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The Influence of Resection Size and Pringle Maneuver on Operating Time and Intraoperative Bleeding in Patients with Colorectal Metastases in the Liver

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Abstract

BACKGROUND: The extent of the resection, whether clamped or non-clamping resection is factor that influences the operating time and intraoperative bleeding, the development of modern techniques for vascular control and resection, and determine of lesser blood loss, morbidity, and mortality.

AIM: The aim of this study was to determine the experience of General and Hepatobiliary Surgery Clinic at Aleksandrovska Hospital Sofia, Republic of Bulgaria in the treatment of patients with colorectal metastases in the liver and to compare literature reports on the influence of the extent of resection and Pringle maneuver (IPM) on operating time and perioperative bleeding.

MATERIALS AND METHODS: This retrospective study covers the time period from January 01, 2006, until December 31, 2015. A total of 239 patients were included, from which: 179 patients were treated with radical surgery, 5 with palliative intervention, and 55 were subjected on operability exploration.

RESULTS: The use of the IPM for vascular control insignificantly influenced the prolonged operative time, while intraoperative blood loss was significantly lower in patients with Pringle <15 min. There was no association between IPM and resection type, while intraoperative blood loss and operating time were significantly greater in patients with major resection.

CONCLUSION: Resection size is directly proportional to operating time and perioperative blood loss, but it does not significantly influence perioperative morbidity. The IPM does not influence operating time, while blood loss is significantly lower in the group of patients with Pringle <15 min.

Introduction

In Republic of Macedonia, the incidence of colorectal cancer (CRC) is 25/100000 people or between 500 and 600 newly diagnosed patients per year, while mortality is 16/100000 in male population and 11/100000 in women population. In Republic of Bulgaria, the incidence of CRC is 41.2/100000 in male population and 32.7 in the women population [1]. The incidence rate of synchronous liver metastases was 6.9/100 000 inhabitants in men and 3.4/100 000 inhabitants in women, with no significant variation since 2000. The 5-year cumulative incidence of metachronous liver metastases decreased from 18.6% (95% CI, 14.9%–22.2%) during the 1976–1980 period to 10.0% (95% CI, 8.8%–11.2%) during the 2006–2011 period [2]. In the era of modern oncology therapy, the survival of patients with colorectal metastases has increased after liver resection (33.3% vs. 49.0%) [3]. Non-anatomic resection had a comparable safety and efficacy profile compared with anatomic resection and did not compromise oncologic outcomes. Non-anatomic resection should be considered an appropriate surgical approach to treatment for patients with colorectal liver metastases (CRLM) that facilitates preservation of hepatic parenchyma [4]. Blood loss and transfusion have increased the length of hospital stay, worsened postoperative outcomes, and increased morbidity in liver resection patients [5], [6]. Pringle maneuver (IPM) is the oldest and simplest method for vascular control and today with more modifications are used from many surgeons [7], [8], [9]. Comparison between continuous and intermittent IPM whit cumulative clamping time between 30 and 50 min can shorten operation time, reduce intraoperative bleeding and perioperative transfusion, and reduce postoperative complications and postoperative liver function injury [10].

Materials and Methods

This retrospective study was conducted at the Clinic of General and Hepatopancreatic

