Comparative Analysis between Simultaneous Resection and Staged Resection for Synchronous Colorectal Liver Metastases – A Single Center Experience on 300 Consecutive Patients

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Rezumat

Analiza comparativă între rezecția simultană și rezecțiile seriate pentru metastaze hepatice colorectale sincrone - experiența a 300 de pacienți consecutivi operați într-un singur centru

Introducere: Rezecția simultană (SR) a tumorii colorectale și a metastazelor hepatice sincrone (SCLMs) nu este utilizată pe scară largă. Majoritatea autorilor preferă încă rezecțiile seriate (SgR), mai ales la pacienții cu cancer de rect sau care necesită efectuarea unei hepatectomii majore.

Material și metodă: Ratele morbidității, mortalității și supraviețuirii, precum și durata medie a spitalizării au fost comparate între cele două grupuri (SR vs. SgR). De asemenea, acești parametri au fost comparați și între diverse subgrupuri de pacienți cu caracteristici similare (tumoră de rect, hepatectomie majoră, metastaze bilobare, chimioterapie preoperatorie, etc).

Rezultate: Între 1995 și 2016, la 234 de pacienți s-a practicat SR, iar la 66 de pacienți SgR. Ratele comparative ale morbidității (41%, respectiv 31.8%, $p = 0.1997$), mortalității (3.8%, respectiv 3%, $p = 1$) și supraviețuirii globale (85.8%, 51.3% și 30%, respectiv 87%, 49.6% și 22.5%, la 1-, 3- și 5-years, $p = 0.386$) nu au fost semnificativ

Abbreviations:

SCLMs – synchronous colorectal
liver metastases;
SgR – staged resections
SR – simultaneous resection;

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statistic diferite între cele două grupuri (SR vs. SgR). Durata medie a spitalizării a fost semnificativ mai scurtă după SR decât după SgR (15.11 ± 8.60 , respectiv 19.42 ± 7.36 zile, $p < 0.0001$). Caracteristicile celor două grupuri au fost similare, cu excepția următorilor parametri: localizarea rectală (mai frecventă în SR grup, $p = 0.0245$), invazia ganglionară (mai frecventă în SgR grup, $p = 0.0383$), metastaze bilobare (mai frecvente în SgR grup, $p = 0.0169$), hepatectomii majore (mai frecvente în SgR grup, $p = 0.025$), chimioterapie neo-adjuvantă (mai frecvent în SgR grup, $p < 0.0001$). A fost efectuată o analiză comparativă a morbidității, mortalității și supraviețuirii pentru fiecare din subgrupurile de pacienți prezentând aceste caracteristici. Pentru fiecare subgrup, SR a fost asociată cu rate similare ale morbidității, mortalității și supraviețuirii ca și SgR ($p > 0.05$).

Concluzii: La pacienții cu SCLMs, SR oferă rezultate pe termen scurt și lung similare SgR și o durată mai scurtă a spitalizării. Pentru majoritatea pacienților cu SCLMs, SR ar trebui considerată abordarea terapeutică de elecție.

Cuvinte cheie: sincron, cancer colorectal, metastaze hepatice, rezecție simultană, rezecție seriată, chimioterapie

Abstract

Introduction: In synchronous colorectal liver metastases (SCLMs), simultaneous resection (SR) of the primary tumor and liver metastases has not gained wide acceptance. Most authors prefer staged resections (SgR), especially in patients presenting rectal cancer or requiring major hepatectomy.

Methods: Morbidity, mortality, survival rates and length of hospital stay were compared between the two groups of patients (SR vs. SgR). A subgroup analysis was performed for patients with similar characteristics (e.g. rectal tumor, major hepatectomy, bilobar metastases, metastatic lymph nodes, preoperative chemotherapy).

