Original Article

A surgical nursing perspective analysis of glucose variability in BCLC stage B–C hepatocellular carcinoma patients with and without T2D within 1 year of hepatectomy: a retrospective cohort study from 2016 to 2020

Li-Ping Wang[1#], Jia-Sha Zhu[2#], Feng-Di Zhan[3#], Tian Fang[4], Li Zhao[2]

[1]Department of Breast Surgery/Plastic Surgery, Xinhua Hospital affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China; [2]Department of General Surgery, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China; [3]Department of Colorectal Surgery, Fudan University Shanghai Cancer Center, Shanghai, China; [4]Department IV of Biliary Tract Surgery, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, China

Contributions: (I) Conception and design: L Zhao, T Fang; (II) Administrative support: L Zhao, T Fang; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Li Zhao, MB. Department of General Surgery, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, 1665 Kongjiang Road, Shanghai 200082, China. Email: zhaomango@yeah.net; Tian Fang, MB. Department IV of Biliary Tract Surgery, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, 225 Changhai Road, Shanghai 200438, China. Email: 1114180809@qq.com.

Background: Previous research has reported that variability in glucose levels is associated with a variety of patient characteristics in colon cancer. However, relevant research is still lacking in relation to hepatocellular carcinoma (HCC).

Methods: A total of 95 HCC patients with Barcelona Clinic Liver Cancer (BCLC) stage B–C who underwent liver resection at the Eastern Hepatobiliary Surgery Hospital and Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine were included in this study. The patients were divided into 2 groups with type 2 diabetes (T2D) and without T2D. The primary outcome variable was blood glucose variability at 1 month and within 1 year of HCC surgery.

Results: In this study, the age of patients with T2D was greater than that of patients without T2D (mean age: 70.3±8.45 *vs.* 60.4±11.27 years, P=0.031). Compared to the patients without T2D, those with T2D had higher blood glucose measurements within 1 month (33 *vs.* 7) and 1 year (46.5 *vs.* 22.5, P<0.001) of surgery. The T2D patients and non-T2D patients did not differ in terms of chemotherapy medication or other characteristics. Among the 95 patients with BCLC stage B–C HCC, those with T2D had higher variability in glucose levels (P<0.001) than those without T2D within 1 month of surgery [standard deviation (SD) =46.43 mg/dL, coefficient of variation (CV) =23.5% *vs.* SD =21.56 mg/dL, CV =13.21%], and within 1 year of surgery (SD =42.49 mg/dL, CV =26.14% *vs.* SD =20.45 mg/dL, CV =17.36%). A correlation was found between a lower body mass index and higher variability in glucose levels within 1 month of surgery among patients with T2D [SD (r=–0.431, P<0.05) and CV (r=–0.464, P<0.01)]. A higher preoperative blood glucose level in T2D patients was correlated with a higher blood glucose variability within 1 year of surgery (r=0.435, P<0.01). Variability in glucose levels was weakly correlated with the demographic and clinical characteristics of patients who do not have T2D.

Conclusions: HCC patients with T2D in BCLC stage B–C showed greater variability in glucose levels within 1 month and 1 year of surgery. Preoperative hyperglycemia, insulin use, and a lower cumulative dose of steroids were clinical features correlated with a higher variability in glucose levels in T2D patients.

Keywords: Hepatocellular carcinoma (HCC); diabetes; glucose; variability in glucose levels; type 2 diabetes (T2D)

© Journal of Gastrointestinal Oncology. All rights reserved.

Submitted Feb 07, 2023. Accepted for publication Apr 19, 2023. Published online Apr 29, 2023.
doi: 10.21037/jgo-23-163
View this article at: https://dx.doi.org/10.21037/jgo-23-163

Introduction

Hepatocellular carcinoma (HCC) remains one of the greatest challenges in the field of liver disease (1-3). Some patients with Barcelona Clinic Liver Cancer (BCLC) B–C stage suffer from chronic hepatitis and cirrhosis, the latter of which is correlated with a poor survival (4,5). In addition, cirrhosis is strongly correlated with diabetes mellitus (DM) as a result of disruptions in glucose metabolism in the damaged liver (5-7). A significant number of patients with HCC suffer from diabetes (8-10). Many epidemiological research studies have shown that DM also leads to an increased risk of cancer, particularly HCC, for every 1 nmol/L increase in blood sugar, the risk of HCC increased by 4% (11,12).