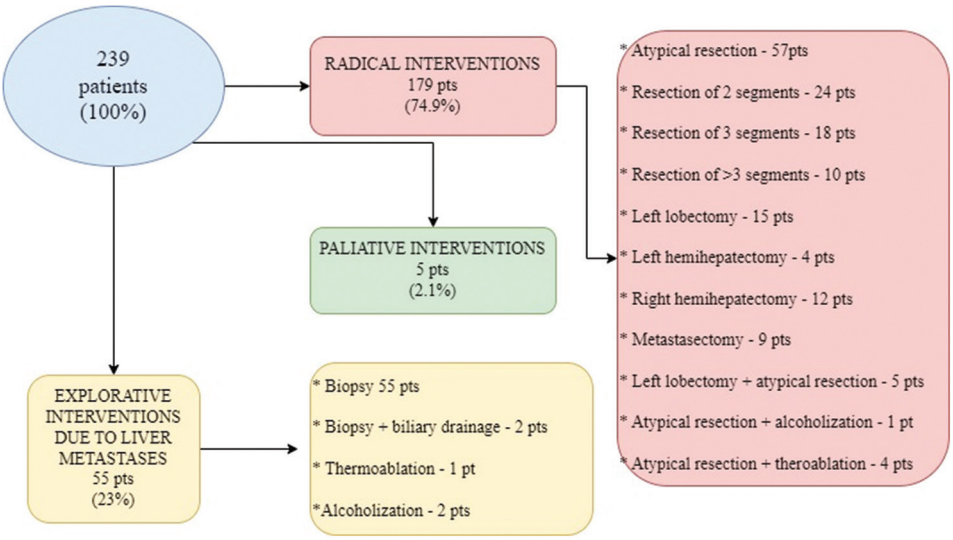

Figure 1: Distribution of patients' population

Surgery at the University Hospital "Aleksandrovska" – Sofia, Bulgaria. The study comprised the period between 01.01.2006 and 31.12.2015. It included a total of 239 patients, of whom: 179 patients (74.9%) underwent radical interventions (atypical resection - 57, resection of 2 segments - 24, resection of 3 segments - 18, resection of >3 segments - 10, left lobectomy - 15, left hemihepatectomy - 4, right hemihepatectomy - 12, metastasectomy - 20, resection with another procedure - 19, atypical resection and metastasectomy - 9, left lobectomy and atypical resection - 5, atypical resection and alcoholization - 1, atypical resection and thermoablation - 4; and 5 palliative and 55 patients underwent explorative interventions due to liver metastases (biopsy - 55, biopsy and biliary drainage - 2, thermoablation - 1, and alcoholization - 2). Furthermore, 119 (49.8%) patients were diagnosed with synchronous metastases, 120 (50.2%) patients with metachronous metastases, and including 7 (2.9%) with metachronous metastases with recurrence on the colon (Figures 1 and 2).

The follow-up period of the patients operated on for CRLM in the Clinic was 5 years after resection of the liver. The study included all patients with liver metastases from CRC regardless of their age and gender; the study included all patients with liver metastases from CRC: synchronous metastases, metachronous metastases, and metastases appearing with local recurrence of cancer; Exclusion criteria were patients who did not meet inclusion criteria and patients who refused to participle in the study. The endpoints were to determine the following: (1) To evaluate the application of the IPM in different types of resections, (2) To assess the duration of the IPM in different types of liver resections, (3) To compare the blood loss volume according duration of the IPM and patients with applied non-clamped technique, (4) To estimate the length of surgery in patients with and without Pringle maneuver, and (5) To assess the connection between the length of surgery with intraoperative blood loss.

Statistical analysis of the collected material to determine the factors for survival was done using the SPSS-19 statistical program.

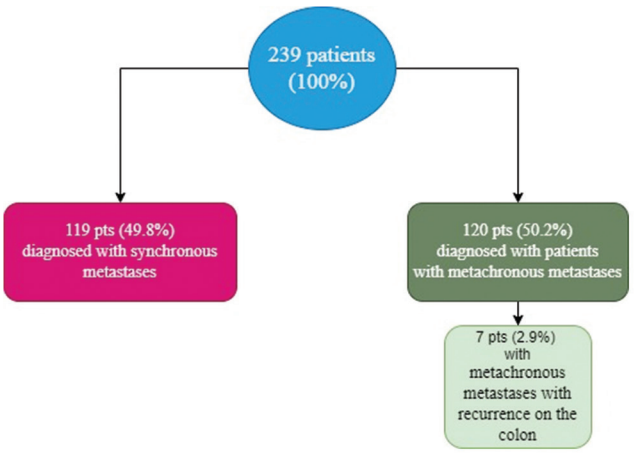

Figure 2: Distribution of patients' population according to metastases

Results

In 31.84% of the patients, who had radical surgery, in time of liver resection, an IPM was used to achieve vascular control. Median time was 16.37 ± 8.3 min. The shortest time of use was 5 min, whereas the longest time was 60 min, in which an intermittent technique was used. Patients, who were subjected to the IPM, were classified into two groups, according time spend – under 15 min and over 15 min. In 18.43% of the patients, the method of vascular control was used shorter than 15 min, median 12.06 ± 2.7 min. In 13.4% of the patients, the method was used longer than 15 min, median 22.3 ± 9.7 min. While using IPM

for longer than 20 min, an intermittent IPM was used. In two patients, ischemic preconditioning with IPM, lasting 20 min was applied. In Table 1 are shown type of liver resection with the use of the IPM. The most used method was right hepatectomy (9/12) and in combined radical surgery (10/19).