Results: Between 1995 and 2016, SR was performed in 234 patients, while 66 patients underwent SgR. Comparative morbidity (41% vs. 31.8%, respectively, $p = 0.1997$), mortality (3.8% vs. 3%, respectively, $p = 1$) and overall survival rates (85.8%, 51.3% and 30% vs. 87%, 49.6% and 22.5%, at 1-, 3- and 5-years, respectively, $p = 0.386$) were similar between the SR and SgR group. Mean hospital stay was significantly shorter in patients undergoing SR than SgR (15.11 ± 8.60 vs. 19.42 ± 7.36 days, respectively, $p < 0.0001$). The characteristics of SR and SgR groups were similar, except the following parameters: rectal tumor (34.1% vs. 19.7%, respectively, $p = 0.0245$), metastatic lymph nodes (68.1% vs. 86.3%, respectively, $p = 0.0383$), bilobar liver metastases (22.6% vs. 37.8%, respectively, $p = 0.0169$), major hepatectomies (13.2% vs. 30.3%, respectively, $p = 0.0025$) and neo-adjuvant chemotherapy (13.2% vs. 77.2%, respectively, $p < 0.0001$). A comparative analysis of morbidity, mortality and survival rates between SR and SgR was performed for subgroups of patients presenting these parameters. In each of these subgroups, SR was associated with similar morbidity, mortality and survival rates compared with SgR (p value > 0.05).

Conclusion: In patients with SCLMs, SR provides similar short-term and long-term outcomes as SgR, with a shorter hospital stay. Therefore, in most patients with SCLMs, SR might be considered the treatment of choice.

Key words: synchronous, colorectal cancer, liver metastases, simultaneous resection, staged resection, chemotherapy

Introduction

Although the treatment of liver metastases

from colorectal cancer is multimodal, the only potentially curative approach to these patients consists in complete resection of liver metas-

tases (LM). In patients with synchronous colorectal metastases (SCLMs), the treatment should aim the curative resection of both primary tumor and LM. To achieve these objectives, three surgical approaches are available: 1. Simultaneous resection (SR) of colorectal cancer and LM; 2. Resection of the primary tumor followed by resection of LM (delayed liver resection – DR); 3. Initial hepatectomy and subsequent colorectal resection (“liver-first” approach).

Because SR implies association of two major operations during the same operative procedure, many authors were skeptical about the safety of this surgical approach to SCLMs. Simultaneous performance of colorectal resection and hepatectomy was considered to be associated with higher morbidity and mortality rates than staged resections (either DR or “liver-first” approach) (1,2). Moreover, most patients undergoing DR will receive chemotherapy during the interval between colorectal resection and liver resection (3,4). Also, in “liver-first” approach the patients usually receive chemotherapy before hepatectomy (5). In patients whose LM progress during chemotherapy, liver resection is frequently abandoned because of the very low survival rates achieved by hepatectomy (5-year overall survival less than 8%) (6). On the other hand, most of the patients who underwent SR did not receive chemotherapy before operation. Thus, it was hypothesized that staged resections (SgR) allow a better selection of patients than SR and this will translate in higher survival rates following SgR (3,7). However, these theoretical assumptions have been challenged during the last decade by the results reported by several centers experienced in colorectal and liver surgery (8-10).

Hereby, are presented the results achieved by SR and SgR in 300 consecutive patients with SCLMs, operated in a single center.

Methods

In “Dan Setlacec” Center of General Surgery and Liver Transplantation from Fundeni Clinical Institute, all the patients diagnosed

with colorectal cancer who did not require emergency surgery, underwent preoperative contrast-enhanced abdominal CT scan or MRI to assess the presence of liver metastases. Whenever preoperative imaging could not rule out the presence of liver metastases, it was performed intraoperative ultrasonography during the operation addressed to the primary tumor. During colorectal resection all patients underwent intraoperative evaluation of the liver. Moreover, in patients requiring urgent operation caused by the complications of the colorectal tumor, who did not underwent preoperative CT scan or MRI, one of the aforementioned investigations has been performed before discharging the patient.

The metastases that were diagnosed in this manner (preoperatively, during operation or during hospitalization after resection of the colorectal tumor) were considered as synchronous metastases. In the present study, there were retrospectively enrolled the first 300 consecutive patients who underwent curative intent resection of primary tumor and liver only synchronous metastases in “Dan Setlacec” Center of General Surgery and Liver Transplantation from Fundeni Clinical Institute, from 1995 to 2015. As well, the patients with initially unresectable SCLMs were excluded.

