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Preoperative pressure pain threshold and solid-food recovery after gastrectomy for gastric cancer: a secondary analysis of a prospective cohort

Wenzhi Zhu
Peking University Cancer Hospital & Institute
Caixia Yang
Peking University Cancer Hospital & Institute
Shuxia Li
Peking University Cancer Hospital & Institute
Xiaoyi Wang
Peking University Cancer Hospital & Institute
Hongyu Tan
galaxyspark@163.com
Peking University Cancer Hospital & Institute

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Authors: Wenzhi Zhu[1†], Caixia Yang[1†], Shuxia Li[1], Xiaoyi Wang[2] and Hongyu Tan[1*]

Affiliations:

[1] Department of Anesthesiology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital & Institute, Beijing 100142, China

2 Department of Medical Record Statistics, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital & Institute, Beijing 100142, China

[†] Wenzhi Zhu and Caixia Yang contributed equally and share first authorship.

Corresponding author:

Hongyu Tan

Tel: +8613693564036

Email: galaxyspark@163.com

No.52 Fucheng Road, Haidian District, Beijing 100142, China

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Study design: Secondary analysis of a prospective observational cohort

Related publication disclosure: All 100 participants reported in Zhu W, Li S, Huang Y, et al. Perioper Med (Lond). 2026;15(1):70 (doi:10.1186/s13741-026-00699-w) are included within the present 262-patient cohort. That publication addressed preoperative sleep disorders and postoperative pain/analgesic/recovery outcomes; the present manuscript addresses PPT and time to first solid diet as a distinct secondary research question. The present cohort is independent of the separate 236-patient 2019 gastric-cancer pain cohort.

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Keywords: gastric cancer; gastrectomy; pressure pain threshold; solid diet; postoperative recovery

CRediT author contributions:

Wenzhi Zhu: conceptualization, data curation, formal analysis, methodology, writing – original draft.

Caixia Yang: data curation, investigation, writing – review and editing.

Shuxia Li: data curation, investigation, validation.

Xiaoyi Wang: formal analysis.

Hongyu Tan: conceptualization, methodology, project administration, supervision, writing – review and editing.

All authors read and approved the final version of the manuscript and agree to be accountable for all aspects of the work. Wenzhi Zhu and Caixia Yang contributed equally and share first authorship.

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Abstract

Background: Recovery of oral intake is an important component of postoperative recovery after gastrectomy, but substantial inter-individual variation remains. We examined whether preoperative pressure pain threshold was associated with postoperative dietary recovery.

Methods: This secondary analysis included 262 patients from a prospective observational cohort undergoing gastrectomy for gastric cancer. Pressure pain threshold was analyzed as a continuous exposure. The primary outcome was time to first solid diet; resumption after postoperative day 7 and postoperative length of stay were secondary outcomes. Multivariable median regression was used for continuous outcomes and logistic regression for binary outcomes, with postoperative opioid exposure examined in sensitivity analyses.

Results: Median time to first solid diet was 6 days (interquartile range 3-7), and 48 patients (18.3%) resumed solid food after postoperative day 7. Each 1-kgf increase in pressure pain threshold was associated with a 0.411-day shorter median time to first solid diet (95% confidence interval -0.627 to -0.194; $P<0.001$). The estimate remained stable after additional adjustment for 48-hour postoperative sufentanil consumption. Pressure pain threshold was not associated with the >7-day binary endpoint or postoperative length of stay.

Conclusions: Lower preoperative pressure pain threshold was associated with slower solid-food recovery when analyzed continuously, but not with the binary delayed-feeding endpoint or postoperative length of stay. The magnitude was modest, and its clinical importance remains uncertain.

Keywords: gastric cancer; gastrectomy; pressure pain threshold; solid diet; postoperative recovery

1. Introduction

Gastric cancer remains a major cause of cancer morbidity and mortality worldwide [1]. Gastrectomy with appropriate lymphadenectomy is central to curative treatment for resectable disease, with perioperative treatment determined by tumor stage and current guidelines [2,3]. As perioperative care has improved, functional recovery after surgery has become an increasingly important clinical outcome.

Recovery of oral intake is a practical marker of early postoperative recovery. ERAS recommendations for gastrectomy and ESPEN guidance on surgical nutrition support early oral intake and avoidance of unnecessary fasting [4-6]. Randomized and prospective studies have shown that oral feeding can often be started within the first few postoperative days after gastrectomy without increasing anastomotic complications [7-10], and meta-analyses have reported earlier gastrointestinal recovery and shorter hospital stay with early feeding strategies [11-13].

Time to first solid diet and postoperative length of stay (PLOS) capture related but distinct aspects of recovery. Time to solid food reflects dietary and gastrointestinal recovery, whereas PLOS is additionally influenced by complications, mobility, discharge criteria, and local practice [14-18].

Substantial variation in recovery persists even within standardized care pathways. Quantitative sensory testing (QST) provides an objective assessment of individual sensory sensitivity, and lower preoperative pain thresholds have been associated with greater postoperative pain in gastric cancer and other surgical populations [19-24]. Whether preoperative sensory sensitivity is also associated with recovery of oral intake after gastrectomy is uncertain.

Postoperative gastrointestinal recovery is influenced by operative stress, inflammation, bowel manipulation, autonomic responses, fluid management, and opioid exposure [25-29]. These factors provide a plausible, but unproven, rationale for examining whether preoperative sensory phenotype is related to postoperative dietary recovery.

The present study examined the association between preoperative PPT and time to first solid diet after gastrectomy for gastric cancer. Delayed resumption of solid diet after postoperative day 7 and PLOS were evaluated as secondary outcomes. Cold and heat pain thresholds and psychological measures were examined as exploratory sensory and psychosocial variables.