The presence of DM has also been shown to be a factor that is independent of the prognosis of HCC patients, hyperglycemia increase the incidence of surgical site infections as low immune system function due to metabolic disorders (13). Individuals who suffer from type 2 diabetes (T2D) are unable to maintain their blood sugar levels within a therapeutic range (4,5). A high level of blood sugar, which is an important part of cellular metabolism, is correlated with DM, which in turn is correlated with an increased risk of HCC (5). Numerous studies have examined the relationship between T2D and HCC, and it has been found that patients with T2D have an increased risk of developing HCC (6-8). The prognosis of HCC patients with or without T2D can be improved by stabilizing their blood glucose (9). The development of a standard definition and practice guidelines for the management of glycemic control in cancer patients is still in its infancy.

Researches indicate that cancer patients, regardless of whether or not they have T2D, have high levels of variability in glucose levels (14,15). Variability in glucose levels is currently measured by the standard deviation (SD) and/or coefficient of variation (CV) of the mean blood glucose level (14,15). Despite the fact that the reporting methods of variability in glucose levels and the definitions of unstable glycemic control scores are not uniform, a CV value of >36% has been identified as the cut-off value for distinguishing between stable glycemic control and unstable glucose control in patients with diabetes using continuous glucose monitoring systems (14). A CV cut-off point for glycemic control in cancer patients has not yet been established.

With the exception of colon cancer, only limited research has been conducted on the association between variability in glucose levels and a variety of patient characteristics in cancer patients. Several factors may contribute to variability in glucose levels, including patient demographics, clinical characteristics, and health behaviors. Further, variability in glucose levels has been shown to increase the risk of adverse events, including positive blood cultures and infections (16-18). This retrospective study sought to describe variability in glucose levels and identify the factors correlated with higher levels of variability in glucose levels in a sample of patients with HCC. We present the following article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-163/rc).

Highlight box

Key findings

- Compared to the hepatocellular carcinoma (HCC) patients without type 2 diabetes (T2D), those with T2D with Barcelona Clinic Liver Cancer (BCLC) stage B–C showed greater variability in glucose levels at 1 month and 1 year post-surgery.

What is known and what is new?

- Variability in glucose levels has been reported to be correlated with a variety of patient characteristics in Colorectal cancer (CRC).
- This retrospective study sought to describe variability in glucose levels and identify the factors correlated with higher levels of variability in glucose levels in a sample of patients with HCC.

What is the implication, and what should change now?

- It is possible that a greater awareness and understanding of variability in glucose levels can be gained by conducting nursing research on patients with HCC.

Methods

Samples

This retrospective study was conducted with BCLC stage B–C HCC patients, with or without T2D, treated at the Eastern Hepatobiliary Surgery Hospital and Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine. To be eligible for inclusion in this

© Journal of Gastrointestinal Oncology. All rights reserved.

study, the patients had to meet the following inclusion criteria: (I) have HCC; (II) be aged ≥18 years; (III) have been diagnosed with BCLC stage B–C between January 2016 and December 2020; (IV) have received surgical therapy with or without chemotherapy; and (V) have had 2 or more blood glucose values recorded within 1 year of surgery. Among the identified patients, 39 met the criteria for T2D. A total of 60 patients with type 1 diabetes (a distinctly different disease) were excluded from the study to ensure the homogeneity of our sample. Additionally, patients who had received chemotherapy for a malignancy other than HCC within 1 year of their surgery were excluded from the research. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional committee of Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine (No. XHECC-D-2023-070) and Eastern Hepatobiliary Surgery Hospital (No. EHBHKY2020-02-011). Informed consent was taken from all the patients. Clinical details were extracted from admission.

