OXFORD

Precision Clinical Medicine, 2023, **6**: pbad032

DOI: 10.1093/pcmedi/pbad032

CORRESPONDENCE

PBS: a prospective longitudinal multi-omics bariatric surgery cohort

Yuwen Jiao,[1] Jiaming Xue,[1] Shuai Chen,[1] Wei Sun ,[2] PBS Cohort Study, Xiangqing Kong,[2,*] Lianmin Chen ,[1,2,*] Liming Tang[1,*]

[1]Department of Gastrointestinal Surgery, The Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University, Changzhou Medical Center, Nanjing Medical University, Changzhou 213164, China

[2]Department of Cardiology, The First Affiliated Hospital of Nanjing Medical University, Nanjing Medical University, Nanjing 210029, China

*Corresponding author. Department of Cardiology, The First Affiliated Hospital of Nanjing Medical University, Nanjing Medical University, Nanjing 210029, China. E-mail: kongxq@njmu.edu.cn; Department of Gastrointestinal Surgery, The Affiliated Changzhou No.2 People's Hospital of Nanjing Medical University, Changzhou Medical Center, Nanjing Medical University, Changzhou 213164, China. E-mail: lianminchen@njmu.edu.cn; Department of Gastrointestinal Surgery, The Affiliated Changzhou No.2 People's Hospital of Nanjing Medical University, Changzhou Medical Center, Nanjing Medical University, Changzhou 213164, China. E-mail: tangliming@njmu.edu.cn

Dear Editor,

Obesity is an increasingly prevalent global health concern affecting ∼13% of the worldwide population and is associated with the development of conditions such as insulin resistance, hypertension, hyperlipidemia, and non-alcoholic fatty liver disease [1]. Despite recent advancements in behavioral interventions (including dietary changes and lifestyle modifications) and medical therapies (such as semaglutide and tirzepatide), bariatric surgery remains the most effective strategy for treating severe and complex obesity [2]. This includes individuals with a body mass index (BMI) > 40 kg/m^2 or a BMI between 35 and 40 kg/m^2 with significant health issues linked to excess body weight [2]. Commonly performed bariatric surgeries include sleeve gastrectomy (SG), SG with jejunojejunal bypass (JJB), one anastomosis gastric bypass (OAGB), and Roux-en-Y gastric banding (RYGB) [1, 2].

Bariatric surgery has been shown not only to result in significant weight loss but also to provide better control of diabetes compared to lifestyle interventions or pharmacotherapy alone [2]. Additionally, it has been observed that bariatric surgery can prevent cancer in patients with obesity and diabetes, and durable diabetes remission is associated with reduced cancer risk [3]. Despite these strengths, a portion of patients achieves only minimal weight reduction after bariatric surgery or regains weight after initially successful weight loss [4, 5]. Therefore, it is crucial to investigate potential underlying mechanisms and identify reliable predictive markers for individual responses to different types of bariatric surgery.

Notably, current research efforts have primarily focused on short-term and long-term weight loss, improvements in comorbidities, mortality, and health-related quality of life after bariatric surgery [1–3]. Additionally, a machine-learning model has been employed to predict accurate individual weight trajectories for up to 5 years post-bariatric surgery. The model is based on seven simple preoperative variables: age, weight, height, smoking history, type 2 diabetes status and duration, as well as the type of intervention [6]. However, a more comprehensive understanding can be gained by delving into additional layers of omics information, such as the metabolome, proteome, microbiome, and immune system profiling [7]. These aspects can provide deeper insights into the molecular basis of bariatric surgery in addressing metabolic syndrome [2]. Furthermore, an extensive collection of phenotypic data, including biochemical parameters, physical measurements, psychosocial characteristics, and environmental factors, along with detailed clinical status information, is of paramount importance [8]. For example, data about dietary habits and medical history can help correct for unrelated environmental biases in molecular analyses [9, 10]. Additionally, longitudinal follow-ups, coupled with these detailed phenotypes, can be immensely valuable for characterizing predictive markers of bariatric surgery efficacy and the suitability of specific bariatric surgery types.

