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ORIGINAL ARTICLE

Impact of postoperative weight gain on complications after liver surgery

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Abstract

Background: Recent data has suggested that excessive perioperative weight gain may be associated with adverse outcomes after abdominal surgery, but this observation remains unexplored following liver surgery. The present study aimed to investigate the predictive value of perioperative weight fluctuation in predicting complications after liver surgery.

Methods: Retrospective monocentric analysis of consecutive patients undergoing liver surgery between 2010 and 2016. Patients without available perioperative weight were excluded. Test variable was postoperative weight change (ΔWeight) measured on day 2 (POD2). Primary outcome was postoperative major morbidity according to Clavien classification (grades III–IV). Secondary outcomes were overall complications, Comprehensive Complication Index (CCI) and length of hospital stay (LoS). Area under the receiver operating characteristic curve (AUROC) and logistic regression with multivariable analysis were performed.

Results: A total of 181 patients met the inclusion criteria. Major and overall postoperative complications were reported in 25 (14%) and 87 (48%) patients, respectively. On POD2, median ΔWeight was 2.6 Kg (IQR: 1.1–4.0). Patients with major complications showed increased ΔWeight of 4.2 Kg (IQR: 2.7–5.7), compared to 2.3 Kg (IQR: 0.9–3.7) in patients without major complications ($p < 0.001$). AUROC of ΔWeight for major complications was 0.74, determining an optimal cut-off of 3.5 Kg, which yielded a negative predictive value of 94%. Multivariable analysis identified ΔWeight ≥3.5 Kg as independent predictor of major complications (OR, 4.73; 95% CI, 1.51–14.80; $p = 0.008$).

Conclusion: ΔWeight ≥3.5 Kg was independently associated with major complications after liver surgery. Perioperative fluctuation of weight appears as an important predictor of adverse outcomes after liver surgery.

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Introduction

Despite important improvements in perioperative management, liver surgery remains associated with substantial morbidity.[1–3] Not only responsible for detrimental clinical burden, postoperative complications also result in a considerable increase of costs.[1] Biomarkers that can predict adverse outcomes after liver resection are lacking.[4]

Recent data have suggested an association between perioperative gain of weight (ΔWeight) and the risk of complications after digestive surgery -such as increased overall and respiratory complications, prolonged length of stay (LoS)[5] as well as postoperative ileus.[6] Considering the physiological stress that liver surgery induces, as well as the challenging fluid management it requires, it was hypothesized that perioperative fluctuation of weight may potentially predict adverse outcomes following liver surgery. Although ΔWeight may be an early predictor of adverse

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complications, it may also represent a modifiable risk factor by pharmacological measures.

This study aimed to investigate the predictive value of the perioperative ΔWeight for postoperative complications in patients undergoing liver surgery.

Methods

Study design

This retrospective study included all consecutive patients undergoing liver surgery at the Department of Visceral Surgery of Lausanne University Hospital (CHUV) between June 2010 and November 2016. Perioperative management adhered to recommendations for liver surgery from the Enhanced Recovery After Surgery (ERAS) Society.[7] Study protocol was approved by the Institutional Review Board (CER-VD # 2017-01169).

Patient selection

Inclusion criteria were age >18 years and patients undergoing elective liver surgery during the study period. Patients without pre- and post-operative measures of weight were excluded. Demographics, surgical details, perioperative variables as well as postoperative outcomes were retrieved from a prospectively maintained database.

Perioperative weight

Patient weight (in kilogram: Kg) was recorded by nurses, preoperatively (on the day before surgery) as well as daily during the postoperative course. Postoperative weight change was measured as ΔWeight on POD2 [weight on POD2 − preoperative weight]. POD2 was chosen for several reasons (I) due to hemodynamics, patients undergoing liver surgery cannot systematically be weighted on POD1, (II) weight fluctuation on POD1 may be too early to accurately reflect perioperative fluid shifts after liver surgery, and (III) weight fluctuation on POD2 is measurable ahead enough of the vast majority of complications to anticipate them and to detect patients at higher risk.