Hepatectomy

An incision was made in the right subcostal region to perform the hepatectomy under general anesthesia. If possible, a surgical margin of at least 1 cm was made when resecting the tumor. A 1-cm surgical margin could not be made when a tumor was adjacent to major blood vessels, but the tumor resection margin made was wide enough to prevent residual tumors. In cases of multiple tumors, a single liver resection or multiple liver resections were performed, depending on the location of the tumors. The procedure was routinely conducted via a 15-minute/5-minute clamp and unclamp cycle using the Pringle's maneuver. The transection of the liver was performed with an ultrasonic scalpel or by clamp crushing.

Measures

The primary outcome variable was blood glucose variability at 1 month and within 1 year of HCC surgery. Variability in glucose levels was determined based on the SD (mg/dL) and CV of all the available blood glucose measurements within 1 year of surgery. To calculate the CV, the following formula was used: CV = (SD/mean value) × 100% (19). In the absence of any information regarding the timing of the glucose testing with respect to eating, glucose scores were considered to represent random, non-fasting assessments. During the hospital follow-up, data on household income were obtained. The variables in the data were recorded and cleaned before the analysis.

Statistical analysis

An analysis of the data was conducted using SPSS 26 (IBM Corporation, Armonk, NY, USA). Null scores were assigned to any missing data. The analyses were conducted within and between groups. The medians [interquartile ranges (IQRs)] are presented for the continuous variables. The frequencies [N (%)] are presented for the categorical variables. Kolmogorov-Smirnov test was used to determine normality. Mann-Whitney U test was used to compare the continuous variables. A Chi-squared (χ^2) test or Fisher's exact test was used to compare the categorical characteristics between the groups. A Spearman's correlation analysis was performed. A P value <0.05 was set as the threshold for statistical significance.

Results

Clinical and demographic characteristics at the baseline

Over the course of the study, 7,106 glucose measurements were taken. *Table 1* provides a detailed description of the demographic characteristics of the patients. The sample comprised 30 patients (31.6%) with a documented diagnosis of T2D before undergoing surgery. The age of patients with T2D was greater than that of patients without T2D (mean age: 70.3±8.45 *vs.* 60.4±11.27 years, P=0.031). Compared to the patients without T2D, those with T2D had higher blood glucose measurements within 1 month (33 *vs.* 7) and 1 year (46.5 *vs.* 22.5, P<0.001) of surgery. As *Table 2* shows, the T2D patients had higher preoperative blood glucose levels (186 mg/dL) than the non-T2D patients (99 mg/dL, P<0.001). Among the T2D patients, 33.33% used insulin, and 43.33% used oral anti-diabetic drugs, such as metformin (40.6%). Within 1 year of surgery, the patients with T2D received a lower cumulative dose of steroids (121 mg) than those without T2D (1,476 mg, P=0.032). The T2D patients and non-T2D patients did not differ in terms of chemotherapy medication or other characteristics.

Patients with and without T2D: variability in glucose levels

Table 3 sets out the mean blood glucose, SD, and CV of the patients with and without diabetes. Compared to the

© Journal of Gastrointestinal Oncology. All rights reserved.

Table 1 Baseline demographic characteristics

Characteristic	With diabetes (N=30)	Without diabetes (N=65)	P value[a]
Baseline BMI (kg/m^2), median [IQR]	28.00 [22.15–38.41]	28.33 [21.17–37.52]	0.372
Age in years, mean ± SD	70.3±8.45	60.4±11.27	0.031
Gender, n			0.635
Male	15	23	
Female	15	42	
Marital status, n			0.361
Married	22	40	
Divorced	5	10	
Widowed	1	6	
Single	2	9	
Insurance status, n			
Private	15	55	0.028
Sociate	15	10	
Median household income (RMB, Yuan), median [IQR]	30,432 [28,130–50,277]	30,086 [28,184–50,662]	0.874

[a], patients with diabetes *vs*. patients without diabetes by Mann-Whitney U, chi-squared (χ^2), or Fisher's exact tests. BMI, body mass index; IQR, interquartile range; SD, standard deviation.

patients without T2D, there was a significant increase in all blood glucose indicators in the T2D patients at 1 month and 1 year post-surgery (P<0.001).