To achieve these goals, we introduce the infrastructure and design of the prospective longitudinal multi-omics bariatric surgery (PBS) cohort study (Fig. 1A). This study involves the collection of relevant phenotypes (supplementary Tables 1 and 2 , see online supplementary material) and biological samples from severe and complex obese patients undergoing various types of bariatric surgeries, including SG, JJB, and OAGB, accompanied by extensive follow-up analyses (Fig. 1B), at affiliated hospitals of Nanjing Medical University, China. The comprehensive baseline information collected includes essential characteristics such as age, gender, and BMI, as well as lifestyle and dietary habits, medical history, vital signs, anthropometric measurements, blood test results, and metabolic syndrome-related status (Fig. 1A). For molecular profiling, we will generate data encompassing the gut microbiome, genome, metabolome, proteome, transcriptome, and more (Fig. 1A). We believe that establishing such a prospective cohort with multiple layers of information collected will reveal the molecular mechanisms underlying the clinical outcomes of bariatric surgery and help identify reliable predictive markers for personalized bariatric surgery type selection.

Between December 2022 and July 2023, we successfully enrolled 285 participants, which accounts for 47.5% of the

Received 28 November 2023; accepted 11 December 2023. **Published:** 12 December 2023

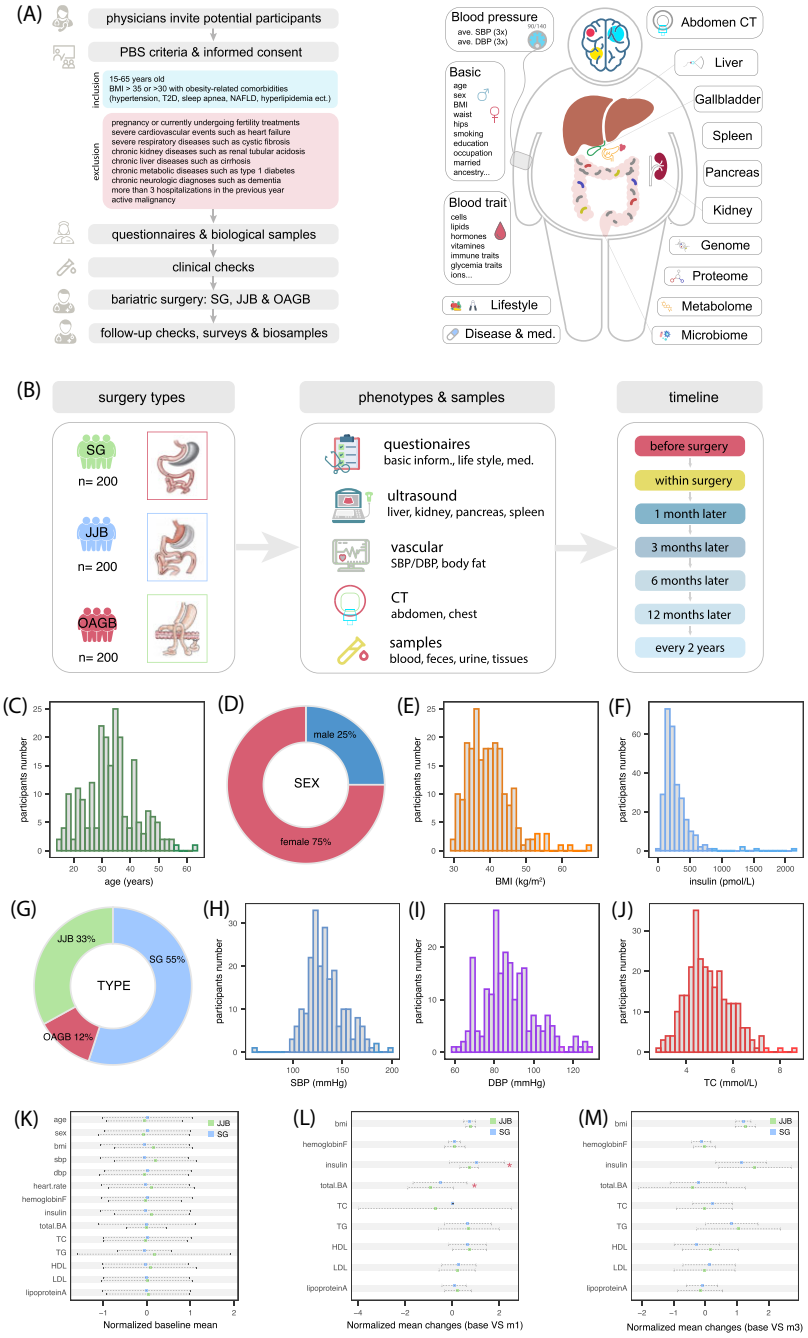

Figure 1. Cohort design and primary outcomes of the PBS cohort study. (**A**) Overview of the recruitment procedure and ongoing data collection from the PBS cohort study. Altogether 600 patients will be recruited who have undergone three major types of bariatric surgery, namely SG, JJB, and OAGB. We will capture >300 phenotypes, encompassing psychosocial characteristics, physical measurements, biochemical parameters, environmental factors, and clinical status. Furthermore, we will collect fasting blood, urine, and stool samples for analyses including genomics, metagenomics, and metabolomics. (**B**) Longitudinal design of the PBS cohort study. Patients will undergo follow-up assessments to monitor changes in their health status following various types of bariatric surgery. These follow-up appointments will be conducted in hospitals, during which comprehensive phenotypic data and biological samples will be collected for further analysis. (**C**) Age distribution of participants. (**D**) Proportion of male and female participants. (**E**) BMI distribution of participants. (**F**) Distribution of serum insulin levels of participants. (**G**) Proportion of patients who underwent SG, JJB, and OAGB bariatric surgeries. (**H**) Systolic blood pressure (SBP) distribution of participants. (**I**). Diastolic blood pressure (DBP) distribution of participants. (**J**) Distribution of serum total cholesterol (TC) levels of participants. (**K**) Comparison of baseline metabolic syndrome (MS)-related traits between the SG and JJB groups. total triglyceride, TG. high-density lipoproteins, HDL. low-density lipoproteins, LDL. (**L**) Temporal differences in MS-related traits between the SG and JJB groups during the 1-month follow-up. (**M**) Temporal differences in MS-related traits between the SG and JJB groups during the 3-months follow-up. The comparison between groups is based on the Kruskal–Wallis test and pink stars indicate significant differences at $P < 0.05$.