2. Materials and Methods

2.1 Study design and participants

This study was a secondary analysis of prospectively collected data from patients who underwent gastrectomy for gastric cancer at Peking University Cancer Hospital. The final analytic cohort comprised 262 patients, and source surgical dates in the current analytic dataset ranged from 17 October 2023 to 31 October 2025. Preoperative quantitative sensory testing and postoperative recovery data were collected prospectively. PPT was available in 261 of 262 patients. The cohort was established under a prospective observational protocol, and the present report follows the STROBE recommendations for observational studies [30]. The present cohort is independent of the previously published 236-patient gastric cancer pain cohort from our institution, which enrolled patients from May to September 2019; there was no participant overlap. Separately, all 100 participants reported in a published analysis of preoperative sleep disorders from the same registered prospective cohort are included within the present 262-patient dataset [31]. That prior report examined sleep disorder status in relation to pain sensitivity, postoperative pain, analgesic consumption, and recovery, whereas the present analysis addresses a distinct secondary research

question with preoperative PPT as the exposure and time to first solid diet as the primary outcome. The participant overlap with that 100-patient report is disclosed explicitly.

For the present secondary analysis, patients were eligible if they underwent gastrectomy for gastric cancer and had postoperative recovery data including time to first solid diet. Preoperative QST was collected as part of the parent cohort; missing PPT or covariate data were handled by complete-case analysis for the relevant multivariable models. The analytic inclusion criteria were defined for this secondary research question and did not alter the original prospective data collection.

2.2 Ethics and registration

The prospective observational protocol was approved by the Institutional Review Board of Peking University Cancer Hospital (No. 2023KT62) and registered in the Chinese Clinical Trial Registry (ChiCTR2400086435). Written informed consent was obtained from all participants. The present secondary analysis used data collected under this approved and registered cohort protocol.

2.3 Preoperative assessment and quantitative sensory testing

Demographic and clinical characteristics, tumor stage, neoadjuvant treatment, psychological measures, and experimental pain thresholds were collected before surgery. Quantitative sensory testing (QST) included pressure, cold, and heat pain thresholds. Pressure pain threshold (PPT) was measured using a mechanical pain meter (Wagner, USA). The probe was placed on the index finger and pressure was increased slowly until the participant first perceived pain, at which point loading was stopped and the displayed value was recorded. The procedure was repeated three times, and the mean of the three measurements was used as the final PPT value and expressed in kilograms-force (kgf); higher values indicate lower pressure-pain sensitivity. The

original cohort protocol specified gradual loading but did not document a numerical loading rate or a more specific device model in the available study record. Cold pain threshold was assessed by immersing the non-dominant hand in a 5°C water bath and recording the time to first pain, with a maximum exposure of 60 s. Heat pain threshold was assessed using a thermostatic metal plate at 47.5°C; the thenar eminence of the non-dominant hand was placed on the plate and time to pain-induced withdrawal was recorded, also with a 60-s safety limit. These procedures were based on the prospective cohort QST protocol and are consistent with standardized QST principles [32].

Anxiety and depression were assessed preoperatively using the Hospital Anxiety and Depression Scale (HADS), which comprises separate 7-item anxiety and depression subscales; a subscale score of 8 or higher indicates clinically relevant symptoms. Cold and heat pain thresholds and HADS anxiety and depression scores were retained for predefined exploratory analyses. Although PPT was measured in triplicate according to the cohort protocol, replicate-level readings were not retained in the analytic dataset used for this secondary analysis; therefore, within-session reliability could not be recalculated.

2.4 Perioperative management, postoperative analgesia, and variables

All patients received general anesthesia and postoperative patient-controlled intravenous analgesia (PCIA) as part of the prospective cohort protocol. The PCIA solution contained sufentanil 5 μg/kg, dexmedetomidine 50 μg, and tropisetron 10 mg diluted with 0.9% sodium chloride to a total volume of 120 mL. Pump settings included a 2-mL loading dose, a background infusion of 0.8 mL/h, a 2-mL patient-controlled bolus, and a 15-min lockout interval. Rescue sufentanil 0.1 μg/kg was administered when the postoperative pain score exceeded 3, with reassessment until adequate analgesia was achieved. Postoperative movement pain was recorded

on a 0-10 numerical rating scale at 12, 24, and 48 h, consistent with the coding in the analytic dataset. Cumulative sufentanil consumption and PCA consumption through 48 h were recorded and were used in sensitivity analyses.

Perioperative covariates included age, sex, body mass index (BMI), TNM stage, neoadjuvant chemotherapy, surgical approach, extent of gastrectomy, operative duration, intraoperative blood loss, crystalloid and colloid infusion, and intraoperative sufentanil dose. In the source case-report form, surgical approach was coded as open surgery, totally laparoscopic surgery, laparoscopic-assisted surgery, or thoracoabdominal incision; no thoracoabdominal-incision case was present in the final cohort, and one unlisted source code was treated as missing. Extent of gastrectomy was coded as total gastrectomy, distal gastrectomy, proximal gastrectomy, or palliative resection. Operative duration was analyzed per 30-min increment and blood loss per 100-mL increment. Postoperative complications and postoperative analgesic consumption were not included in the primary confounder-adjustment model because they occurred after the preoperative exposure and could lie on the recovery pathway. Postoperative opioid exposure was instead examined in separate sensitivity analyses.

2.5 Outcomes

The primary outcome was time from surgery to the first postoperative day on which solid food intake was documented in the clinical record; liquids and non-solid intake were not counted as the endpoint. Delayed resumption of solid diet was defined for the present secondary analysis as first solid diet after postoperative day 7 (>7 days), based on clinical interpretability and previous literature. Secondary outcomes were postoperative length of stay (PLOS), time to first flatus, and postoperative complications. A distribution-based sensitivity analysis defined prolonged PLOS as >9 days; this cutoff was not treated as a validated clinical threshold.

202 2.6 Data cleaning

203 Data were checked before analysis. Implausible values were verified against source records and

204 corrected before analysis. No patient was excluded as a result of data cleaning.

205 2.7 Statistical analysis

206 Continuous variables are presented as median (IQR) and categorical variables as number (%).

207 Patients with and without delayed solid-diet resumption were compared using the Mann-Whitney

208 U test for continuous variables and the chi-square test or Fisher exact test for categorical

209 variables, as appropriate. Spearman correlation was used to assess the relationship between time

210 to first solid diet and PLOS.

211 Because time to first solid diet and PLOS were right-skewed, multivariable median regression

212 was used for adjusted continuous-outcome analyses [33]. Covariates were selected a priori on the

213 basis of clinical knowledge and a simple causal framework rather than univariable P-value

214 screening. The core adjustment set comprised demographic factors (age, sex, BMI),

215 disease/treatment factors (TNM stage, neoadjuvant chemotherapy), and markers of operative

216 burden considered strong determinants of postoperative recovery (operative duration and blood

217 loss). Regression coefficients (β) represent adjusted differences in median outcome days.