Indicators of variability in glucose levels and demographic and clinical characteristics

Table 4 shows the Spearman correlation coefficients for variability in glucose levels and the demographic and clinical characteristics of the patients with T2D. In the T2D patients, a higher 1-month SD was correlated with a lower cumulative dose of steroids (r=–0.645, P<0.01) and a lower baseline body mass index (BMI) (r=–0.431, P<0.05) within 1 year of surgery, and administering insulin during surgery (r=0.355, P<0.05). A correlation was found between a higher 1-month CV and a lower baseline BMI (r=–0.464, P<0.01). Additionally, correlations were found between a higher 1-year SD and preoperative blood glucose levels >140 mg/dL (r=0.423, P<0.01), being male (r=0.368, P<0.05), being married (r=–0.339, P<0.05).

Patients without T2D

As *Table 5* shows, among the patients without T2D, higher SDs at 1 month and 1 year were correlated with an older age (r=0.253, r=0.291, P<0.05) and being prescribed more antibiotics within 1 month of surgery (r=0.292, r=0.139, P<0.05). Additionally, higher 1-month and 1-year CVs were correlated with a greater number of antibiotic prescriptions within 1 month of surgery (r=0.136, r=0.122; P<0.05).

Discussion

Recent research has shown that DM negatively affects the prognosis of HCC patients following hepatectomy (20-22). As far as we know, this was the first study to evaluate postoperative variability in glucose levels among HCC patients with BCLC stage B–C using 2 calculation methods (SD and CV). Only a few studies have examined variability in glucose levels in HCC patients, and no research appears to have been conducted that incorporated variability in glucose levels as an outcome measure (23). We found that patients with T2D had higher blood glucose variability at 1 month and 1 year post-surgery than patients without T2D. The variability in the glucose levels of patients with T2D has been reported to be higher than that of non-T2D patients (24) and the range of variability in the glucose levels is broader (25).

© Journal of Gastrointestinal Oncology. All rights reserved.

Table 2 Clinical characteristics and cancer treatment

Characteristic	With diabetes (N=30)	Without diabetes (N=65)	P value[a]
Preoperative glucose, mg/dL (n=72), median [IQR]	186 [153–231] (n=28)	99 [97–109] (n=44)	<0.001
Preoperative glucose >140 mg/dL, n	25	9	<0.001
BCLC stage, n			0.215
B	20	55	
C	10	10	
Number of oral diabetes medications, n			
1	10	0	
2	1	0	
Diabetes therapy at time of surgery, n			<0.001
Insulin	10	0	<0.001
Oral therapy[b]	13	0	<0.001
Insulin and oral therapy	7	0	<0.001
Steroid dose over 1 month following surgery, prednisolone equivalent (mg), median [IQR]	53 [22–67] (n=10)	67 [52–103] (n=20)	0.783
Steroid dose over 12 months following surgery, prednisolone equivalent (mg), median [IQR]	121 [56–872] (n=10)	1,476 [68.5–2,367.5] (n=20)	0.032
Antibiotic use over 12 months, n			0.261
None	27	50	
1 time	0	5	
2 times	2	8	
≥3 times	1	2	
Positive blood cultures within 1 month following surgery, n	2	6	0.873
Positive blood cultures within 12 months following surgery, n	1	5	0.452

[a], patients with diabetes *vs*. patients without diabetes by Mann-Whitney U, chi-squared (χ^2), or Fisher's exact tests. [b], DPP-4 inhibitors, metformin, SGLT2 inhibitors, sulfonylureas. BCLC, Barcelona Clinic Liver Cancer; IQR, interquartile range.

