

# Oral Carbohydrate Administration in Patients Undergoing Cephalomedullary Nailing for Proximal Femur Fractures: An Analysis of Clinical Outcomes and Patient Satisfaction

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## Abstract

**Purpose:** The purpose of this study was to investigate the clinical effects of oral carbohydrate intake for cephalomedullary nailing on proximal femoral fractures and patient satisfaction. **Subjects and Methods:** 88 patients were admitted to our hospital with proximal femoral fracture from July 2019 to December 2019. All patients were treated with closed reduction and internal fixation (CR&IF, Cephalomedullary nailing) under spinal anesthesia. The exclusion criteria included the presence of endocrine disorders including diabetes mellitus (DM), patients treated with steroids, and cognitive impairment. Additionally, those with fasting blood glucose levels above 126 mg / dl or HbA1C > 6.5% were considered as having undiagnosed DM. After obtaining informed consent, the subjects were randomized into either the preoperative oral carbohydrate (POC) group or control group. Patients who were assembled into the control group fasted including water from midnight of the day of the surgical procedure according to the conventional method. Patients assembled into the POC group received 400 ml of oral carbohydrate solution (Nucare NONPO, DAESANG, 12.8%, 1 kcal/ml) between 21-24 hours on the day before operation and 400 ml oral carbohydrate solution 2 hours before the administration of anesthesia. Serum glucose on the day before operation at 7 am (before breakfast, baseline), immediately before anesthesia, at skin incision, 1 hour, 4 hours, 6 hours, 24 hours after anesthesia, and 3 days after surgery (before breakfast) was measured, and insulin, cortisol, and IL-6 were measured at baseline 7 am at day before operation, immediately before anesthesia, 4 hours and 24 hours after anesthesia, and 3 days after surgery (before breakfast). The patients completed questionnaires about their satisfaction (thirst, hunger, nausea and vomiting, and anxiety) in the morning (before the surgery) on the day of the surgery. Additionally, the length of hospital stay (LOS) and preoperative opioid usage was also investigated. **Results:** The operative characteristics of the patients did not differ between the groups except for the actual fasting time. The glucose levels were higher in the control group at skin incision; however, there were no significant differences in both groups at other time points. Additionally, insulin, insulin resistance, cortisol, and IL-6 also did not differ significantly between the 2 groups at all time-points. Among the factors related to patient satisfaction, the POC group showed significantly higher scores for thirst and hunger factors and shorter LOS than the control group. **Conclusion:** The intake of oral carbohydrates in patients treated with closed reduction and internal fixation for proximal femoral fractures does not affect the improvement of post-operative insulin resistance. However, there was significant improvement in patients' thirst and hunger before surgery and LOS.

## Keywords

carbohydrate, femur fracture, insulin resistance

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## Introduction

Surgical treatments induce catabolic responses such as stress hormones, inflammatory mediator secretion, and insulin resistance.<sup>1</sup> Insulin resistance leads to hyperglycemia, which leads to immune suppression and increased inflammatory cytokines and is an important risk factor for surgical site infections. Additionally, persistent fasting before and after the surgery exacerbates this condition.<sup>2</sup> Given that proximal femoral fractures occur predominantly in older patients, complications following these surgical treatments can cause increased fatal consequences for the patient. It is notable that fasting has been performed generally on the night prior to surgery for reducing the risk of gastro-esophageal reflux and aspiration pneumonia during anesthesia.<sup>1</sup> However, scientific evidence regarding this phenomenon is yet to be elucidated. Additionally, long-term fasting before surgery is known to cause dehydration, anxiety, thirst, hunger, dry mouth, and headaches.<sup>3</sup>

For these reasons, the Enhanced Recovery after Surgery protocol, which includes oral carbohydrates preoperatively, is recommended as one of several methods to minimize such surgical stress.<sup>4</sup> Preoperative carbohydrate oral administration can reduce the insulin resistance and contribute to shorter hospital stays and alleviate thirst, hunger, and anxiety.<sup>4</sup> Kwak et al. reported that preoperative oral carbohydrates had a significant effect on reducing the insulin resistance in patients undergoing coronary artery bypass surgery.<sup>5</sup> Nygren et al. argued that preoperative oral carbohydrate administration has a positive role in reducing the thirst, hunger, and tension and contributes to shorter hospital stays.<sup>1</sup> By contrast, Doris et al. reported that oral carbohydrate administration had no positive effect on insulin resistance in patients undergoing cardiopulmonary bypass surgery.<sup>6</sup> Mathur et al. reported that preoperative oral carbohydrates did not show superior results in terms of hospital stays and fatigue in major abdominal surgeries.<sup>7</sup>

However, there is no study on the effect of oral carbohydrate intake in patients undergoing orthopedic surgery such as closed reduction and internal fixation (CR&IF, Cephalomedullary nailing) after proximal femur fracture (PFF). The purpose of this study was to investigate the effects of oral carbohydrate intake for CR&IF after PFFs on the clinical effects of postoperative insulin resistance and patient satisfaction.