218 Multivariable logistic regression using the same covariates was performed for delayed solid-diet

219 resumption (>7 days) and prolonged PLOS (>9 days). Surgical approach and extent of

220 gastrectomy were added in an extended sensitivity model.

221 Postoperative analgesia was assessed in sensitivity analyses by adding cumulative 48-h

222 postoperative sufentanil consumption to the core model. A separate model added 48-h PCA

223 consumption because the two postoperative analgesia measures were strongly correlated and

224 were not entered simultaneously. Exploratory models examined cold and heat pain thresholds

and anxiety and depression scores using the same clinical adjustment set; Benjamini-Hochberg false-discovery-rate correction was applied within the four exploratory exposure tests for each outcome family. Other secondary and cutoff sensitivity analyses were not multiplicity-adjusted and are interpreted as supportive or hypothesis-generating. Missing data were handled by complete-case analysis. No formal sample-size calculation was performed for the present secondary analysis; all eligible participants available in the cohort were included. The extent and pattern of missingness were summarized, and complete cases were compared with patients excluded from the core model. Two-sided P values <0.05 were considered statistically significant for the primary analysis. Effect estimates are reported with 95% confidence intervals. All statistical analyses were performed using Python version 3.13.5 (Python Software Foundation, Wilmington, DE, USA), with pandas version 2.2.3, SciPy version 1.17.0, and statsmodels version 0.14.6. To examine the influence of the right-skewed blood-loss distribution and the apparently different continuous-outcome estimates, an additional sensitivity analysis replaced continuous blood loss with a binary term (>100 versus ≤100 mL) using the same core adjustment set.

3. Results

3.1 Cohort characteristics and postoperative recovery

A total of 262 patients were included. Median time to first solid diet was 6 days (IQR 3-7), and 48 patients (18.3%) resumed solid food after postoperative day 7. Fifty patients (19.1%) developed at least one postoperative complication. Median time to first flatus was 4 days (IQR 3-6), and median PLOS was 8 days (IQR 7-9). Surgical approach comprised 79 open, 37 totally laparoscopic, and 145 laparoscopic-assisted procedures; one source record had an unlisted

approach code and was treated as missing. Extent of gastrectomy comprised 104 total, 128 distal, 25 proximal, and 5 palliative resections (Tables 1 and 2).

Compared with patients who resumed solid food by postoperative day 7, those with delayed resumption had longer operative duration (241.5 vs 216.5 min, P=0.030), received more crystalloid (median 1550 vs 1350 mL, P=0.033), had later first flatus (6 vs 4 days, P<0.001), and had longer PLOS (9 vs 7 days, P<0.001). Postoperative complications were also more frequent in the delayed group (41.7% vs 14.0%, P<0.001). Median PPT was lower in the delayed group (6.39 vs 7.14 kgf), although the unadjusted difference was not statistically significant (P=0.082). Cold and heat pain thresholds, anxiety and depression scores, male sex, intraoperative sufentanil dose, and blood loss did not differ significantly between groups (Table 1).

3.2 Primary analysis: time to first solid diet

In multivariable median regression, higher preoperative PPT was associated with earlier resumption of solid food (Table 3). Each 1-kgf increase in PPT was associated with a 0.411-day shorter median time to first solid diet (95% CI -0.627 to -0.194; P<0.001). Male sex was associated with a 1.244-day longer median time to first solid diet (95% CI 0.408-2.079; P=0.004). Blood loss showed a negative but imprecise association with time to first solid diet (β -0.422 days per 100 mL; 95% CI -0.861 to 0.016; P=0.059); this estimate was not interpreted as a protective effect. Age, BMI, TNM stage, neoadjuvant chemotherapy, and operative duration were not associated with the primary outcome.

3.3 Delayed solid-diet resumption >7 days

In the multivariable logistic regression model, PPT was not independently associated with delayed resumption of solid diet after postoperative day 7 (aOR 0.844 per 1 kgf; 95% CI 0.688-1.034; P=0.102; Table 4). Operative duration showed the same direction of association but did

not reach statistical significance in the core model (aOR 1.153 per 30 min; 95% CI 0.992-1.340; P=0.064).

3.4 PPT quartiles and cutoff sensitivity analyses

Delayed resumption occurred in 22.1% of patients in the lowest PPT quartile, 25.4% in Q2, 13.8% in Q3, and 12.3% in the highest quartile. Thus, the crude quartile pattern was not strictly monotonic. The adjusted trend analysis nevertheless showed lower odds with higher PPT quartile (aOR 0.711 per quartile; 95% CI 0.520-0.971; P=0.032; Table 5), and this analysis was treated as supportive rather than evidence of a dose-response relationship.

Sensitivity analyses using alternative delayed-feeding thresholds showed stronger associations for >6 days (aOR 0.744; 95% CI 0.625-0.887; P<0.001) and >8 days (aOR 0.733; 95% CI 0.559-0.960; P=0.024) than for the >7-day endpoint (Supplementary Table S1). The >7-day definition was retained for the main binary analysis, and alternative cutoffs were considered sensitivity analyses rather than data-driven outcome definitions.

Of the 262 patients, TNM stage was missing in 18 (6.9%), PPT in 1 (0.4%), cold pain threshold in 1 (0.4%), and surgical approach in 1 (0.4%). The patient with missing PPT was among those with missing TNM stage, resulting in 244 complete cases for the core model and 243 for the extended surgical-category model. Patients included in and excluded from the core complete-case model did not differ materially in age, BMI, PPT, operative duration, blood loss, sex, neoadjuvant chemotherapy, postoperative complications, time to first solid diet, or PLOS (all P>0.18; Supplementary Table S4).

In exploratory sensory and psychological models, heat pain threshold was inversely associated with time to first solid diet after clinical adjustment (β -0.011 days per second; 95% CI -0.019 to -0.003; P=0.0047; FDR-adjusted q=0.019). Cold pain threshold, anxiety score, and depression

score were not associated with the continuous outcome. None of these exploratory variables was associated with the >7-day endpoint after FDR correction (Supplementary Table S5).