intended 600 patients scheduled for bariatric surgery. Specifically, the mean age of participants was 33.45 years, with 75% of them being female (Fig. 1C and D). The average BMI stood at 39.67 kg/m^2 and the mean insulin level was 274.85 pmol/l (Fig. 1E and F). At this stage, 55% of patients had undergone SG, 33% had undergone JJB, while the remaining 12% had undergone OAGB (Fig. 1G). Other metabolic syndrome (MS)-related traits, including systolic blood pressure (SBP), diastolic blood pressure (DBP), and total cholesterol (TC), exhibited normal distribution patterns (Fig. 1H–J).

With a significant number of participants having completed 1- and 3-month follow-ups for both SG and JJB procedures, we investigated potential differences in MS-related traits between the two surgery types. Initially, we examined 12 existing MS traits, along with age and sex, and found no significant differences between SG and JJB at baseline ($P > 0.05$, Fig. 1K). These results indicate that baseline characteristics were evenly balanced between the groups.

However, noteworthy trends emerged during the 1-month follow-up. Specifically, we observed a significant decrease in insulin levels in the SG group ($P = 0.03$, Fig. 1L), while total bile acid levels showed a significant increase in the JJB group ($P = 0.04$, Fig. 1L). Similar trends were noted at the 3-month follow-up, although they did not reach statistical significance ($P > 0.05$, Fig. 1M) due to the smaller sample size at this stage, as many participants had not yet completed the 3-month follow-up. These findings suggest that SG and JJB may have differing impacts on the regulation of MS traits following bariatric surgery.

In summary, the PBS is a prospective cohort comprising 600 patients who have undergone three major types of bariatric surgery, including SG, JJB, and OAGB. This cohort encompasses an extensive array of phenotypic data, spanning biochemical parameters, physical measurements, psychosocial characteristics, and environmental factors, in addition to detailed clinical information. Furthermore, multiple layers of omics datasets, including the gut microbiome, genotype, metabolomics, and proteomics, will be generated. This comprehensive collection of diverse phenotypic and deep omics data represents a valuable resource for clinical research. To the best of our knowledge, the PBS is a unique bariatric surgery cohort that may address critical questions concerning the molecular mechanisms underlying the impact of bariatric surgery on MS from a multi-omics perspective. Additionally, its prospective design and long-term follow-up offer the potential to identify reliable predictive markers that can aid in tailoring bariatric surgery approaches to individual responses, thereby enhancing treatment effectiveness.

However, it is important to also acknowledge several limitations in the current study. While we aim to compare differences in multiple layers of omics datasets to unveil potential mechanisms underlying the impact of bariatric surgery on MS, this study is observational in nature, which limits our ability to establish causality. Addressing this limitation would require conducting randomized clinical trials and wet lab experiments to validate potential causal relationships. Furthermore, it is plausible that selection bias may be present due to the self-assignment of participants and the exclusion of individuals with specific medical conditions within this particular population. Such bias could potentially affect the generalizability of associations between interventions and outcomes. Therefore, the inclusion of multiple centers and replication in independent cohorts with diverse ancestry may serve to enhance the robustness of the observations and emphasize their clinical significance.