We found an association between a higher variability in glucose levels and demographic and clinical characteristics among T2D patients and non-T2D patients. We observed that the differences in the demographic and clinical variables were correlated with a higher variability in glucose levels over 1 month and 1 year post-surgery, and in the measurement method (i.e., SD and CV). Consistent with previous research (26), we also found that an older age was correlated with greater variability in glucose levels among patients without T2D. Variability in glucose levels may be caused by age-related changes in the cells, such as increased oxidative stress and cellular senescence (27), which are known risk factors for inflammation and hyperglycemia. T2D patients had higher overall blood glucose levels and lower age variability. Despite the fact that T2D is correlated with a higher BMI, higher variability in glucose levels cannot be predicted among patients with T2D and a high BMI (27). There may be differences in pathophysiology between overweight and obese patients and non-overweight and obese patients in relation to pancreatic β-cell function and body fat percentage, which may affect variability in glucose levels (28,29). Further research should be conducted to determine whether other factors, including a patient's overall health, underlying physiology, and comorbidities, may have contributed to such findings.

A weak association was found between men with T2D and higher 1-year SDs. We also observed a moderate association involving a higher 1-year SD and marital status among the

© Journal of Gastrointestinal Oncology. All rights reserved.

Table 3 Comparison of mean glucose, SD, and CV between patients with and without type 2 diabetes within 1 year of surgery

Study variable	With diabetes (N=30), median [IQR]	Without diabetes (N=65), median [IQR]	P value[a]
Mean of glucose measurements, n[b]			<0.001
1 month	33 [13.5–46.50]	7 [4.50–12.0]	
1 year	46.5 [23.50–69.50]	22.5 [11.00–46.50]	
Mean glucose, mg/dL[b]			<0.001
1 month	145.33 [117.96–179.56]	115.36 [103.44–135.96]	
1 year	139.55 [121.25–200.06]	113.32 [102.13–135.44]	
SD, mg/dL[b]			<0.001
1 month	46.43 [31.88–59.37]	21.56 [13.28–29.77]	
1 year	42.49 [30.61–57.13]	20.45 [13.92–29.32]	
CV[b]			<0.001
1 month	23.50 [21.33–35.48]	13.21 [11.54–26.21]	
1 year	26.14 [21.59–37.49]	17.36 [12.96–25.64]	

Glycemic variability was determined by the SD (mg/dL) and CV. [a], with diabetes *vs*. without diabetes by Mann-Whitney U; [b], Tukey's hinges. SD, standard deviation; CV, coefficient of variation; IQR, interquartile range.

Table 4 Correlation between demographic and clinical characteristics and mean glucose, SD, and CV in patients with type 2 diabetes

Covariate	1 month mean glucose	1 month SD	1 month CV	1 year mean glucose	1 year SD	1 year CV
Age at surgery	0.103	0.115	–0.035	–0.066	–0.036	–0.229
BMI	–0.077	–0.431*	–0.464**	0.062	–0.235	–0.336
Gender[a]	0.361	0.243	0.192	0.452**	0.368*	0.136
Employment status[b]	0.016	–0.112	–0.155	0.078	0.162	0.161
Marital status[c]	–0.235	–0.162	–0.123	–0.328	–0.339*	–0.225
Median household income	0.135	0.024	–0.063	0.123	0.236	0.192
Preoperative glucose	0.322	0.192	0.037	0.505**	0.435**	0.292
Preoperative glucose >140 mg/dL	0.298	0.135	0.064	0.436**	0.423**	0.265
Cumulative steroid dose 1 month following surgery	–0.250	–0.230	–0.105	–0.436	–0.288	0.123
Cumulative steroid dose 1 year following surgery	–0.636**	–0.645**	–0.252	–0.298	–0.305	0.064
Taking insulin at time of surgery	0.359*	0.355*	0.196	0.343*	0.286	0.164
Taking insulin 1 year following surgery	0.323*	0.246	0.193	0.361*	0.335*	0.282
Positive blood culture within 1 month following surgery	–0.166	–0.235	–0.286	–0.113	–0.262	–0.295
Positive blood culture within 1 year following surgery	–0.182	–0.236	–0.262	–0.176	–0.246	–0.262
Number of antibiotics prescribed within 1 month following surgery	–0.035	–0.160	–0.126	–0.145	–0.029	0.056
Number of antibiotics prescribed within 1 year following surgery	–0.192	–0.138	–0.067	–0.248	–0.119	0.035