Postoperative analgesia sensitivity analyses did not materially alter the primary PPT estimate. After addition of cumulative 48-h postoperative sufentanil consumption, the PPT coefficient was -0.406 days per 1 kgf (95% CI -0.626 to -0.187; P<0.001). In a separate model adding 48-h PCA consumption, the coefficient was -0.398 days per 1 kgf (95% CI -0.618 to -0.179; P<0.001). The two analgesia measures were strongly correlated (Spearman ρ=0.766) and were therefore not entered together (Supplementary Table S6).

3.5 Secondary analysis: postoperative length of stay

Time to first solid diet was positively correlated with PLOS (Spearman ρ=0.236; P<0.001). In multivariable median regression, PPT was not associated with PLOS (β -0.048 days per 1 kgf; 95% CI -0.197 to 0.101; P=0.526; Table 6). Longer operative duration (β 0.126 days per 30 min; 95% CI 0.008-0.244; P=0.037) and greater blood loss (β 0.847 days per 100 mL; 95% CI 0.545-1.149; P<0.001) were associated with longer PLOS. Male sex showed a borderline association with longer PLOS (β 0.575 days; 95% CI 0.000-1.150; P=0.050).

Fifty-nine patients (22.5%) had PLOS >9 days. Among 244 complete cases, PPT was not associated with prolonged PLOS (aOR 0.874 per 1 kgf; 95% CI 0.716-1.067; P=0.185; Supplementary Table S3). Greater blood loss was associated with higher odds of prolonged PLOS (aOR 1.833 per 100 mL; 95% CI 1.264-2.658; P=0.001), whereas higher BMI was associated with lower odds (aOR 0.868 per 1 kg/m²; 95% CI 0.779-0.968; P=0.011).

When blood loss was categorized as >100 versus ≤100 mL, 29 of 244 complete-case patients were in the >100-mL group. The 100-mL value corresponded to the 75th percentile of blood loss in the full cohort and was selected as a distribution-based, clinically interpretable threshold to

test robustness to the right-skewed blood-loss distribution; it was not treated as a validated clinical cutoff. The dichotomized blood-loss variable was not associated with time to first solid diet or the >7-day endpoint, but was associated with longer median PLOS and higher odds of PLOS >9 days; the PPT estimates remained materially unchanged (Supplementary Table S7). After additional adjustment for surgical approach and extent of gastrectomy, the association between PPT and time to first solid diet remained significant (β -0.422 days per 1 kgf; 95% CI -0.630 to -0.214; P<0.001; n=243; Supplementary Table S2). PPT remained unrelated to the >7-day endpoint (aOR 0.857; 95% CI 0.694-1.057; P=0.150). Operative duration was associated with delayed solid-diet resumption in the extended model (aOR 1.212 per 30 min; 95% CI 1.019-1.441; P=0.030), whereas the corresponding core-model estimate was borderline (P=0.064), indicating model sensitivity rather than a uniformly robust binary-outcome association. Findings for PLOS were otherwise similar to those of the core model.

4. Discussion

In this prospective cohort analysis, lower preoperative PPT was associated with a longer time to first solid diet after gastrectomy. Each 1-kgf increase in PPT corresponded to a 0.411-day difference in median recovery time, or approximately 9.9 hours. Among all patients with available PPT data (n=261), the interquartile range was 5.76-8.07 kgf; applying the core-model coefficient across this 2.31-kgf range corresponds to an estimated difference of about 0.95 day. No established minimally important difference exists for time to first solid diet after gastrectomy, so the clinical importance of this magnitude is uncertain. PPT was not associated with the >7-day binary endpoint or with PLOS.

Previous QST studies in surgical patients have focused mainly on postoperative pain [19-24]. In the present study, the primary PPT association persisted after adjustment for conventional

clinical factors and after separate adjustment for postoperative sufentanil or PCA consumption. Heat pain threshold also showed an exploratory inverse association with time to first solid diet after false-discovery-rate correction (β -0.011 days per second; q=0.019), whereas cold pain threshold, anxiety, and depression did not. The direction of the heat-threshold finding was concordant with the PPT result: lower pain sensitivity was associated with slightly earlier dietary recovery. However, the effect was small (approximately 0.11 day per 10-s higher heat pain threshold), was not reproduced for the >7-day binary endpoint, and arose from a secondary set of four exploratory exposures. It should therefore be regarded as hypothesis-generating rather than evidence for a second independent sensory predictor.

A biological link between preoperative pain sensitivity and dietary recovery remains speculative. Pain sensitivity, autonomic responses, inflammation, opioid exposure, and postoperative gastrointestinal motility may share neurophysiological pathways [25-28], but the present study did not measure the intermediate mechanisms required to test such a pathway. The results therefore support an association, not a mechanistic or causal explanation.

The difference between the continuous and binary analyses is important. Dichotomization at a single postoperative day discards information and reduced the number of delayed events to 48. The crude quartile pattern was also non-monotonic, with a slightly higher event rate in Q2 than Q1, so the quartile analysis should not be interpreted as a simple dose-response relation. Variation in results across >6-, >7-, and >8-day definitions further supports treating the continuous outcome as primary and cutoff analyses as supportive.

Male sex was associated with a longer median time to first solid diet and showed a borderline association with PLOS, but it was not associated with the >7-day binary endpoint. In our earlier independent gastric cancer pain cohort, female sex was associated with greater postoperative

pain, whereas in the present cohort male sex was associated with a longer median time to solid diet [19]. The opposite directions across different outcomes argue against a simple extension of sex-related pain sensitivity to dietary recovery. Unmeasured differences in body composition, operative complexity, mobilization, or feeding tolerance could contribute, but these mechanisms were not tested. Because sex was not the primary exposure and the association was inconsistent across outcomes, the finding should be considered exploratory and may reflect residual confounding.

Operative duration was not significantly associated with the >7-day endpoint in the core model but became significant after adjustment for surgical approach and extent of gastrectomy. The change in estimate suggests confounding or model sensitivity rather than a uniformly robust effect. Longer operative duration was, however, associated with longer PLOS, consistent with operative duration serving as a marker of procedural burden.