Table 1: Classification of type of liver resection based on the use of the Pringle maneuver

Type of liver resection	Pringle maneuver	
	Without Pringle n = 122	With Pringle n = 57
Atypical resection n = 57	49	8
Resection of 2 segments n = 24	12	12
Resection of 3 segments n = 18	11	7
Resection of more than 3 segments n = 10	6	4
Left lobectomy n = 15	11	4
Left hemihepatectomy n = 4	2	2
Right hemihepatectomy n = 12	3	9
Metastasectomy n = 20	19	1
Resection+other procedures n = 19	9	10
atypical resection+metastasectomy	3	6
left lobectomy+atypical resection	3	2
atypical resection+thermoablation	2	2
atypical resection+alcohol ablation	1	0

Table 1 shows surgical interventions classified into three groups based on the use of the IPM and its time of duration.

The IPM was used in 34.17% of the patients, subjected to major resections, while 27.12% of the patients had small resections. There was no statistically significance in dividing patients with and without Pringle according resection size (p = 0.34) (Table 2 and Figure 3). A more significant factor for use of the method was localization of metastases to major blood vessels of the liver.

Table 2: Types of liver resection with and without Pringle maneuver

Type of liver resection	Pringle maneuver		
	Without Pringle n = 122	Pringle< 15 min n = 33	Pringle> 15 min n = 24
Atypical resection	49	7	1
Resection of 2 segments	12	10	2
Resection of 3 segments	11	5	2
Resection of more than 3 segments	6	1	3
Left lobectomy	11	4	0
Left hemihepatectomy	2	1	1
Right hemihepatectomy	3	1	8
Metastasectomy	19	1	0
Resection+other procedures	9	3	7

Blood loss was another factor, who has influence over perioperative mortality. Comparison between patients, who had postoperative complications, with those who had no postoperative complications, showed that the former group had greater blood loss – 488.10 mL versus 319.35 mL (p = 0.000). For the reasons, mentioned above, we analyzed the volume of blood loss in different groups of patients (with and without the use of IPM and duration of the method <15 min and >15 min). The lowest blood loss was observed in patients, in which the IPM was used for under 15 min (Table 3).

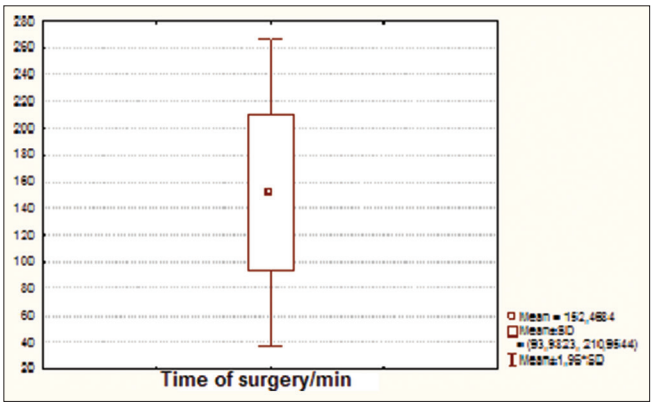

Figure 3: Operating time of liver resection

Table 3: Comparison of blood loss volume according duration of the Pringle maneuver and patients with applied non-clamped technique

Variable	Pringle	Descriptive statistics		p-value
		Mean ± SD	SE (median)	
Blood loss	Without Pringle	488.10 ± 170.5	18.6	0.972
	Pringle> 15 min	486.96 ± 123.6	25.77	
Blood loss	Without Pringle	488.1 ± 170.5	18.6	0.000
	Pringle< 15 min	319.35 ± 55.8	10.02	
Blood loss	Pringle> 15 min	486.96 ± 123.6	25.77	0.000
	Pringle< 15 min	319.35 ± 55.8	10.02	

*SD: Standard deviation; SE (median): Standard error of the median

The use of IPM and resection size has influence over time of surgery. Liver resection was between 50 min (shortest time) and 340 min (longest time), with median operating time of 152.5 ± 58.5 min (Figure 3).

The average operating time was the longest in patients' group, who had resection of three liver segments (175 ± 48.8 min), followed by the group of patients, who had right hepatectomy (168 ± 56.1 min) (Table 4). It is worth of noting that operating time depends on the experience of the surgeon with different procedures and liver resection techniques and thus operating time of discussed techniques is of significance.