Supplementary data

Supplementary materials are available at *PCMEDI Journal* online.

Acknowledgments

We are grateful for the participation of all the volunteers and the members of the PBS cohort study. This project was funded by the National Natural Science Foundation of China (Grant No. 32270077, 32394052 and Excellent Young Scientists Fund Program Overseas-2022); Jiangsu Shuangchuang Project (Medical Expert & JSSCBS20221815); the Natural Science Foundation of Jiangsu (Grant No. BK20220709); Nanjing Medical University (Grants No. CMCM202204, 303073572NC21, and YNRCZN0301); and Development of Jiangsu Higher Education Institutions Priority Academic Program (PAPD). We thank the High-Performance Computing Centre of Nanjing Medical University for providing computational resources. The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflict of interest statement: None declared.

Data availability

Diverse layers of omics datasets will be stored at the China National Center for Bioinformation (CNCB, https://www.cncb.ac.cn). Access to individual-level data is available for research and scientific purposes, if it aligns with the informed consent signed by the PBS participants. This consent specifies that the collected samples and data will not be used for commercial purposes. To gain access to individual-level data, researchers must obtain approval from the management board of the PBS consortium and adhere to the policies and approvals outlined by the Human Genetic Resource Administration, Ministry of Science and Technology of the People's Republic of China.

Ethics approval

The PBS cohort study was approved by the ethics committee of the Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University (2021YLA001 & 2023KY124-01) and has been registered at the Chinese Clinical Trial Registry (ChiCTR) under accession id ChiCTR2200060809. Informed consent was obtained from all participants of this study.

Author contributions

X.K., L.C., and L.T. contributed to conceptualization and funding. Y.J., J.X., S.C., and the PBS cohort study staff contributed to data and sample collection. Y.J. and L.C. drafted the manuscript. W.S., X.K., L.C., and L.T. contributed to discussion of the content. All authors read and approved the final manuscript.

References

1 Zeng Q, Li N, Pan XF *et al.* Clinical management and treatment of obesity in China. *Lancet Diabetes Endocrinol* 2021:**9**:393–405. doi: 10.1016/S2213-8587(21)00047-4.

2 Sandoval DA, Patti ME. Glucose metabolism after bariatric surgery: implications for T2DM remission and hypoglycaemia. *Nat Rev Endocrinol* 2023;**19**:164–76. doi: 10.1038/s41574-022-00757-5.

3 Sjoholm K, Carlsson LMS, Svensson PA *et al.* Association of bariatric surgery with cancer incidence in patients with obesity and diabetes: Long-term results from the Swedish obese subjects study. *Diabetes Care* 2022;**45**:444–50. doi: 10.2337/dc21-1335.
4 Salminen P, Helmio M, Ovaska J *et al.* Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass on weight loss at 5 years among patients with morbid obesity: The SLEEVEPASS randomized clinical trial. *JAMA* 2018;**319**:241–54. doi: 10.1001/jama.2017.20313.
5 Peterli R, Wolnerhanssen BK, Peters T *et al.* Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass on weight loss in patients with morbid obesity: The SM-BOSS randomized clinical trial. *JAMA* 2018;**319**:255–65. doi: 10.1001/jama.2017.20897.
6 Saux P, Bauvin P, Raverdy V *et al.* Development and validation of an interpretable machine learning-based calculator for predicting 5-year weight trajectories after bariatric surgery: a multinational retrospective cohort SOPHIA study. *Lancet Digital Health* 2023;**5**:e692–702. doi: 10.1016/S2589-7500(23)00135-8.
7 Tremaroli V, Karlsson F, Werling M *et al.* Roux-en-Y gastric bypass and vertical banded gastroplasty induce long-term changes on the human gut microbiome contributing to fat mass regulation. *Cell Metab* 2015;**22**:228–38. doi: 10.1016/j.cmet.2015.07.009.
8 Wijmenga C, Zhernakova A. The importance of cohort studies in the post-GWAS era. *Nat Genet* 2018;**50**:322–8. doi: 10.1038/s41588-018-0066-3.
9 Sun W, Wang Y, Zhang H *et al.* eHypertension: A prospective longitudinal multi-omics essential hypertension cohort. *iMeta* 2022; **1**: e22 doi: 10.1002/imt2.22.
10 Hou C, Yang H, Qu Y *et al.* Health consequences of early-onset compared with late-onset type 2 diabetes mellitus. *Precis Clin Med* 2022;**5**: pbac015. doi: 10.1093/pcmedi/pbac015.

Received 28 November 2023; accepted 11 December 2023. **Published:** 12 December 2023