Postoperative complications were substantially more frequent among patients with delayed solid-diet resumption. Their temporal relationship to feeding recovery is complex: a complication may delay oral intake, while delayed gastrointestinal recovery may also occur as part of an evolving postoperative complication. Because complications occurred after the preoperative exposure and could function as mediators, consequences, or time-dependent co-occurring events, they were not included in the primary adjustment set. The observed group difference is therefore descriptive and should not be interpreted as evidence that complications confound the PPT association.

Blood loss showed apparently different directions across outcomes: the coefficient for time to first solid diet was negative but imprecise and crossed the null, whereas greater blood loss was strongly associated with longer PLOS and with PLOS >9 days. An additional sensitivity analysis that dichotomized blood loss at >100 versus ≤100 mL clarified this pattern. Blood loss >100 mL

was not associated with time to first solid diet (β -0.901 days; 95% CI -2.024 to 0.222; P=0.117) or delayed solid-diet resumption (aOR 0.566; 95% CI 0.177-1.811; P=0.338), but it was associated with a 1.559-day longer median PLOS (95% CI 0.796-2.322; P<0.001) and higher odds of PLOS >9 days (aOR 4.625; 95% CI 1.942-11.013; P<0.001; Supplementary Table S7). The nonsignificant negative dietary-recovery estimate should therefore not be interpreted as beneficial; the more reproducible blood-loss signal in this dataset concerns hospital stay rather than solid-diet recovery.

Higher BMI was associated with lower odds of prolonged PLOS >9 days in the dichotomized sensitivity model (aOR 0.868 per 1 kg/m²), but BMI was not associated with continuous median PLOS. This isolated threshold-specific association should not be interpreted as evidence that higher BMI is protective. It may reflect differences in nutritional reserve or body composition, selection effects, or residual confounding, and requires confirmation in larger cohorts using more direct measures of nutritional and sarcopenic status.

This study has several strengths. Data were collected prospectively, and PPT was measured before surgery. The primary exposure and outcome were analyzed continuously, and the main estimate was stable after additional adjustment for surgical categories and postoperative analgesia. Covariates were chosen from a clinically informed causal framework rather than by significance screening, and post-exposure complications were excluded from the primary confounder set. Missingness was quantified and complete-case patients were compared with those excluded from the core model.

Several limitations should be acknowledged. This was a single-center secondary analysis, and feeding and discharge practices may differ across institutions. TNM stage was missing in 6.9% of patients, although complete-case and excluded patients were similar on observed

characteristics. First solid diet was a clinical milestone rather than a direct physiological measurement. For PPT, the source protocol identified a Wagner mechanical pain meter and specified gradual loading to first pain, but the exact device model and a numerical pressure-loading rate were not documented in the available study record. Although PPT was measured three times and averaged, replicate-level readings were not retained in the analytic dataset; within-session reliability (for example, intraclass correlation or coefficient of variation) therefore could not be recalculated. These limitations reduce methodological reproducibility and may introduce measurement error. Detailed reconstruction technique, inflammatory biomarkers, surgeon-level complexity, and the temporal sequence between complications and feeding decisions were not available. Postoperative opioid adjustment was necessarily secondary because opioid use may lie on the causal pathway between sensory phenotype and recovery. The binary delayed-feeding analysis included only 48 events, limiting precision and the number of covariates that could be estimated reliably in logistic models. Finally, the observational design precludes causal inference.

These findings do not support using PPT alone to guide feeding or discharge decisions. The observed effect was modest and its clinical importance is uncertain. Multicenter studies using standardized feeding protocols, fully documented QST procedures, repeated sensory measurements, and time-resolved postoperative analgesia and complication data are needed to determine whether sensory phenotyping adds clinically useful information beyond conventional perioperative factors.

5. Conclusion

Lower preoperative PPT was associated with a longer time to first solid diet after gastrectomy for gastric cancer, and the estimate remained stable in analyses accounting for postoperative

analgesic consumption. The association was not observed for delayed resumption beyond postoperative day 7 or for PLOS. The magnitude was modest, and these findings should be considered evidence of association rather than a basis for clinical decision-making or causal inference.

Declarations

Ethics approval and consent to participate: The prospective observational protocol was approved by the Institutional Review Board of Peking University Cancer Hospital (No. 2023KT62) and registered in the Chinese Clinical Trial Registry (ChiCTR2400086435). Written informed consent was obtained from all participants.

Consent for publication: Not applicable.

Data availability: The data supporting the findings of this study are available from the corresponding author subject to institutional and ethical requirements.

Conflicts of interest: The authors declare no conflicts of interest.

Related publication: All 100 participants reported in Zhu et al. (Perioperative Medicine, 2026) are included within the present 262-patient cohort. The prior publication evaluated preoperative sleep disorders and postoperative pain, analgesic use, and recovery; the present manuscript evaluates preoperative PPT and time to first solid diet as a distinct secondary research question. This overlap has been disclosed in the Methods and to the journal editors.

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References

[1] Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-263. doi:10.3322/caac.21834.

[2] Lordick F, Carneiro F, Cascinu S, et al. Gastric cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2022;33(10):1005-1020. doi:10.1016/j.annonc.2022.07.004.

[3] Japanese Gastric Cancer Association. Japanese Gastric Cancer Treatment Guidelines 2021 (6th edition). Gastric Cancer. 2023;26(1):1-25. doi:10.1007/s10120-022-01331-8.

[4] Mortensen K, Nilsson M, Slim K, et al. Consensus guidelines for enhanced recovery after gastrectomy: Enhanced Recovery After Surgery (ERAS) Society recommendations. Br J Surg. 2014;101(10):1209-1229. doi:10.1002/bjs.9582.

[5] Weimann A, Braga M, Carli F, et al. ESPEN practical guideline: Clinical nutrition in surgery. Clin Nutr. 2021;40(7):4745-4761. doi:10.1016/j.clnu.2021.03.031.

[6] Hu Y, Hsu AW, Strong VE. Enhanced Recovery After Major Gastrectomy for Cancer. Ann Surg Oncol. 2021;28(12):6947-6954. doi:10.1245/s10434-021-09906-y.