0.00–0.19 = very weak; 0.20–0.39 = weak; 0.40–0.59 = moderate; 0.60–0.79 = strong; 0.80–1.0 = very strong. [a], Female = 0, male = 1. [b], retired = 0, working = 1, other = 2. [c], married = 0, not married = 1. *, P<0.05; **, P<0.01. SD, standard deviation; CV, coefficient of variation; BMI, body mass index.

© Journal of Gastrointestinal Oncology. All rights reserved.

Table 5 Correlation between demographic and clinical characteristics and mean glucose, SD, and CV in patients without diabetes

Covariate	1 month mean glucose	1 month SD	1 month CV	1 year mean glucose	1 year SD	1 year CV
Age at surgery	0.188*	0.253*	0.179	0.235**	0.291*	0.168
BMI	–0.006	–0.061	–0.055	0.195	0.134	0.077
Gender[a]	0.029	–0.124	–0.136	–0.085	–0.119	–0.146
Employment status[b]	–0.144	–0.163	–0.092	–0.173	–0.035	–0.065
Marital status[c]	0.166	0.191	0.122	0.236*	0.164	0.123
Median household income	–0.065	–0.133	–0.105	–0.111	–0.166	–0.114
Preoperative glucose	0.373**	0.162	0.055	0.316**	0.135	0.062
Preoperative glucose>140 mg/dL	0.182	0.065	–0.013	0.176	0.089	0.023
Cumulative steroid dose 1 month following surgery	–0.012	–0.046	–0.099	–0.022	0.025	0.038
Cumulative steroid dose 1 year following surgery	–0.236	–0.222	–0.116	–0.263	–0.191	–0.127
Positive blood culture within 1 month following surgery	–0.070	0.053	0.029	0.066	–0.031	–0.085
Positive blood culture within 1 year following surgery	–0.136	0.063	0.055	0.062	0.163	0.194
Number of antibiotics prescribed within 1 month following surgery	0.166	0.292*	0.136*	0.166	0.139*	0.122*
Number of antibiotics prescribed within 1 year following surgery	0.153	0.142	0.163	0.105	0.176*	0.184*

0.00–0.19 = very weak; 0.20–0.39 = weak; 0.40–0.59 = moderate; 0.60–0.79 = strong; 0.80–1.0 = very strong. [a], Female = 0, male = 1. [b], retired = 0, working = 1, other = 2. [c], married = 0, not married = 1. *, P<0.05; **, P<0.01. SD, standard deviation; CV, coefficient of variation; BMI, body mass index.

T2D patients. Preoperative hyperglycemia, insulin use, and a lower cumulative dose of steroids were clinical features correlated with a higher variability in glucose levels in T2D patients. According to limited evidence, variability in glucose levels is correlated with an increased risk of infection in cancer patients (24,30). We intended to investigate the relationship between blood glucose changes and infection by identifying positive blood cultures; however, only a few patients had positive blood cultures. Despite the finding that prescribing more antibiotics within 1 month and 1 year of surgery was weakly correlated with the1-month and 1-year SDs among patients without T2D, it is unclear whether these antibiotics were prescribed prophylactically or as a result of active infection. To enable interventions to be established to improve outcomes for cancer patients, further research needs to be conducted to investigate the relationship between infection and variability in glucose levels.

