilizing RYGB [1, 3, 4, 6, 7, 9, 14, 15, 18–22, 24, 27–29, 31, 34, 36–38, 40–45, 47]. Even with continued HFD diet intake (nearly half of the RYGB studies reviewed here), mice did not return to preoperative weight [1, 3, 4, 15, 19–22, 27, 29, 31–34, 38, 40, 42, 44, 45]. The only time in which a return to preoperative weight has been observed is when non-obese mouse models were used [2, 26, 30].

For studies at least 8 weeks in duration, the final percent weight loss was an average of 25% [1, 4, 6, 14, 15, 19, 21, 24, 25, 27, 31, 32, 36, 44, 47]. In a 2016 study, Hao et al. demonstrated that weight loss (or lean mass gain in the case of a lean starting weight) was relative to pre-surgical adiposity and that final weight bottle-necked to an average of approximately 32.5 g [26]. In 26 of the RYGB studies examined in this review whose results included final weight information [1, 3, 7, 14, 15, 18–21, 24–29, 31, 33, 34, 36, 40–45, 47], final weight was examined and the mean was approximately 32 ± 4 g, nearly identical to Hao et. al.'s 2016 study.

Of the 21 studies of RYGB [1, 3, 4, 14, 15, 19, 22, 25, 31, 33–36, 38, 40–43, 45, 47] in which fat mass changes were recorded, all but one [28] found a significant reduction in fat mass. The results concerning lean mass are less clear: 9 showed no change [1, 3, 4, 15, 25, 28, 31, 42, 47], 7 showed decreased amounts [14, 19, 34–36, 41, 45], and even one, using a DIO model, showed an increase in lean mass [40].

RYGB vs VSG

It is evident that RYGB and VSG are both potent procedures in which significant reductions to adiposity can be achieved. However, the effects of RYGB, unlike VSG, demonstrate durable, long-term effects on weight loss in mice. Even between different laboratories using different surgical models, administering either normal or HFD, sustained and consistent alterations to body weight can be expected. However, as discussed above in the section on anemia, RYGB is often linked with several nutritional complications post-operatively, such as vitamin B12 and D deficiencies [99]. It is possible that changes

seen in lean mass, like the increased risk of anemia and bone mass loss [44], may also depend on nutritional malabsorption. There are also suggestions that changes in lean mass may be related to alterations in energy expenditure [100]. Nevertheless, these lean mass alterations indicate a difference between the outcomes of VSG and RYGB and should be examined further.

The data from VSG studies oblige us to consider that in terms of sustained weight loss, other factors such as caloric restriction, dietary weight loss, or surgical model might play a greater role than previously assumed and may explain some of the variability seen in mouse studies. As has been pointed out above, choice of surgical model may impact outcomes, and so extreme variance in weight related outcomes from study to study might represent some of the first clues in revealing why a particular surgical model is or is not suited for study. Body weight remains a critical marker of overall health and expectations of consistent and dependable changes in body weight after VSG should be established.

Studies having found that VSG mice are the same weight or heavier than controls often go on to highlight some of the weight-independent effects observed after VSG on hepatic insulin sensitivity [48], hepatic inflammation [55, 66], bile acid synthesis [66], lipid metabolism [55], and endoplasmic reticular stress [64], as well as one study finding that post-VSG, mice show a preference for HFD [14]. These studies suggest that VSG can have beneficial, perhaps weight-independent effects and these lines of inquiry should be pursued further, but with the understanding that complete weight regain is a possibility.

Discussion

Automated data collection methods, such as creating simple computer programs to perform keyword and text-string searches, can be employed to decrease the human error inevitably involved in a manual search without turning into meta-analysis. To increase the accuracy of our conclusions, more automated methods of data acquisition could have been used. Additionally, the authors have experience performing VSG-lembert, VSG-stapler, RYGB-fundus, and RYGB-small pouch models but little experience with VSG-single layer, VSG-clip, and RYGB-esophagus. This review, as well as the illustrations, would have been enhanced through first-hand experience performing and troubleshooting all of the reviewed models. Lastly, when information of interest was not found in an article, the original authors could have been solicited for additional information.

Selecting an appropriate surgical model of mouse RYGB or VSG is complicated by two major factors: execution and translation. Replicating the anatomical alterations of the human surgery is important, but difficult due to the microanatomy of the mouse. Though the difficulty of performing bariatric surgery on mice will always remain high, methods attempting to circumvent surgical struggles by employing less than ideal models should be avoided, while those best replicating the human form of the surgery should be promoted. VSG-lembert and RYGB-small pouch mouse models of bariatric surgery, particularly those developed by Hao et al. [1, 14], are closest to the human forms of surgery. They are demonstrably robust in terms of weight outcomes and have low mortality rates. Additionally, to prevent inadvertent or undesirable effects on weight and metabolic changes after surgery, protocols that minimize the use of liquid diet should be favored. Again, through repeated demonstration, it is particularly those models of VSG-lembert and RYGB-small pouch developed by Hao et al. establishing that caloric restriction can be mitigated and liquid diet avoided altogether so that more immediate gastrointestinal alterations can be examined more accurately.

Unreasonable or unnecessary deviations from the human form of VSG and RYGB surgeries should be examined closely as the translation of outcomes depends on how well the human to mouse relationship is maintained. So, while it seems evident that for studies using RYGB and VSG in mice that RYGB is superior in terms of lasting transformations to body weight homeostasis, it is not clear whether this holds true for humans. In other words, it is not clear whether these results demonstrate a fundamental difference between mice and humans in their response to bariatric surgery or if this is a consequence of the increased control researchers can exert when performing mouse studies.

The answers to this and other questions regarding the translational potential of mouse bariatric studies would be best framed in standardized surgical models of VSG and RYGB. Furthermore, it is important that information concerning all aspects of the surgical protocols (i.e., perioperative caloric restriction, anemia, mortality) as well as basic data on weight and body composition be consistently reported. For example, as initial studies are uncovering how gut microbiota and antibiotic use may impact weight and metabolic changes after bariatric surgery [59, 72], the use of antibiotics in mouse studies should also be examined and more generally reported (only 13% of studies reviewed here reported antibiotic administration). By favoring full disclosure, more consistent results can be achieved between laboratories and more accurate predictions made concerning the overlap of outcomes between humans and mice after bariatric surgery.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval Statement For this type of study, formal consent is not required.

Informed Consent Statement Does not apply

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