[7] Hur H, Kim SG, Shim JH, et al. Effect of early oral feeding after gastric cancer surgery: a result of randomized clinical trial. Surgery. 2011;149(4):561-568. doi:10.1016/j.surg.2010.10.003.

[8] Jeong O, Ryu SY, Jung MR, Choi WW, Park YK. The safety and feasibility of early postoperative oral nutrition on the first postoperative day after gastrectomy for gastric carcinoma. Gastric Cancer. 2014;17(2):324-331. doi:10.1007/s10120-013-0275-5.

[9] Shimizu N, Oki E, Tanizawa Y, et al. Effect of early oral feeding on length of hospital stay following gastrectomy for gastric cancer: a Japanese multicenter, randomized controlled trial. Surg Today. 2018;48(9):865-874. doi:10.1007/s00595-018-1665-4.

[10] Wang Q, Yang KL, Guo BY, et al. Safety of early oral feeding after total laparoscopic radical gastrectomy for gastric cancer (SOFTLY-1): a single-center randomized controlled trial. Cancer Manag Res. 2019;11:4839-4846. doi:10.2147/CMAR.S199552.

[11] Tweed T, van Eijden Y, Tegels J, et al. Safety and efficacy of early oral feeding for enhanced recovery following gastrectomy for gastric cancer: a systematic review. Surg Oncol. 2019;28:88-95. doi:10.1016/j.suronc.2018.11.017.

[12] He H, Ma Y, Zheng Z, Deng X, Zhu J, Wang Y. Early versus delayed oral feeding after gastrectomy for gastric cancer: a systematic review and meta-analysis. Int J Nurs Stud. 2022;126:104120. doi:10.1016/j.ijnurstu.2021.104120.

[13] Xu D, Li J, Liu J, Wang P, Dou J. An updated systematic review and meta-analysis of the efficacy and safety of early oral feeding vs. traditional oral feeding after gastric cancer surgery. Front Oncol. 2024;14:1390065. doi:10.3389/fonc.2024.1390065.

[14] Kang SH, Lee Y, Min SH, et al. Multimodal Enhanced Recovery After Surgery (ERAS) Program is the optimal perioperative care in patients undergoing totally laparoscopic distal gastrectomy for gastric cancer: a prospective, randomized, clinical trial. Ann Surg Oncol. 2018;25(11):3231-3238. doi:10.1245/s10434-018-6625-0.

[15] Beamish AJ, Chan DSY, Blake PA, Karran A, Lewis WG. Systematic review and meta-analysis of enhanced recovery programmes in gastric cancer surgery. Int J Surg. 2015;19:46-54. doi:10.1016/j.ijsu.2015.05.021.

[16] Wee IJY, Syn NLX, Shabbir A, Kim G, So JBY. Enhanced recovery versus conventional care in gastric cancer surgery: a meta-analysis of randomized and non-randomized controlled trials. Gastric Cancer. 2019;22(3):423-434. doi:10.1007/s10120-019-00937-9.

[17] Lee Y, Yu J, Doumouras AG, Li J, Hong D. Enhanced recovery after surgery (ERAS) versus standard recovery for elective gastric cancer surgery: a meta-analysis of randomized controlled trials. Surg Oncol. 2020;32:75-87. doi:10.1016/j.suronc.2019.11.004.

[18] Jin H, Song S, Lu T, et al. The application of enhanced recovery after surgery in minimally invasive gastrectomy for gastric cancer: a meta-analysis of randomized controlled trials. Expert Rev Gastroenterol Hepatol. 2022;16(11-12):1089-1100. doi:10.1080/17474124.2022.2145944.

[19] Tan H, Wei J, Li S, et al. Pain threshold, anxiety and other factors affect intensity of postoperative pain in gastric cancer patients: a prospective cohort study. Chin J Cancer Res. 2021;33(3):343-351. doi:10.21147/j.issn.1000-9604.2021.03.06.

[20] Wu F, Liu J, Zheng L, et al. Preoperative pain sensitivity and its correlation with postoperative acute and chronic pain: a systematic review and meta-analysis. Br J Anaesth. 2024;133(3):591-604. doi:10.1016/j.bja.2024.05.010.

[21] Braun M, Bello C, Riva T, et al. Quantitative Sensory Testing to Predict Postoperative Pain. Curr Pain Headache Rep. 2021;25(1):3. doi:10.1007/s11916-020-00920-5.

[22] Abrishami A, Chan J, Chung F, Wong J. Preoperative pain sensitivity and its correlation with postoperative pain and analgesic consumption: a qualitative systematic review. Anesthesiology. 2011;114(2):445-457. doi:10.1097/ALN.0b013e3181f85ed2.

[23] van Helmond N, Aarts HM, Timmerman H, et al. Is preoperative quantitative sensory testing related to persistent postsurgical pain? A systematic literature review. Anesth Analg. 2020;131(4):1146-1155. doi:10.1213/ANE.0000000000004871.

[24] Sangesland A, Støren C, Vaegter HB. Are preoperative experimental pain assessments correlated with clinical pain outcomes after surgery? A systematic review. Scand J Pain. 2017;15:44-52. doi:10.1016/j.sjpain.2016.12.002.

[25] Story SK, Chamberlain RS. A comprehensive review of evidence-based strategies to prevent and treat postoperative ileus. Dig Surg. 2009;26(4):265-275. doi:10.1159/000227765.

[26] Luckey A, Livingston E, Tache Y. Mechanisms and treatment of postoperative ileus. Arch Surg. 2003;138(2):206-214. doi:10.1001/archsurg.138.2.206.

[27] Beard TL, Leslie JB, Nemeth J. The opioid component of delayed gastrointestinal recovery after bowel resection. J Gastrointest Surg. 2011;15(7):1259-1268. doi:10.1007/s11605-011-1500-3.

[28] Buscail E, Deraison C. Postoperative ileus: a pharmacological perspective. Br J Pharmacol. 2022;179(13):3283-3305. doi:10.1111/bph.15800.

[29] Huang DD, Zhuang CL, Wang SL, et al. Prediction of prolonged postoperative ileus after radical gastrectomy for gastric cancer: a scoring system obtained from a prospective study. Medicine (Baltimore). 2015;94(51):e2242. doi:10.1097/MD.0000000000002242.