Conclusions

As expected, a higher variability in glucose levels was observed in BCLC stage B–C HCC patients within 1 month and 1 year of surgery. To effectively manage the care of cancer patients and those with T2D, it is important to understand blood glucose fluctuations, especially their amplitudes. Future studies will focus on greater awareness and understanding of variability in glucose levels that can be gained by conducting nursing research on patients with HCC. There are many uncertainties in retrospective research, which increase the deviation of research results. We will enlarge sample size and bias analysis to solve the problem.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-163/rc

Data Sharing Statement: Available at https://jgo.amegroups.

© Journal of Gastrointestinal Oncology. All rights reserved.

com/article/view/10.21037/jgo-23-163/dss

Peer Review File: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-163/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-163/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional committee of Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine (No. XHECC-D-2023-070) and Eastern Hepatobiliary Surgery Hospital (No. EHBHKY2020-02-011). Informed consent was taken from all the patients.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

References

1. Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2022. CA Cancer J Clin 2022;72:7-33.
2. Chen D, Liu J, Zang L, et al. Integrated Machine Learning and Bioinformatic Analyses Constructed a Novel Stemness-Related Classifier to Predict Prognosis and Immunotherapy Responses for Hepatocellular Carcinoma Patients. Int J Biol Sci 2022;18:360-73.
3. Tang Y, Xu L, Ren Y, et al. Identification and Validation of a Prognostic Model Based on Three MVI-Related Genes in Hepatocellular Carcinoma. Int J Biol Sci 2022;18:261-75.
4. Jin H, Qin S, He J, et al. New insights into checkpoint inhibitor immunotherapy and its combined therapies in hepatocellular carcinoma: from mechanisms to clinical trials. Int J Biol Sci 2022;18:2775-94.
5. Liu P, Zhong Q, Song Y, et al. Long noncoding RNA Linc01612 represses hepatocellular carcinoma progression by regulating miR-494/ATF3/p53 axis and promoting ubiquitination of YBX1. Int J Biol Sci 2022;18:2932-48.
6. Wlazlo N, Beijers HJ, Schoon EJ, et al. High prevalence of diabetes mellitus in patients with liver cirrhosis. Diabet Med 2010;27:1308-11.
7. Nielsen MF, Caumo A, Aagaard NK, et al. Contribution of defects in glucose uptake to carbohydrate intolerance in liver cirrhosis: assessment during physiological glucose and insulin concentrations. Am J Physiol Gastrointest Liver Physiol 2005;288:G1135-43.
8. Poon RT, Fan ST, Wong J. Does diabetes mellitus influence the perioperative outcome or long term prognosis after resection of hepatocellular carcinoma? Am J Gastroenterol 2002;97:1480-8.
9. Toyoda H, Kumada T, Nakano S, et al. Impact of diabetes mellitus on the prognosis of patients with hepatocellular carcinoma. Cancer 2001;91:957-63.
10. Wang YY, Huang S, Zhong JH, et al. Impact of diabetes mellitus on the prognosis of patients with hepatocellular carcinoma after curative hepatectomy. PLoS One 2014;9:e113858.
11. Kasmari AJ, Welch A, Liu G, et al. Independent of Cirrhosis, Hepatocellular Carcinoma Risk Is Increased with Diabetes and Metabolic Syndrome. Am J Med 2017;130:746.e1-7.
12. He S, Wang J, Shen X, et al. Cancer and its predictors in Chinese adults with newly diagnosed diabetes and impaired glucose tolerance (IGT): a 30-year follow-up of the Da Qing IGT and Diabetes Study. Br J Cancer 2022;127:102-8.
13. Cho WR, Wang CC, Tsai MY, et al. Impact of metformin use on the recurrence of hepatocellular carcinoma after initial liver resection in diabetic patients. PLoS One 2021;16:e0247231.
14. Ceriello A, Monnier L, Owens D. Glycaemic variability in diabetes: clinical and therapeutic implications. Lancet Diabetes Endocrinol 2019;7:221-30.
15. Kovatchev B. Glycemic Variability: Risk Factors, Assessment, and Control. J Diabetes Sci Technol 2019;13:627-35.
16. Hammer MJ, Casper C, Gooley TA, et al. The contribution of malglycemia to mortality among allogeneic hematopoietic cell transplant recipients. Biol Blood Marrow Transplant 2009;15:344-51.
17. Sato H, Hosojima M, Ishikawa T, et al. Glucose Variability Based on Continuous Glucose Monitoring Assessment

© Journal of Gastrointestinal Oncology. All rights reserved.