## Material and Methods

This study was approved by our hospital's ethics committee. 88 patients were admitted to our hospital with PFF (femoral neck fracture: 0 cases, Intertrochanteric fracture: 61 cases, subtrochanteric fracture: 27 cases) from July 2019 to December 2019. All patients were treated with CR&IF under spinal anesthesia. Patients treated for endocrine diseases or treated with steroids, including diabetes mellitus (DM), were excluded. Fasting blood glucose levels above 126 mg / dl or HbA1C values > 6.5% were considered as undiagnosed DM.

After obtaining informed consent, the subjects were randomized into either the preoperative oral carbohydrate (POC) or

control groups. Randomization was performed using a computer-generated random number assigned to the patient. This was done at time of admission and blinding of the patient was not possible. Patients who were assembled into the control group fasted including water from midnight of the day of the surgical procedure according to the conventional method and patients assembled into the POC group received 400 ml of oral carbohydrate solution (Nucare NONPO, DAESANG, 12.8%, 1 kcal/ml) between 21-24 hours on the day before operation and 400 ml oral carbohydrate solution 2 hours before the administration of anesthesia. Carbohydrate solution contains maltodextrin, isomaltooligosaccharide, dextrose, vitamin A, B, C, D, E, and K (*carbohydrate 15 g, fat 3 g, protein 4 g, vitamin A 75ug, B1 0.13 mg, B2 0.15 mg, B6 0.15 mg, C 14 mg, D 1ug, E 1.5 mg, K 7.5 ug per 100 ml*). After surgery, liquid intake was allowed if there was no specificity in vital signs and level of consciousness.

The measurements of serum glucose at 7 am on the day of the surgery (before breakfast, baseline), immediately before anesthesia, at skin incision, 1 hour, 4 hours, 6 hours, 24 hours after anesthesia, and 3 days after surgery (before breakfast) were carried out, and insulin, cortisol, and IL-6 were measured at baseline 7 am on the day of the operation (before the operation), immediately before anesthesia, 4 hours and 24 hours after skin incision, and 3 days after the surgery (before breakfast).

Insulin resistance was measured in the blood at 7 am on the day of the operation, immediately before anesthesia, 4 hours after anesthesia, 24 hours after anesthesia (postoperative day 1), and postoperative day 3 (before breakfast). HOMA-IR (Homeostasis model assessment) = insulin concentration (uU/ml) X glucose concentration (mg/dl) / 405 was used and IR > 1.0 or higher was considered to signify insulin resistance.<sup>6</sup>

To control pain before surgery, 1 ample of Fentanyl citrate (100 mcg/2 ml) per day were infused intravenously and additional administration was given according to pain control. If fentanyl citrate was not used due to allergy or hypersensitivity, morphine sulfate or hydromorphone was used. Morphine sulfate or hydromorphone doses were converted to fentanyl citrate using the formula: 1 mg of morphine = 10mcg of fentanyl citrate, 1 mg of hydromorphone = 50mcg of fentanyl citrate.<sup>8</sup> **Oral medications were not prescribed, but femoral nerve block was performed by an anesthesiologist just before surgery.** In the rehabilitation protocol, full weight bearing with assisted was allowed from the next day of surgery (POD1). The weight bearing time was gradually increased as much as it could withstand until POD3 and gait training with walker was implemented from POD 4. By POD 6, it was notified that patient could be discharged if there was no abnormality of x-ray and rehabilitation protocol compliance.

A 5-point scale (5: very satisfied, 4: generally satisfied, 3: moderate, 2: somewhat dissatisfied, 1: very dissatisfied) on 4 criteria of patient satisfaction (thirst, hunger, nausea and vomiting, and tension) was used for the evaluation. The evaluation was performed on the morning of the surgery (prior to surgery).

The length of hospital stay (LOS), from the operation day to the discharge day was also investigated. To compare the difference between the 2 groups, the independent paired t test, the Wilcoxon rank sum test and 2-way ANOVA were used. The post hoc power analysis was performed to determine if the study was sufficient to detect as statistically significant difference between 2 groups. Statistical analysis was performed using R Statistical Software (Foundation for Statistical Computing, Vienna, Austria) and defined as significant when  $p < 0.05$ .