Study outcomes

Clavien classification was used to grade postoperative complications within 30 days after surgery.[8] Minor and major complications were defined as grades I/II and grades III/IV, respectively. Grade V was defined as mortality.

Primary endpoint was major morbidity. Secondary endpoints were overall complications, Comprehensive Complication Index (CCI)[9] and LoS, calculated from day of surgery until discharge, consistently with previous definition.[10,11]

Statistical analyses

Continuous variables were provided as mean with standard deviations (SD) or standard error to the mean (SEM), or with median and interquartile range (IQR), according to the distribution. Student's t-test and Mann−Whitney U test were used to compare continuous variables depending on the normality of the distribution. Likewise, categorical variables were displayed as frequencies with valid percentages, and compared with χ^2 test or Fisher's exact test. Several variables were dichotomized as followed: age (≥70 years), ASA (≥III), ECOG (>1), BMI (≥25 Kg/m^2), extent of the resection (≥3 segments), duration of surgery (≥300 min), estimated blood loss (≥500 mL). Correlations were assessed with Pearson's (r) or Spearman's (ρ) tests depending on the distribution of the variable. Receiver operating characteristic (ROC) were generated and area under the curve (AUC) was calculated. Ideal cut-offs were determined to obtain equal sensitivity and specificity. Logistic regression was performed to identify independent predictors of major complications. Factors with significance <0.1 on univariable analysis were integrated in the multivariable model. Statistical significance was defined as a p-value <0.05. All statistical analyses were performed with IBM SPSS Statistics 25.

Results

During the study period, 307 patients underwent liver surgery. After exclusion of patients without signed consent (n = 32) and patients without available perioperative weight values (n = 94), a total of 181 (59%) patients were analyzed. Characteristics of the patients and surgical details are summarized in Table 1.

Detailed outcomes are provided in Table 2. Minor, major and overall complications were reported in 78 (43%), 25 (14%) and 87 (48%) patients, respectively. No case of postoperative mortality was observed. Median LoS was 8 days (6−12).

Perioperative ΔWeight

Fig. 1 illustrates the perioperative weight change. Median perioperative fluctuation of weight measured on POD2 (ΔWeight) was 2.6 Kg (1.1−4.0). Patients with major complications showed an increased ΔWeight of 4.2 Kg (2.7−5.7), as opposed to 2.3 Kg (0.9−3.7) in patients without major complications ($p < 0.001$).

A correlation analysis was performed, to understand whether this gain of weight was due to fluid management during surgery. ΔWeight poorly correlated with the amount of intravenous fluid received intraoperatively ($r = 0.385$, $p < 0.001$) (Fig. 2).

Cut-off, performance and predictive value of ΔWeight

ROC curve analysis of ΔWeight for major complications revealed an AUC of 0.74 (Fig. 3), determining an optimal cut-off of 3.5 Kg. This cut-off yielded a sensitivity of 72%, specificity of 71%, positive predictive value (PPV) of 28% and a negative predictive value (NPV) of 94%.

Patients showing ΔWeight above this cut-off of 3.5 Kg showed worse outcomes with increased complication rates ($p = 0.005$), higher CCI ($p < 0.001$) as well as prolonged LoS ($p < 0.001$) (Table 2).

Multivariable analysis for major complications integrating multiple potential confounding factors is detailed in Table 3.