Table 4: Operating time distribution of surgical procedures in patients with CRC, according average operating time, P (ANOVA)

Resection type	Descriptive statistics operating time/minutes		p-value
	Mean ± SD	min–max	
Atypical resection	150.1 ± 60.6	60–300	p = 0.6
Resection of 2 segments	132.7 ± 48.8	70–240	
Resection of 3 segments	175 ± 48.8	100–280	
Resection of more than 3 segments	152.5 ± 61.4	60–240	
Left lobectomy	155.7 ± 48	100–240	
Left hemihepatectomy	137.5 ± 29.9	100–170	
Right hemihepatectomy	168 ± 56.1	120–280	
Metastasectomy	161.4 ± 76.6	60–340	
Resection+other procedures	151.7 ± 68.1	50–340	

CRC: Colorectal cancer

We confirmed that the duration of operative time is directly proportional with the number of resected segments (p = 0.0001). Liver resection had longer operating time in patients with greater by-volume procedures (164.9 ± 56.5 vs. 127.2 ± 54.7 min) (Table 5).

Table 5: Operating procedures distribution according volume and mean operating time, P (Student t-test)

Volume of operation according the number of resected segments	Descriptive statistics operating time/minutes		p-value
	Mean ± SD	min–max	
Major	164.9 ± 56.5	60–340	p = 0.0001**
Small	127.2 ± 54.7	50–340	

Operating time was insignificantly longer in patients who had liver resection carried out using the IPM compared with the group of patients, in which method of vascular control during liver resection was

Table 6: Operating time analysis in patients with applied Pringle maneuver and time duration, P (Student t test)

Operating time	Pringle maneuver	Descriptive statistics operating time/minutes		p-value
		Mean ± SD	Min–Max	
Operating time	Pringle	158.9 ± 52.5	60–340	p = 0.3
	Without Pringle	148.9 ± 61.6	50–280	
Operating time	Pringle< 15 min	150.7 ± 50.9	60–250	p = 0.25
	Pringle> 15 min	170.0 ± 53.6	90–340	

not used (158.9 ± 52.5 vs. 148.9 ± 61.6).

In the patients' group, that had been applied the IPM, the operating time was insignificantly longer when Pringle was used for more than 15 min versus intervention with clamped resection under 15 min (170.0 ± 53.6 vs. 150.7 ± 50.9) (Table 6 and Figure 4). Those results are easily read due to the fact that usually bigger by volume liver resections require more precise vascular control because of procedural complexity, which affects the duration of surgery, making the operating time longer.

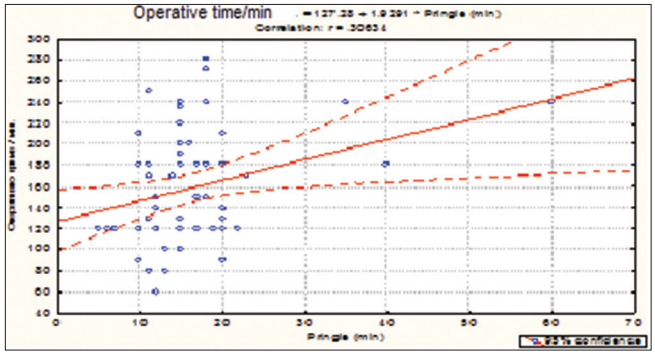

Figure 4: Influence of the clamped technique on general operating time (r = 0.306, p = 0.02 *p < 0.05)*

As we established that operative blood loss affects postoperative complications, we analyzed the potential association between intraoperative blood loss and operating time. The association between these two operating factors was statistically significant (p = 0.008), which in turn, underlines the importance of the surgeon's experience. The correlation is directly proportional (r = 0.21) – blood loss volume is greater with longer operating time and vice versa (Figure 5).