**Table 1.** Patients' Demographics.

	Control group (n = 45)	POC group (n = 43)
<b>Sex(M/F)</b>	15/30	13/30
<b>ASA(I/II/III/IV)</b>	1/19/25/0	0/21/22/0
<b>Age(yr)<sup>#</sup></b>	75.24 ± 11.36	78.14 ± 9.27
<b>Anesthesia time(min)<sup>#</sup></b>	79.55 ± 10.32	77.26 ± 11.45
<b>Surgery time(min)<sup>#</sup></b>	48.15 ± 7.84	42.68 ± 8.95
<b>HbA1c(%)<sup>#</sup></b>	5.52 ± 0.85	5.49 ± 0.81
<b>Actual fasting time(hour)<sup>#</sup></b>	11.55 ± 1.27	2.30 ± 0.28
<b>Mean time from admission to surgery(day)<sup>#</sup></b>	2.15 ± 0.35	2.04 ± 0.25
<b>Preoperative Opioid(mcg)<sup>#</sup></b>	230.30 ± 30.52	225.15 ± 35.11

<sup>#</sup>; Values are given as mean ± Standard deviation. ASA, American Society of Anesthesiologists.

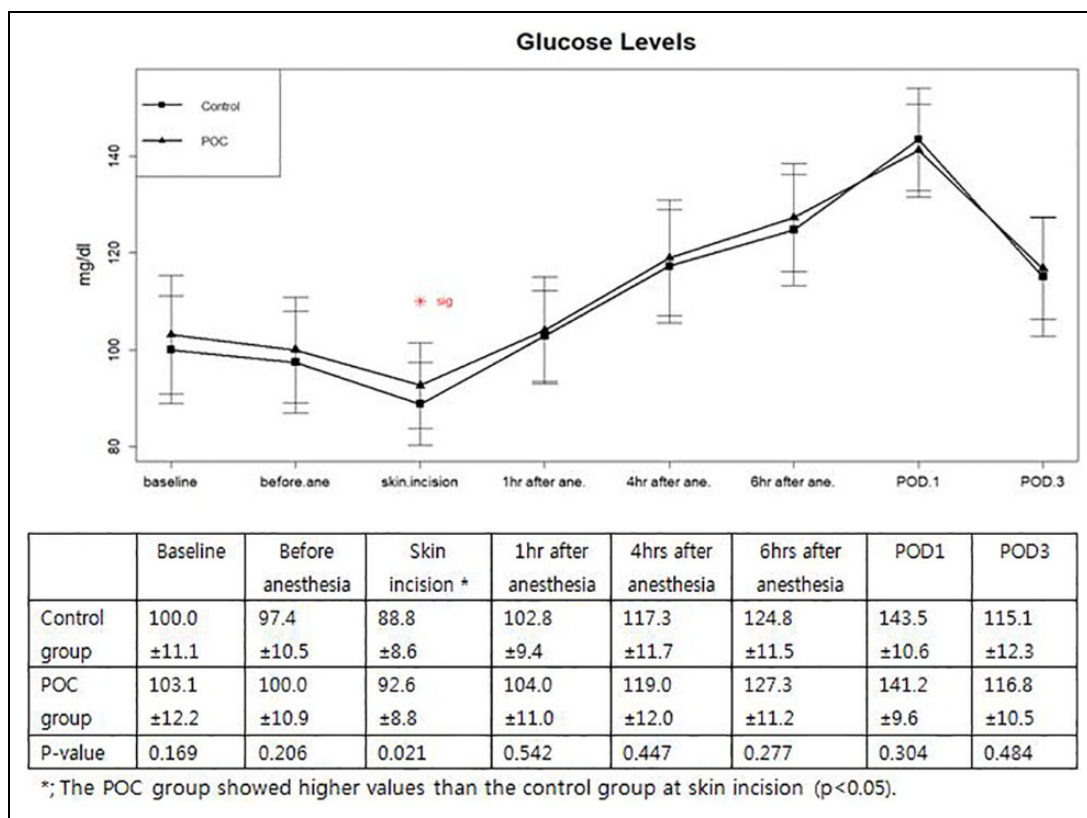
No significant differences were noted between the control and POC groups except for the actual fasting time.