[30] von Elm E, Altman DG, Egger M, et al; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med. 2007;147(8):573-577. doi:10.7326/0003-4819-147-8-200710160-00010.

[31] Zhu W, Li S, Huang Y, Wang X, Tan H. The impact of preoperative sleep disorders on postoperative pain and recovery in patients undergoing gastrectomy: a prospective cohort study. Perioper Med (Lond). 2026;15(1):70. doi:10.1186/s13741-026-00699-w.

[32] Rolke R, Baron R, Maier C, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): standardized protocol and reference values. Pain. 2006;123(3):231-243. doi:10.1016/j.pain.2006.01.041.

[33] Koenker R, Bassett G Jr. Regression quantiles. Econometrica. 1978;46(1):33-50. doi:10.2307/1913643.

Table 1. Baseline and perioperative characteristics according to delayed resumption of solid diet

Variable	≤7 days (n=214)	>7 days (n=48)	P value
Age, years	61.00 (53.25, 67.75)	60.50 (54.00, 66.00)	0.779
BMI, kg/m²	23.91 (21.26, 25.71)	24.27 (22.46, 26.42)	0.146
Pressure pain threshold, kgf	7.14 (5.77, 8.29)	6.39 (5.60, 7.35)	0.082
Cold pain threshold, s	8.91 (6.13, 13.56)	9.47 (7.32, 17.63)	0.251
Heat pain threshold, s	16.68 (8.05, 46.69)	13.46 (6.26, 42.29)	0.349
Anxiety score	3.00 (1.00, 6.00)	3.00 (0.75, 6.25)	0.721
Depression score	2.00 (0.00, 6.00)	2.50 (0.00, 6.00)	0.330
Intraoperative sufentanil, μg	26.00 (23.00, 30.00)	25.00 (21.50, 30.50)	0.584
Crystalloid volume, mL	1350.00 (1350.00, 1500.00)	1550.00 (1287.50, 1850.00)	0.033
Colloid volume, mL	1000.00 (700.00, 1000.00)	1000.00 (575.00, 1000.00)	0.553
Blood loss, mL	50.00 (50.00, 100.00)	50.00 (50.00, 100.00)	0.319
Operative duration, min	216.50 (185.00, 253.75)	241.50 (205.00, 300.00)	0.030
Male sex	149 (69.6%)	35 (72.9%)	0.783
Neoadjuvant chemotherapy	79 (36.9%)	19 (39.6%)	0.857
Hypertension	69 (32.2%)	10 (20.8%)	0.167
Diabetes	30 (14.0%)	8 (16.7%)	0.807
PSQI >7	43 (20.1%)	10 (20.8%)	1.000
TNM stage, n (%) [N=262]			0.846
Stage 1	37 (17.3%)	8 (16.7%)	
Stage 2	32 (15.0%)	7 (14.6%)	
Stage 3	114 (53.3%)	28 (58.3%)	
Stage 4	16 (7.5%)	2 (4.2%)	
Missing	15 (7.0%)	3 (6.3%)	
Surgical approach, n (%) [N=262]			0.684
Open surgery	62 (29.0%)	17 (35.4%)	
Totally laparoscopic surgery	31 (14.5%)	6 (12.5%)	
Laparoscopic-assisted surgery	120 (56.1%)	25 (52.1%)	
Missing	1 (0.5%)	0 (0.0%)	
Extent of gastrectomy, n (%) [N=262]			0.077
Total gastrectomy	84 (39.3%)	20 (41.7%)	
Distal gastrectomy	110 (51.4%)	18 (37.5%)	
Proximal gastrectomy	16 (7.5%)	9 (18.8%)	
Palliative resection	4 (1.9%)	1 (2.1%)	

Data are median (IQR) or n (%). Mann-Whitney U test was used for continuous variables; chi-square or Fisher exact test was used for categorical variables. Downstream postoperative outcomes are reported separately in Table 2. Source case-report-form coding defined surgical approach as open surgery (1), totally laparoscopic surgery (2), laparoscopic-assisted surgery (3), or thoracoabdominal incision (4); no code-4 case was present in the final cohort, and one unlisted source code was treated as missing. Extent of gastrectomy was coded as total (1), distal (2), proximal (3), or palliative resection (4).

Table 2. Postoperative outcomes according to delayed resumption of solid diet (≤7 versus >7 postoperative days)

Variable	≤7 days (n=214)	>7 days (n=48)	P value
Any postoperative complication	30 (14.0%)	20 (41.7%)	<0.001
Time to first flatus, days	4.00 (3.00, 6.00)	6.00 (3.00, 9.00)	<0.001
Postoperative length of stay, days	7.00 (7.00, 8.75)	9.00 (8.00, 11.00)	<0.001

Data are median (IQR) or n (%). These postoperative variables were not entered as predictors in the primary preoperative/intraoperative regression models.

Table 3. Multivariable median regression for time to first solid diet

Variable	β, days	95% CI	P value
Pressure pain threshold, per 1 kgf	-0.411	-0.627 to -0.194	<0.001
Age, per 10 years	-0.057	-0.388 to 0.274	0.733
Male sex	1.244	0.408 to 2.079	0.004
BMI, per 1 kg/m²	0.081	-0.032 to 0.193	0.158
TNM stage, per 1 stage	-0.019	-0.449 to 0.411	0.930
Neoadjuvant chemotherapy	-0.048	-0.829 to 0.732	0.903
Operative duration, per 30 min	0.035	-0.136 to 0.207	0.686
Blood loss, per 100 mL	-0.422	-0.861 to 0.016	0.059

β represents the adjusted change in median days to first solid diet. Negative values indicate earlier resumption. Core model used complete cases (n=244). See Supplementary Table S4 for variable-specific missingness and the comparison of patients included in versus excluded from the core complete-case model. CI, confidence interval; BMI, body mass index.