Table 1 Demographics and surgical characteristics

	Whole cohort (n = 181)	Major complications (n = 25)	No major complications (n = 156)	P-value
	n (%)	n (%)	n (%)	
Age (≥70 years)	42 (24)	6 (24)	36 (24)	0.828
Gender (Female)	73 (40)	11 (44)	62 (40)	0.687
ASA score (III/IV)	39 (22)	7 (32)	32 (21)	0.244
Cirrhosis	14 (8)	4 (18)	10 (7)	0.06
Cancer	134 (74)	19 (76)	115 (74)	0.809
Diabetes	24 (14)	6 (27)	18 (12)	0.128
BMI (≥25 Kg/m^2)	88 (49)	11 (44)	77 (50)	0.598
Surgical approach (Open)	144 (81)	23 (96)	121 (79)	0.146
Resection extent (≥3 segments)	75 (42)	15 (60)	60 (39)	0.048
Surgery duration (≥300 min)	61 (35)	13 (59)	48 (31)	0.01
Blood loss (≥500 mL)	95 (59)	17 (85)	78 (55)	0.011

Abbreviations: ASA: American Society of Anesthesiologists; BMI: Body mass index; ECOG: Eastern Cooperative Oncology Group.

Table 2 Outcomes

	Whole cohort (n = 181)	ΔWeight		
		<3.5 Kg (n = 117)	≥3.5 Kg (n = 64)	p-value
Complications				
Minor (I–II)	78 (43)	43 (37)	35 (55)	0.028
Major (III–IV)	25 (14)	7 (6)	18 (28)	<0.001
Overall	87 (48)	47 (40)	40 (63)	0.005
Median CCI	0 (0–20.9)	0 (0–20.9)	20.9 (0–33.5)	<0.001
Mean CCI	12.6 (16.0)	8.9 (12.4)	19.3 (19.5)	<0.001
LoS	8 (6–12)	8 (6–10)	10 (8–18)	<0.001

Abbreviations: CCI: Comprehensive Complication Index; LoS: Length of stay.

Cirrhosis (OR, 6.45; 95% CI, 1.35–30.81; p = 0.02) and ΔWeight ≥3.5 Kg (OR, 4.73; 95% CI, 1.51–14.80; p = 0.008) appeared as independent predictors of major complications.

Discussion

The present study suggested that a weight gain on POD2 (ΔWeight) of ≥3.5 Kg was associated with postoperative adverse outcomes after liver surgery, in particular major complications.

Previous data have shown associations between ΔWeight and delayed gastrointestinal function, decreased mobilization or anastomotic leak.[12–16] The rapid weight gain observed after liver surgery raises the question of its underlying mechanisms and causes. Although it may be speculated that such a weight fluctuation resulted from intraoperative fluid management, the

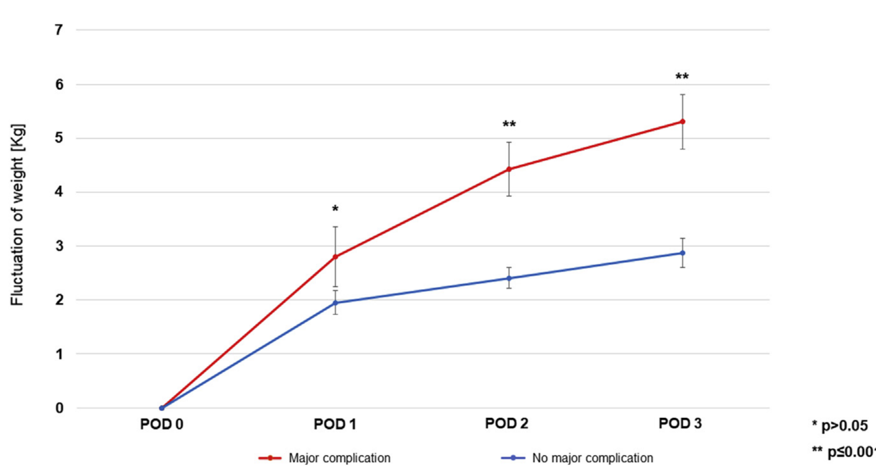

Figure 1 Perioperative fluctuation of weight. Perioperative fluctuation of weight in patients undergoing liver surgery. Curves illustrate the mean values of weight fluctuation, and bars represent standard error of the mean. Blue curve indicates patients without major complication (Clavien III–IV) and red curve illustrates patients with major complications