## Results

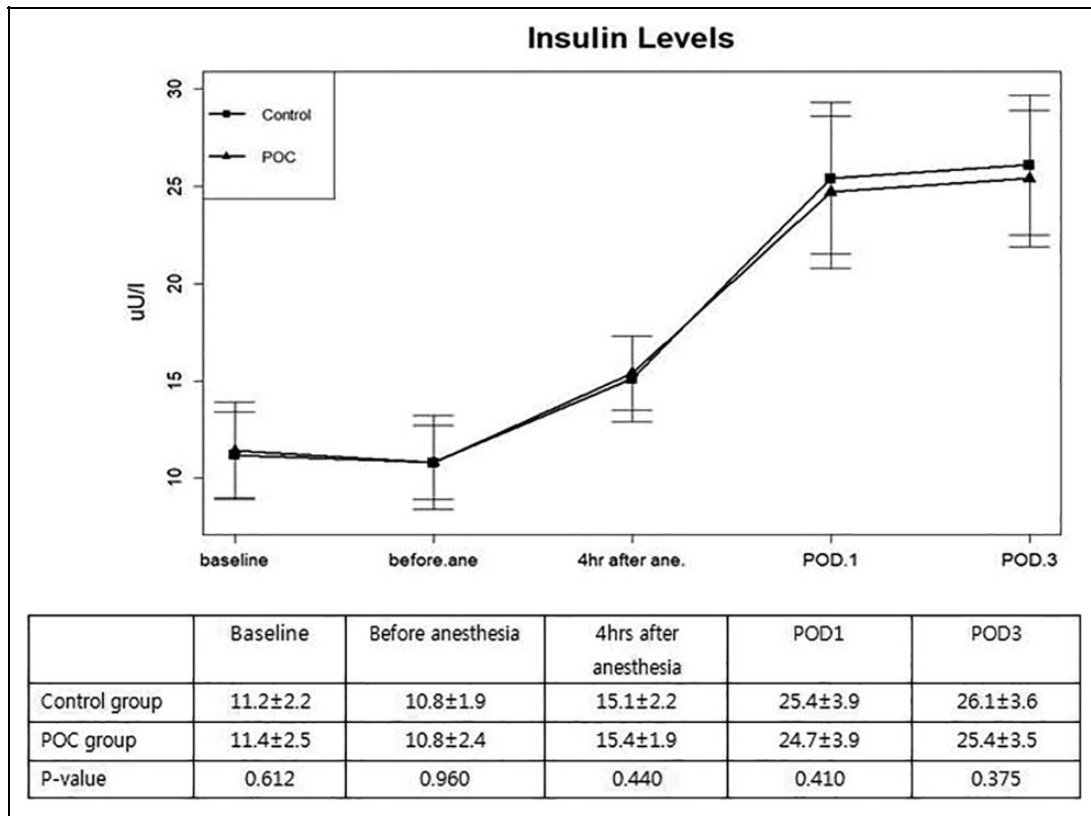
A total of 88 patients were included as subjects. There was no significant difference in patients between the 2 groups in gender, age, ASA, anesthesia and operation time, HbA1c, time from admission to operation and preoperative opioid usage except for the actual fasting time (Table 1).

Glucose was higher in the POC group at skin incision; however, there were no significant differences in both groups at other time points. The blood glucose levels of the POC and control groups were 100.0 ± 11.1 vs 103.1 ± 12.2 (mg/dl)( $p = 0.169$ ), 97.4 ± 10.5 vs 100.0 ± 10.9 (mg/dl)( $p = 0.206$ ), 88.8 ± 8.6 vs 92.6 ± 8.8 (mg/dl)( $p = 0.021$ ), 102.8 ± 9.4 vs 104.0 ± 11.0 (mg/dl)( $p = 0.542$ ), 117.3 ± 11.7 vs 119.0 ± 12.0 (mg/dl)( $p = 0.447$ ), 124.8 ± 11.5 vs 127.3 ± 11.2 (mg/dl)( $p = 0.277$ ), 143.5 ± 10.6 vs 141.2 ± 9.6 (mg/dl)( $p = 0.304$ ), and 115.1 ± 12.3 vs 116.8 ± 10.5 (mg/dl)( $p = 0.484$ ) at baseline, immediately before anesthesia, skin incision, 1 hour, 4 hours, 6 hours, 24 hours (POD 1) after anesthesia, and POD 3 days, respectively (Figure 1).