Table 4. Multivariable logistic regression for delayed resumption of solid diet (>7 days)

Variable	Adjusted OR	95% CI	P value
Pressure pain threshold, per 1 kgf	0.844	0.688 to 1.034	0.102
Age, per 10 years	1.027	0.752 to 1.403	0.867
Male sex	1.157	0.522 to 2.563	0.720
BMI, per 1 kg/m²	1.071	0.964 to 1.189	0.200
TNM stage, per 1 stage	1.004	0.668 to 1.509	0.985
Neoadjuvant chemotherapy	1.061	0.507 to 2.220	0.875
Operative duration, per 30 min	1.153	0.992 to 1.340	0.064
Blood loss, per 100 mL	0.874	0.574 to 1.332	0.532

OR, odds ratio; CI, confidence interval; BMI, body mass index. Core model used complete cases (n=244). Postoperative variables were intentionally excluded from the predictor model.

Table 5. Pressure pain threshold quartiles and delayed resumption of solid diet

PPT quartile	N	Median first solid diet, days	>7-day events	Event rate, %
Q1 (lowest)	68	6	15	22.1
Q2	63	6	16	25.4
Q3	65	6	9	13.8
Q4 (highest)	65	6	8	12.3

Adjusted trend per higher PPT quartile: OR 0.711 (95% CI 0.520-0.971), P=0.032. This quartile analysis is supportive/exploratory; the primary exposure analysis treats PPT continuously.

Table 6. Multivariable median regression for postoperative length of stay

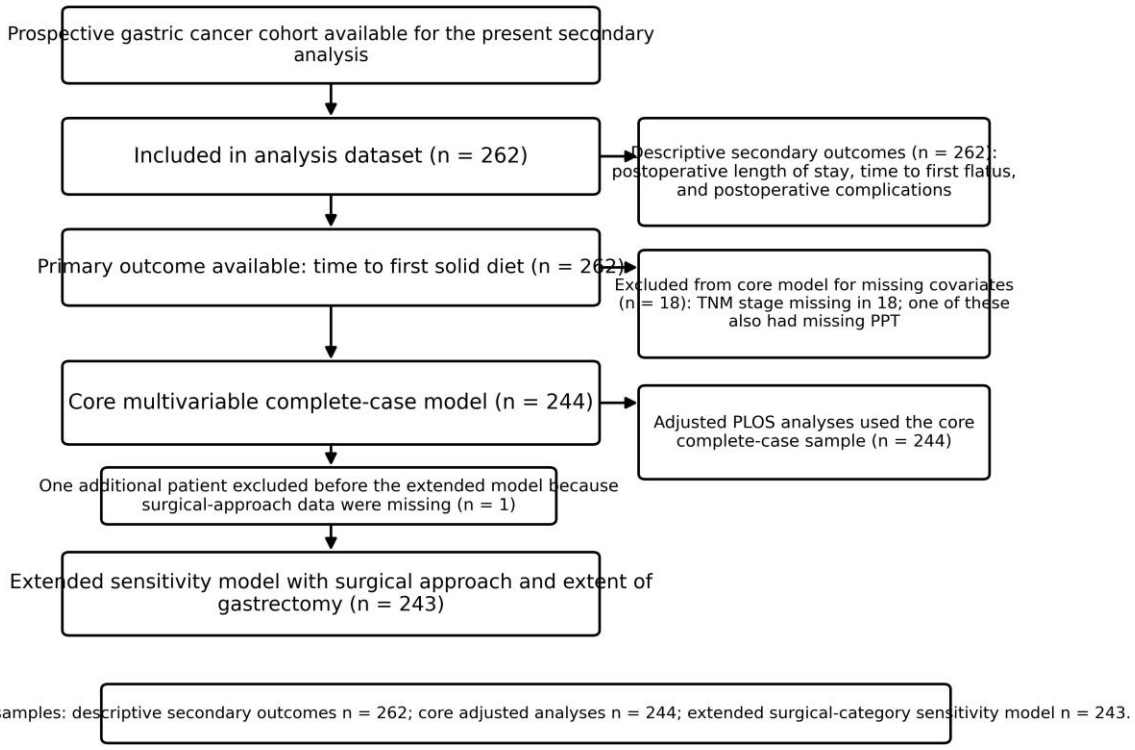
Variable	β, days	95% CI	P value
Pressure pain threshold, per 1 kgf	-0.048	-0.197 to 0.101	0.526
Age, per 10 years	0.010	-0.218 to 0.238	0.929
Male sex	0.575	0.000 to 1.150	0.050
BMI, per 1 kg/m²	-0.058	-0.136 to 0.019	0.137
TNM stage, per stage	0.026	-0.270 to 0.322	0.861
Neoadjuvant chemotherapy	-0.138	-0.676 to 0.399	0.613
Operative duration, per 30 min	0.126	0.008 to 0.244	0.037
Blood loss, per 100 mL	0.847	0.545 to 1.149	<0.001

β represents the adjusted change in median postoperative length of stay in days. Core model used complete cases (n=244). See Supplementary Table S4 for variable-specific missingness and the comparison of patients included in versus excluded from the core complete-case model. PPT, pressure pain threshold; CI, confidence interval; BMI, body mass index.

Figure Legend

Figure 1. Study flow diagram and analysis samples. All 262 patients contributed to the primary dietary-recovery outcome and to descriptive secondary-outcome analyses. Eighteen patients were excluded from the core multivariable complete-case analysis because of missing covariate data (TNM stage missing in 18 patients; one of these also had missing PPT), leaving n=244. One additional patient lacked a valid surgical-approach category, leaving n=243 for the extended model. Descriptive analyses of PLOS, time to first flatus, and postoperative complications used the full cohort (n=262), whereas adjusted PLOS analyses used the core complete-case sample (n=244). PPT, pressure pain threshold; PLOS, postoperative length of stay; TNM, tumor-node-metastasis.

Alt text: Study flow diagram distinguishing descriptive and adjusted analysis samples. The full cohort of 262 patients contributed to the primary outcome and descriptive secondary outcomes. Eighteen patients with missing core-model covariates were excluded from multivariable complete-case analyses, leaving 244 patients; one further patient with missing surgical-approach information was excluded from the extended model, leaving 243. Adjusted PLOS analyses used the 244-patient core complete-case sample.



Note: Descriptive analyses of postoperative length of stay, first flatus, and postoperative complications used the full cohort (n = 262). Adjusted postoperative length-of-stay analyses used the core complete-case sample (n = 244). PPT, pressure pain threshold; PLOS, postoperative length of stay; TNM, tumor-node-metastasis.

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Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryMaterial.docx