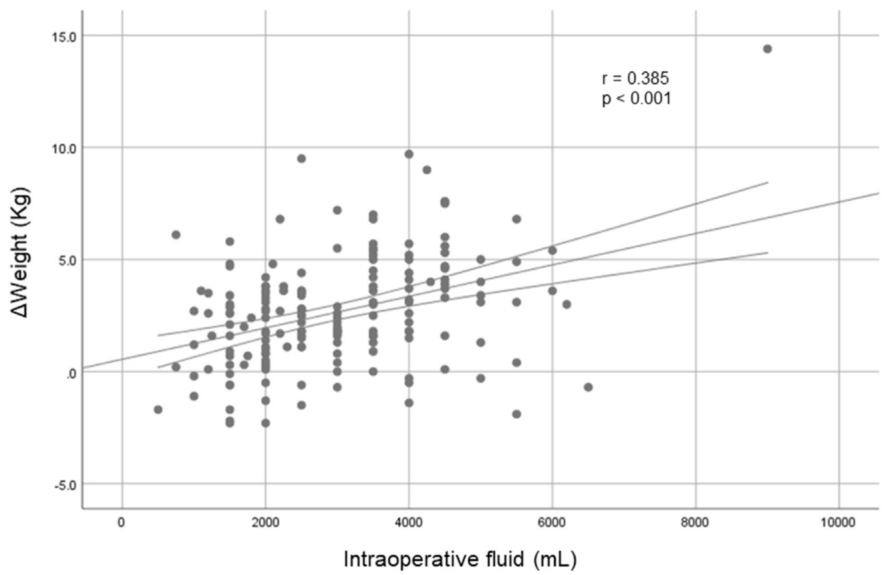

Figure 2 Correlation between ΔWeight and intraoperative fluid administration. Correlation analysis between the volume of intravenous fluid received intraoperatively (mL) and perioperative weight fluctuation measured on POD2 (ΔWeight)

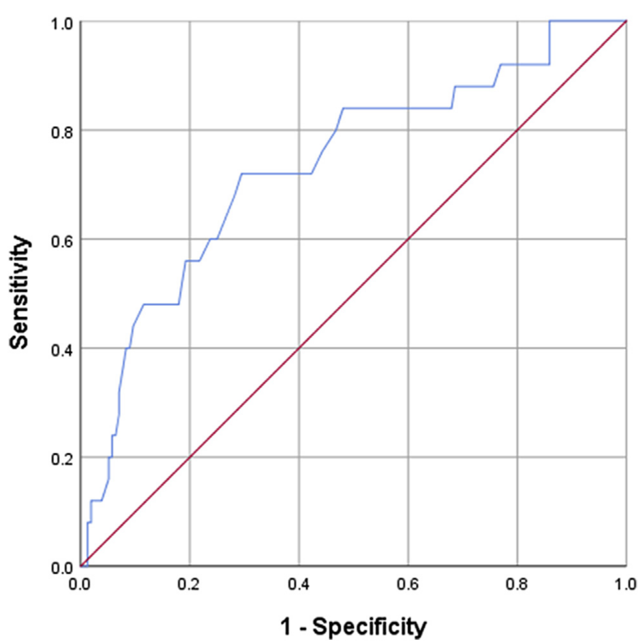

Figure 3 ROC curve of ΔWeight for major complications. Receiver operating characteristic (ROC) curve of ΔWeight for major complications (blue line). Calculated area under the curve (AUC) was 0.74

present results suggest that intraoperative fluid administration alone does not entirely explain ΔWeight since these factors poorly correlated (Fig. 2). However, present results showed continuous postoperative gain of weight beyond POD1. Therefore, it remains possible the ongoing weight gain resulted from ongoing postoperative fluid administration. Although it seems reasonable to hypothesize that ΔWeight reflects different effects induced by surgery such as metabolic stress response which induces capillary leak, responsible of fluid sequestration, hematocrit and albuminemia decreases,[2,17] one must remain cautious about physiological explanations. The present study was not designed to explore the underlying causes of ΔWeight. Dedicated studies are needed to decipher these complex physiological mechanisms.