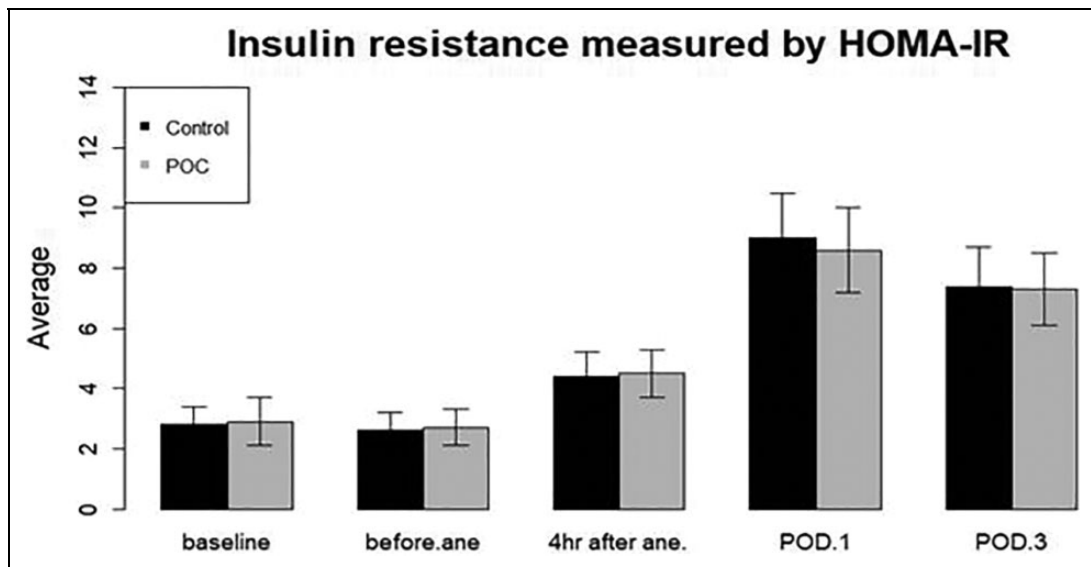
Insulin did not show a statistically significant difference between the 2 groups at any time point. Insulin concentrations in the POC and control groups were 11.2 ± 2.2 vs 11.4 ± 2.5 (uU/l)( $p = 0.612$ ), 10.8 ± 1.9 vs 10.8 ± 2.4 (uU/l)( $p = 0.960$ ), 15.1 ± 2.2 vs 15.4 ± 1.9 (uU/l)( $p = 0.440$ ), 25.4 ± 3.9 vs 24.7 ± 3.9 (uU/l)( $p = 0.410$ ), and 26.1 ± 3.6 vs 25.4 ± 3.5 (uU/l)( $p = 0.375$ ) at baseline, immediately before anesthesia, 4 hours, 24 hours after anesthesia (POD 1), and POD 3,