Is Associated with Postoperative Complications after Cardiovascular Surgery. Ann Thorac Cardiovasc Surg 2017;23:239-47.
18. Luo J, Xu L, Li L, et al. Diabetes mellitus and postoperative blood glucose value help predict posthepatectomy liver failure in patients with hepatocellular carcinoma. J Gastrointest Oncol 2021;12:2377-87.
19. Zhang L, Li F, Liu HH, et al. Glycaemic variability and risk of adverse cardiovascular events in acute coronary syndrome. Diab Vasc Dis Res 2022;19:14791641221137736.
20. Chen J, Han Y, Xu C, et al. Effect of type 2 diabetes mellitus on the risk for hepatocellular carcinoma in chronic liver diseases: a meta-analysis of cohort studies. Eur J Cancer Prev 2015;24:89-99.
21. Zheng Z, Zhang C, Yan J, et al. Diabetes mellitus is associated with hepatocellular carcinoma: a retrospective case-control study in hepatitis endemic area. PLoS One 2013;8:e84776.
22. Koh WP, Wang R, Jin A, et al. Diabetes mellitus and risk of hepatocellular carcinoma: findings from the Singapore Chinese Health Study. Br J Cancer 2013;108:1182-8.
23. Mandolfo N, Berger A, Hammer M. Glycemic variability in patients with gastrointestinal cancer: An integrative review. Eur J Oncol Nurs 2020;48:101797.
24. Xia J, Xu J, Li B, et al. Association between glycemic variability and major adverse cardiovascular and cerebrovascular events (MACCE) in patients with acute coronary syndrome during 30-day follow-up. Clin Chim Acta 2017;466:162-6.
25. Rasmussen Mandolfo N, Berger AM, Struwe LA, et al. Glycemic Variability in Patients With Stage II-III Colon Cancer Treated With Surgery and Adjuvant Chemotherapy. Oncol Nurs Forum 2022;49:571-84.
26. Gude F, Díaz-Vidal P, Rúa-Pérez C, et al. Glycemic Variability and Its Association With Demographics and Lifestyles in a General Adult Population. J Diabetes Sci Technol 2017;11:780-90.
27. Wang J, Yan R, Wen J, et al. Association of lower body mass index with increased glycemic variability in patients with newly diagnosed type 2 diabetes: a cross-sectional study in China. Oncotarget 2017;8:73133-43.
28. Dybala MP, Olehnik SK, Fowler JL, et al. Pancreatic beta cell/islet mass and body mass index. Islets 2019;11:1-9.
29. Echouffo-Tcheugui JB, Zhao S, Brock G, et al. Visit-to-Visit Glycemic Variability and Risks of Cardiovascular Events and All-Cause Mortality: The ALLHAT Study. Diabetes Care 2019;42:486-93.
30. Hammer MJ, Voss JG. Malglycemia and cancer: introduction to a conceptual model. Oncol Nurs Forum 2012;39:E275-87.

Cite this article as: Wang LP, Zhu JS, Zhan FD, Fang T, Zhao L. A surgical nursing perspective analysis of glucose variability in BCLC stage B–C hepatocellular carcinoma patients with and without T2D within 1 year of hepatectomy: a retrospective cohort study from 2016 to 2020. J Gastrointest Oncol 2023;14(2):943-951. doi: 10.21037/jgo-23-163

© Journal of Gastrointestinal Oncology. All rights reserved.