Major abdominal surgery such as liver resection suffers from the lack of reliable and early biomarkers capable of predicting complications. Laboratory markers currently utilized in clinical practice such as C-Reactive Protein (CRP) or procalcitonin (PCT) are limited by their slow kinetics.[17,18] Furthermore, being metabolized by the liver, CRP is not likely to be highly informative after hepatic surgery. While serum albumin changes can predict overall complications, it has not specifically predicted major complications.[2,19] ΔWeight appears as a promising biomarker displaying several advantages: early predictive, easy to measure, reproducible and cost-effective. Although it showed a low PPV that precludes from detecting patients at high risk of major complications, its high NPV (94%) may allow to identify patients at low risk.

What is unclear from this study is whether modifying ΔWeight by pharmacological or fluid restrictive measures following liver resection could potentially alter the incidence of complications. A more detailed prospective study would be required to answer this question.

Available data on ΔWeight are limited and comparison with similar studies is thus difficult. A recent study from the same institution as the current study investigated ΔWeight in patients undergoing open colorectal surgery. The authors identified ΔWeight ≥3.5 Kg as predictor of overall and respiratory complications as well as prolonged LoS.[5] Consistently, another study showed that ΔWeight ≥1.2 Kg was associated with an increased

Table 3 Multivariable analysis for the prediction of major postoperative complications

	Univariate			Multivariate		
	HR	95% CI	p-value	HR	95% CI	p-value
Age (≥70 years)	1.12	0.41–3.05	0.828			
Gender (Female)	1.19	0.51–2.79	0.687			
ASA score (III/IV)	1.78	0.67–4.73	0.248			
Cirrhosis	3.18	0.90–11.19	0.072	6.45	1.35–30.81	0.020
Cancer	1.13	0.42–3.02	0.809			
Diabetes	1.94	0.76–4.95	0.164			
BMI (≥25 Kg/m^2)	0.80	0.34–1.86	0.599			
Extent of resection	2.35	0.99–5.57	0.052	1.00	0.32–3.14	0.999
Surgery duration (≥300 min)	3.19	1.28–7.97	0.013	2.08	0.65–6.67	0.216
Blood loss (≥500 mL)	4.65	1.30–16.58	0.018	2.53	0.65–9.90	0.183
Surgical approach (open)	1.11	0.74–1.64	0.621			
ΔWeight (≥3.5 Kg)	6.15	2.41–15.72	<0.001	4.73	1.51–14.80	0.008

Abbreviations: ASA: American Society of Anesthesiologists; BMI: Body mass index; CI: Confidence interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard ratio.

risk of postoperative ileus.[6] Limitations of the current study include retrospective single-center design and the limited patient sample with a limited data set. The current results underscore the relevance of monitoring perioperative weight and provide a cut-off that may help to identify patients at lower risk for major complications which can be of precious help. However this cut-off will need to be confirmed and validated through external, independent cohorts.

In summary, the present findings highlighted an association between postoperative weight gain and adverse outcomes after liver surgery, emphasizing the pertinence to monitor perioperative weight in this specific type of surgery.

Author's contribution

1. Study concept and design: IL, ND, MH.
2. Acquisition of data: IL, GRJ, GJ.
3. Analysis and interpretation of data: IL, GRJ, FG, GJ, ND, MH.
4. Drafting of the manuscript: IL, MH.
5. Critical revision of the manuscript for important intellectual content: IL, GRJ, FG, GJ, NH, ND, MH.

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Conflicts of interest
None declared.

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