**Figure 1.** Serum glucose.



**Figure 2.** Plasma insulin.

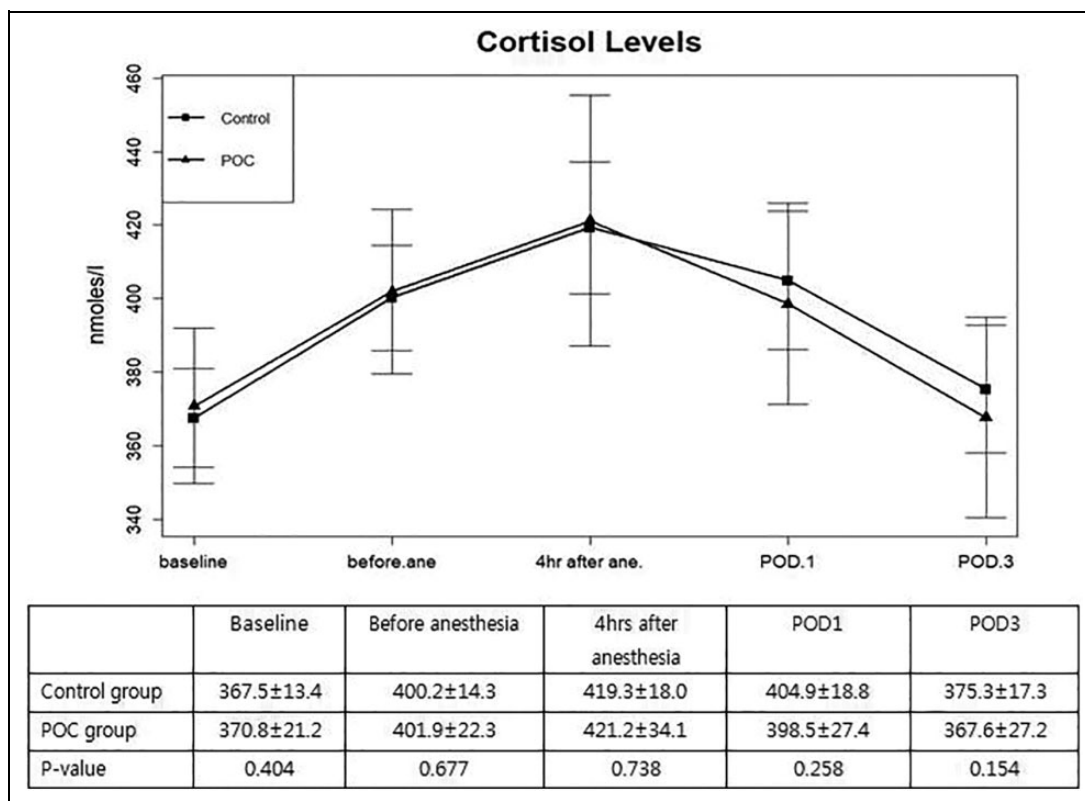


**Figure 3.** HOMA-IR.

respectively (Figure 2). Insulin resistance measured by HOMA-IR did not show a significant difference at any measurement point in the comparison between the 2 groups. The HOMA-IR was  $2.8 \pm 0.6$  vs  $2.9 \pm 0.8$  ( $p = 0.329$ ),  $2.6 \pm 0.6$  vs  $2.7 \pm 0.6$  ( $p = 0.665$ ),  $4.4 \pm 0.8$  vs  $4.5 \pm 0.8$  ( $p = 0.355$ ),  $9.0 \pm 1.5$  vs  $8.6 \pm 1.4$  ( $p = 0.195$ ), and  $7.4 \pm 1.3$  vs  $7.3 \pm 1.2$  ( $p = 0.744$ ) at baseline,

immediately before anesthesia, 4 hours after anesthesia, 24 hours after anesthesia (POD 1), and POD 3, respectively (Figure 3).

Similarly, cortisol also did not show any statistically significant differences between the 2 groups at any time point. Cortisol levels in the POC and control groups were



**Figure 4.** Plasma cortisol.

367.5 ± 13.4 vs 370.8 ± 21.2 (nmol/l)(p = 0.404), 400.2 ± 14.3 vs 401.9 ± 22.3 (nmol/l)(p = 0.677), 419.3 ± 18.0 vs 421.2 ± 34.1 (nmol/l)(p = 0.738), 404.9 ± 18.8 vs 398.5 ± 27.4 (nmol/l)(p = 0.258), and 375.3 ± 17.3 vs 367.6 ± 27.2 (nmol/l)(p = 0.154) at baseline, immediately before anesthesia, 4 hours after anesthesia, 24 hours (= POD 1), and POD 3, respectively (Figure 4).

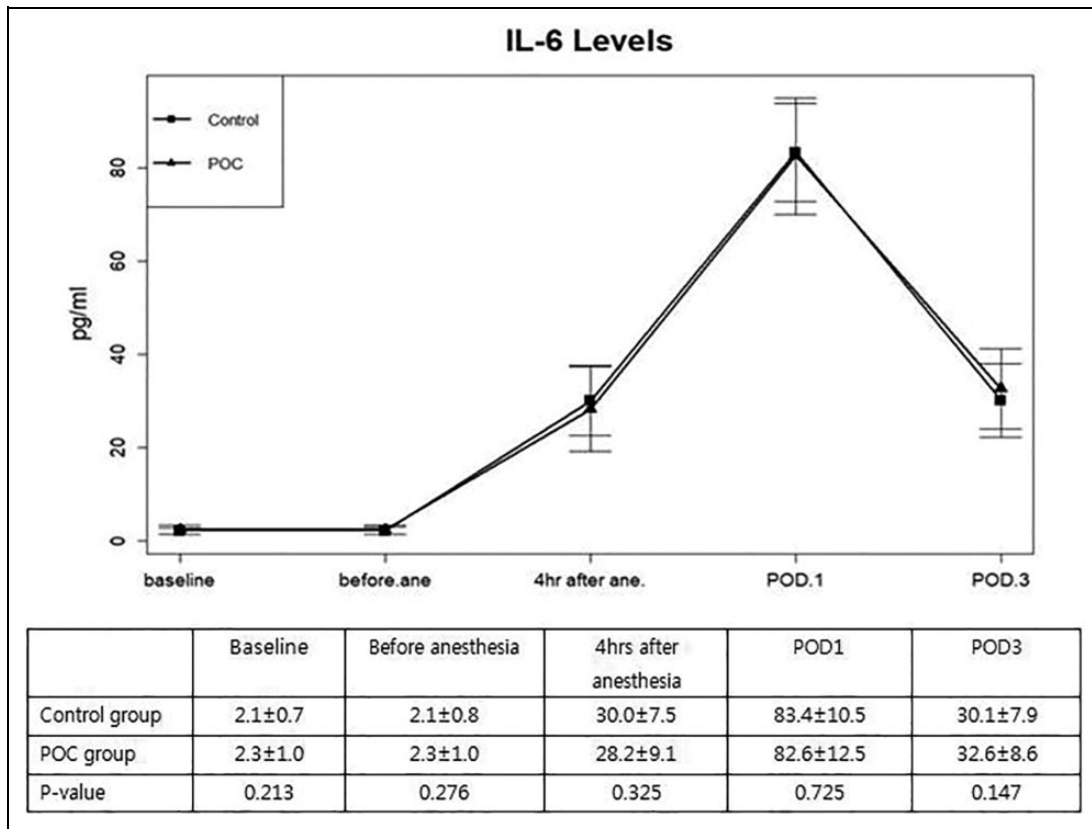
Additionally, IL-6 also showed no statistically significant differences between the 2 groups at any time point. The IL-6 levels in the POC and control groups were 2.1 ± 0.7 vs 2.3 ± 1.0 (pg/ml)(p = 0.213), 2.1 ± 0.8 vs 2.3 ± 1.0 (pg/ml)(p = 0.276), 30.0 ± 7.5 vs 28.2 ± 9.1 (pg/ml)(p = 0.325), 83.4 ± 10.5 vs 82.6 ± 12.5 (pg/ml)(p = 0.725), and 30.1 ± 7.9 vs 32.6 ± 8.6 (pg/ml)(p = 0.147) at baseline, immediately before anesthesia, 4 hours after anesthesia, 24 hours (= POD 1), and POD 3, respectively (Figure 5).