Discussion

Perioperative blood transfusion has increased the length of hospital stay, worsened postoperative outcomes, and increased morbidity in liver resection patients [5], [6]. Hepatic vascular occlusion methods, mostly the PM, are still frequently used by surgeons to control bleeding during liver resection and to decrease perioperative blood transfusion [7], [8], [9]. The IPM is associated with a significant reduction of a blood during surgery when is it combined with stapler technique for transection of hilar structures [11]. The use of continuing Pringle under 15 min, in our study, has shown significant intraoperative blood loss reduction versus resections done without vascular control method, from 319.35 mL to 488.10 mL, respectively (p = 0.000). The intermittent IPM does not cause additional liver damage during hepatectomy, and use of the IPM results in shorter hospital stays compared to surgery without using the IPM [12]. In patients' group, that had been applied IPM over 15 min, where intermittent technique was used, greater blood loss was noticed compared with the group that had been applied continuing Pringle under 15 min, 486.96 ± 123.6 mL versus 319.35 mL (p = 0.000), respectively. Intermittent IPM with a 25-min ischemic interval can be applied safely and efficiently in open or laparoscopic hepatectomy [13]. There was no significant difference in blood loss between the use of intermittent technique and resection, without vascular control method (488.10 ± 170.5 mL).

Compared with IPM, CPM with a cumulative

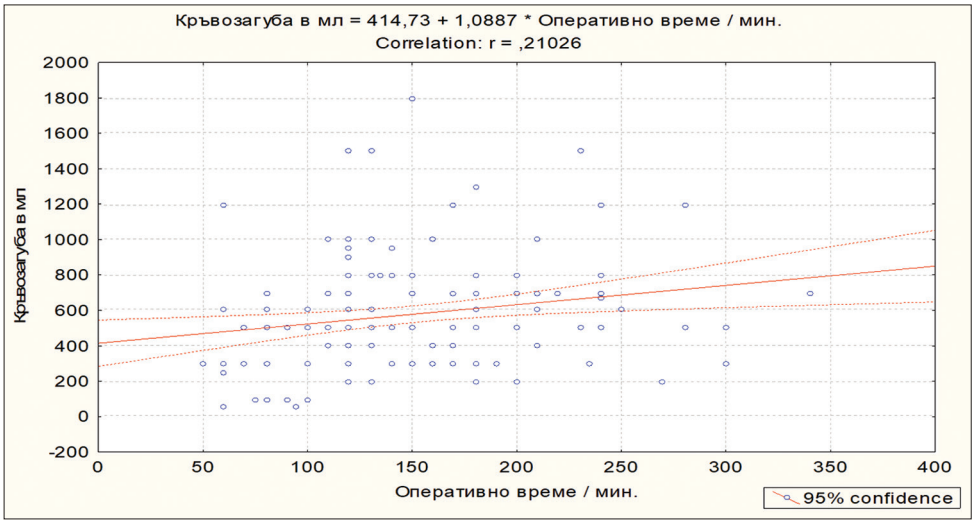

*Figure 5: Dependence of blood loss volume from operating time r = 0.21 p = 0.008** **p < 0.01*

clamping time between 30 and 50 min can shorten operation time, reduce intraoperative bleeding and perioperative transfusion, and reduce postoperative complications and postoperative liver function injury in patients who underwent complex hepatectomy [10]. The IPM had lost its value in patients with CRLM, although it remained controversial in patients with hepatocellular carcinoma [14]. Performing selective vascular hepatic exclusion in major hepatectomy may result in reduced rates of morbidity and mortality when compared to an IPM [15]. Continuous half-IPM offers the advantages of less operative time and blood loss, less injury, and better recovery [16]. Applying infrahepatic inferior vena cava clamping combined with the IPM can effectively reduce intraoperative bleeding, blood transfusion rates, and postoperative complications, while adding minimal time to the operation [17]. In our study, resection without IPM had an insignificant shorter operative time compared with the group with IPM, especially in group with Pringle over 15 min. Resections, that were greater in volume (major resections), have shown significant influence on operating time ($p = 0.0001$), i.e., they take a great deal of time. There was no statistical significance in IPM on operating time, regardless of time duration for its use. The correlation between intraoperative blood loss and operative time was found to be significant, i.e., longer and larger resections have greater blood loss.

Conclusion

Short-term use of the IPM showed a significant reduction of intraoperative blood loss, longer-term use of the intermittent Pringle does not affect the reduction of blood loss and is comparable to the group of resections without the use of Pringle. This method of vascular control does not affect the operative time, which directly affects the blood loss.

Study limitations

The retrospective design is a limitation of this study due to the inability to follow patients and directly observe the effects of surgical treatment and possible early or late complications. The use and decision to apply the IPM were based on surgeon preference and were not influenced by patient-related factors.

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