

## Peer Review File

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### Review comments

This study aimed to develop a new formula for predicting standard pancreas volume (SPV) in Chinese adults using body surface area (BSA). The authors obtained the total pancreas volume (TPV) of 377 Chinese adults via CT 3D reconstruction estimation, with 287 used to construct the formula and 90 for validation. They found that BSA was the only independent associated factor for TPV, leading to the formula:  $SPV (cm^3) = 52.40 \times BSA (m^2) - 21.33$  ( $R^2 = 0.384$ ). The study's strength is its use of advanced 3D CT reconstruction technology for accurate volume measurement. However, the study is limited by its focus on a Chinese population, which may affect the formula's applicability to other ethnic groups, and the relatively small sample size, which could impact the generalizability of the results. In addition, the study did not account for all potential factors that could influence pancreas volume, which have limited the formula's accuracy. According to the  $R^2 = 0.384$ , the predictive accuracy is poor. For prediction, the  $R^2$  should be at least 0.8.

Reply1: We have added some content in Discussion.

While the  $R^2$  (0.384) reflects moderate explanatory power, biological variability in pancreas volume and unaccounted factors (e.g., genetics, lifestyle) likely contribute. Despite this, our formula provides a pragmatic tool for clinical scenarios where pre-disease TPV is unavailable. Comparable studies in liver volumetry report similar  $R^2$  values (0.3–0.5), yet their formulas remain clinically useful.

Changes in the text: See Page 8-9, line 260-265.

Reply 2: We have expanded limitations in Discussion.

Expanded in Discussion:

Limitations include ethnic specificity to Chinese adults and unmeasured confounders. Future studies should incorporate larger, diverse cohorts and explore additional predictors (e.g., genetic, metabolic factors).

Changes in the text: See Page 9, line 283-285.

I suggest the title to be revised as the development and validation of the formula.

Reply: We have modified our title as advised. The title has been revised to: Development and validation of a new formula to predict standard pancreas volume in Chinese adults using body surface area.

Changes in the text: See Page 1, line 1-2.

In the abstract, please clarify the clinical needs for the estimation of SPV and why 3D CT reconstruction cannot be used to directly assess SPV in the background, describe the inclusion of subjects, how the gold criterion for SPV and TPV by using 3D CT reconstruction was administered, how the training and validation samples were generated, and how the predictive accuracy was measured in the methods, report the characteristics of the patient sample and accuracy measure of the prediction model in the results, and consider to tone down the current conclusion because of the above concerns in the conclusion.

**Comment 1:** Clarify the clinical needs for the estimation of SPV and why 3D CT reconstruction cannot be used to directly assess SPV in the background, describe the inclusion of subjects, how the gold criterion for SPV and TPV by using 3D CT reconstruction was administered

**Reply 1:** We have modified our text as advised in Background section.

Changes in pancreas volume have been reported in many disorders. In clinical practice, pre-disease total pancreas volume (TPV) is often unavailable for patients with pancreatic pathologies (e.g., tumors, cysts, or pancreatitis), as prior imaging may not exist or may reflect abnormal volumes. While three-dimensional (3D) computed tomography (CT) reconstruction provides accurate TPV measurements, its utility is limited in these scenarios, necessitating a predictive formula.

Changes in the text: See Page 2, line 13-18.

**Comment 2:** Clarify how the training and validation samples were generated, and how the predictive accuracy was measured in the methods, report the characteristics of the patient sample and accuracy measure of the prediction model in the results.

**Reply 2:** We have added some contents in Methods.

Subjects were randomly split into training (287) and validation (90) cohorts. This retrospective cohort study utilized convenience sampling, with sample size informed by similar organ volume prediction studies. Training and validation cohorts were randomly stratified by age and gender to ensure representativeness. Validation accuracy thresholds ( $\pm 10\%$ ,  $\pm 15\%$ ) between SPV and TPV were based on prior liver volume studies by Ling-Mei Feng et al.

Changes in the text: See Page 5, line 120-125.

**Comment 3:** Consider to tone down the current conclusion because of the above concerns in the conclusion.

**Reply 3:** We have modified our text in Conclusion.

**Revised Conclusion:**

This preliminary BSA-based formula offers a practical method for SPV estimation in Chinese adults, particularly when pre-disease TPV is inaccessible. Further multi-ethnic studies are warranted to enhance generalizability.

Changes in the text: See Page 9, line 288-290.

The introduction is inadequate. The authors need to clearly indicate the clinical needs for the indirect estimation of TPV or SPV and whether the clinical factors and BSA could accurately predict. There has been direct assessment of TPV and the current formula is poor, so the rationale for this research focus is questionable.

Reply: We have modified our text in Background and Discussion section.

Background section.

Changes in pancreas volume have been reported in many disorders. In clinical practice, pre-disease total pancreas volume (TPV) is often unavailable for patients with pancreatic pathologies (e.g., tumors, cysts, or pancreatitis), as prior imaging may not exist or may reflect abnormal volumes. While three-dimensional (3D) computed tomography (CT) reconstruction provides accurate TPV measurements, its utility is limited in these scenarios, necessitating a predictive formula.

Changes in the text: See Page 2, line 13-18.

Discussion section.

In total, clinically, SPV estimation is critical for preoperative planning in pancreatic surgery and assessing volume loss in diseases like diabetes. BSA is prioritized due to its strong correlation with TPV ( $r=0.619$ ) and practicality as a single variable.

Changes in the text: See Page 9, line 272-275.

In the methodology, please specify the clinical research design of this study and sample size estimation procedures. The authors need to describe how the training and validation samples were generated and specify the methods for assessing the predictive accuracy of the formula and the threshold accuracy value for a satisfactory formula.

Reply: We have modified our text in Methods and Results section.

Methods section.

Subjects were randomly split into training (287) and validation (90) cohorts. This retrospective cohort study utilized convenience sampling, with sample size informed by similar organ volume prediction studies. Training and validation cohorts were randomly stratified by age and gender to ensure representativeness.

Validation accuracy thresholds ( $\pm 10\%$ ,  $\pm 15\%$ ) between SPV and TPV were based on prior liver volume studies by Ling-Mei Feng et al.

Changes in the text: See Page 4, line 120-125.

Results section.

In the validation cohort, 41% and 53% of SPV estimates fell within  $\pm 10\%$  and  $\pm 15\%$  of TPV, respectively.

Changes in the text: See Page 7, line 191-192.

Please consider to cite several related papers: 1. Miao Q, Li G, Wáng YXJ, Wang J, Wang H, Chen W, Shao Y. Feasibility study of low-dose computed tomography (CT) technology for maxillofacial bone three-dimensional (3D) printing in skeletal class III malocclusion. *Quant Imaging Med Surg* 2024;14(12):8238-8248. doi: 10.21037/qims-22-1266. 2. Wakker AM, Van Lieshout EMM, De Boer AS, Cornelissen BMW, Verhofstad MHJ, Van Walsum T, Visser JJ, Van Vledder MG. A novel method to perform morphological measurements on three-dimensional (3D) models of the calcaneus based on computed tomography (CT)-imaging. *Quant Imaging Med Surg* 2024;14(6):3778-3788. doi: 10.21037/qims-24-142.

Reply: We have added some related papers in Discussion.

Recent advancements in 3D CT reconstruction, as demonstrated in skeletal and calcaneal imaging (20, 21), underscore its reliability for volumetric assessments.

Changes in the text: See Page 7, line 203-205.