In the survey on patient satisfaction measured in the morning (before surgery) on the day of surgery, the control and POC groups had scores of 2.02 ± 0.78 vs 2.98 ± 0.84 in thirst (p < 0.05), 1.36 ± 0.48 vs 2.78 ± 0.52 in hunger (p < 0.05), and 3.20 ± 0.54 vs 3.24 ± 0.65 in nausea and vomiting (p = 0.813), and 1.33 ± 0.48 vs 1.22 ± 0.43 in the anxiety categories (p = 0.318). The POC group showed statistically significant superiority with respect to thirst and hunger. The POC group showed shorter LOS than the control group (7.78 ± 1.22 vs 8.95 ± 1.36 days)(P < 0.05)(Table 2).

## Discussion

In the present study, preoperative oral carbohydrate administration showed no significant differences in the blood glucose except during skin incision, insulin, insulin resistance, cortisol, and IL-6 compared with the control group. However, among the indicators of patient satisfaction measured on the morning of the surgery, thirst and hunger were superior to that of the control group.

Insulin resistance is affected by a variety of factors, including the patient's general condition, the type and invasiveness of the operation, the amount of bleeding during surgery, the type of anesthesia, and the drug used during anesthesia. Jan-P et al. reported that preoperative oral carbohydrates affect the insulin resistance in ASA I / II patients undergoing cardiac surgery, but not in ASA III / IV patients.<sup>9</sup> In previous studies regarding total hip arthroplasty (THR), Nygern et al. reported that preoperative oral carbohydrates were effective in reducing the insulin resistance,<sup>10</sup> but not in studies conducted by Stenfan and Celiksular.<sup>11</sup> Ozlem et al also reported that preoperative oral carbohydrates in patients undergoing lumbar disc surgery did not affect the insulin resistance.<sup>12</sup> Moreover, it might be reasoned that lumbar disc surgery may be a minor surgery compared to abdominal or hip arthroplasty.<sup>12</sup> M.sem et al. reported that epidural anesthesia suppresses the surgical stress response compared to general anesthesia in THR surgery.<sup>13</sup> We assumed that those factors may have influenced our study results. Be specifically, it is relatively less invasive factors



**Figure 5.** Plasma IL-6.

**Table 2.** Four Parameters of Patient Satisfaction and LOS.

	Control group	POC group	p-value
<b>Thirst *</b>	1.87 ± 0.73	3.09 ± 1.04	P < 0.05
<b>Hunger *</b>	1.73 ± 0.72	3.07 ± 0.94	P < 0.05
<b>Nausea &amp; vomiting</b>	3.07 ± 0.90	3.00 ± 0.80	0.813
<b>Anxiety</b>	1.64 ± 0.71	1.78 ± 0.67	0.318
<b>LOS *</b>	7.78 ± 1.22	8.95 ± 1.36	P < 0.05

\*; P < 0.05, The Wilcoxon rank-sum test was used for evaluation. LOS; length of hospital stay.

Four parameters representing patient satisfaction (thirst, hunger, nausea and vomiting, and anxiety) were assessed by a 5-point scale (5: very satisfied, 4: generally satisfied, 3: moderate, 2: somewhat dissatisfied, 1: very dissatisfied).

such as shorter surgery time and lesser bleeding than surgeries such as THR and ASA II or III.

In addition, there are clamp approaches and homeostasis model assessment (HOMA) methods for measuring the insulin sensitivity. Although the clamp approach is a gold standard method for measuring insulin sensitivity. In order to implement this method, continuous glucose level monitoring is needed and accordingly, insulin infusion rate needs to be adjusted to maintain a constant glucose concentration. For these reasons, this method is time-consuming, labor-intensive, and expensive, so it is difficult to apply in practice.<sup>7</sup> The HOMA-IR method is a method of measuring the serum fasting glucose and basal insulin concentration,<sup>12</sup> which is economical in terms of

convenience and cost that can be measured simply by blood tests. Matthews et al. reported that the insulin resistance measured using HOMA correlated strongly with insulin sensitivity measured using the clamp technique.<sup>14</sup> However, Bonora et al. suggested that the clamp approach mainly reflects peripheral insulin resistance due to the insulin's non-basal and active levels,<sup>15</sup> while HOMA-IR reflects the hepatic insulin resistance as insulin is based on fasting blood glucose.<sup>7</sup> Mireille et al. reported that oral supplements containing carbohydrates slightly attenuate the decrease in peripheral insulin sensitivity after surgery,; however, they do not prevent the decrease in insulin sensitivity.<sup>16</sup> In this study, insulin resistance was measured using the HOMA-IR method. Additionally, it can be inferred that the peripheral insulin sensitivity was difficult to reflect properly, considering that it mainly reflects hepatic insulin resistance.

Surgical stress causes neuroendocrine responses mediated by stress hormones such as cortisol and glucagon and pro-inflammatory cytokines. It is noted that the cortisol levels in blood were proportional to insulin resistance. Moreover, Doris et al. reported that the cortisol levels were higher than baseline and there were no statistical significances between the POC and control groups.<sup>6</sup> In the present study, cortisol was elevated in both groups from 4 hours after skin incision.

Cytokines such as IL-6 mediate the systemic response to trauma. It is observed that IL-6 rises 2-6 hours after the start of the operation and the degree of its increase is different according to the type of surgery. Fasting before surgery leads

to an increase in the inflammatory markers and preoperative oral carbohydrate intake is reported to alleviate this effect. By contrast, Takahiko et al. noted that cytokines such as IL-6 did not display a significant difference between the 2 groups. This may be due to the fact that cytokines do not play a major role in the deterioration of insulin resistance caused by fasting.<sup>3</sup> In the present study, postoperative IL-6 was elevated in both groups from 4 hours after anesthesia compared to the baseline. However, there was no statistical difference between the 2 groups. This means that the preoperative oral carbohydrate administration has no significant effect on patients undergoing CR&IF under spinal anesthesia or it is thought that cortisol and IL-6 do not significantly affect the catabolic response after surgery.

Large-scale studies have shown that preoperative oral carbohydrate administration shortens hospital stay but does not affect the well-being of patients.<sup>4</sup> Nygren et al. also found that the administration of oral carbohydrates significantly affects the thirst, hunger, and anxiety of the patient<sup>1</sup>; however, thyroidectomy surgery<sup>4</sup> and lumbar disc surgery<sup>12</sup> did not significantly affect the well-being of the patients. This may be due to the relatively high level of well-being of the control group. In our study, the patient's thirst and hunger showed significantly better results in the POC group and LOS was reduced by 1.2 days. Therefore, POC could contribute to the partial improvement of patients' satisfaction and LOS.

The limitations of this study were that it is a relatively small, single-center study and the clamp approach was not applied when measuring insulin resistance, and the actual fasting time was not controlled under the same conditions for each patient. Another limitation of this study was that difference in rehabilitation rate immediately after surgery and mortality rate, reoperation rate during long-term follow-up were not conducted. *Due to the design of this study, the fasting time had to differ between the 2 groups, and the effect of this difference in fasting time on insulin resistance was not precisely controlled.* Hence, further research is needed to address these shortcomings.

## Conclusion

The intake of whole oral carbohydrates in the patients treated with CR&IF for PFFs does not affect the improvement of postoperative insulin resistance. However, there was a significant improvement in patients' thirst and hunger before surgery and LOS.

## Declaration of Conflicting Interests

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