Out of the 300 patients, 234 underwent SR while 66 patients underwent SgR (61 patients with DR and 5 patients with “liver-first” approach).

The parameters that were evaluated were: age, gender, location of the primary tumor, T status and N status (according to the 7th edition of TNM staging system), number and the largest size of liver metastases, distribution of liver metastases (unilobar vs. bilobar), chemotherapy before liver resection, extent of liver resection (minor vs. major hepatectomy), completeness of hepatectomy, estimated blood loss, number of patients receiving transfusion, total operative time and the length of hospital stay.

Total operative time represented the duration of the operation for patients undergoing SR. In patients who underwent SgR, the total operative time was calculated as the sum of the

operative times of the two procedures. The length of hospital stay represents the days of hospitalization for patients undergoing SR and the sum of the days of hospital stay after colorectal resection and liver resection, in SgR patients.

The Mann-Whitney test was used to compare quantitative variables. A *p* value below 0.05 was considered to be statistically significant.

Any complication that occurred during hospitalization or within 30 postoperative days (POD) was recorded and reported when the postoperative morbidity was calculated. For patients who underwent a SgR, complications were generated as the sum from colorectal and liver procedure. Mortality was calculated taking into account any death occurring during hospitalization after liver resection or within 30 days after hepatectomy.

The morbidity and mortality rates between different groups of patients were compared with Chi-square test or Fischer exact test. The difference was considered statistically significant when *p* value < 0.05.

The survival was defined as the interval between the liver resection and the last follow-up or the date of patient's decease. The 1-, 3- and 5-year overall survival rates and the median survival were estimated with Kaplan-Meier test. The survival rates between different groups of patients were compared with Log-rank test. When the *p*-value was lower than 0.05, the difference was considered statistically significant.

In patients undergoing SR, neo-adjuvant chemotherapy was delivered before resection of the primary tumor and liver metastases. In patients who underwent SgR, it was delivered either during the interval between colorectal resection and liver resection (in DR), or before hepatectomy in patients undergoing "liver-first approach".

Results

Characteristics of the SR Group and SgR Group

The comparative analysis of the two groups

(SR group and SgR group, respectively), revealed that age, gender, T-stage, number and size of SCLMs, completeness of liver resection, estimated blood loss and the number of patients who required transfusion were similarly distributed in the two groups (*Table 1*). However, some characteristics related to the primary tumor, liver metastases, surgical procedure and oncologic treatment were significantly different between the two groups (*Table 1*).

Primary Tumor

In the SR group, significantly more patients had a rectal tumor than in the SgR group (34.1% vs. 19.6%, *p* value = 0.0245).

The proportion of patients without lymph-nodes metastases (N0) was significantly higher in SR group than in SgR group (31.8% vs. 13.6%, *p* value = 0.0383).

Liver Metastases

Regarding the distribution of SCLMs, the bilobar involvement of the liver was more frequent in the SgR group than in the SR group (37.8% vs. 22.6%, *p* value = 0.0169).

Operative Procedure

Major hepatectomy was significantly more frequently performed in SgR group, comparative with the number of patients undergoing major liver resection in SR group (30.3% vs. 13.2%, *p* value = 0.0025).

In the SgR group, the mean total operative time was 315.405 ± 76.634 minutes (median 320 minutes), while in patients undergoing SR, the mean operative time was 229.414 ± 100.47 minutes (median 200 minutes). The duration of operative time was highly significant longer in SgR group than in SR group (*p* value < 0.0001).

The mean lengths of hospital stay was statistically significant longer in SgR group than in SR group (19.421 ± 7.363 days vs. 15.111 ± 8.604 days, *p* value < 0.0001; median 18 vs. 12 days).

Oncologic Treatment

A significantly higher number of patients underwent neo-adjuvant chemotherapy in

Table 1. Comparative analysis of patients' characteristics in SR group and SgR group

	SR (n=234)	SgR (n=66)	p value
Age (year-old)	62	59	0.1601
Median (mean $\pm$ SD)	(60.659 $\pm$ 10.528)	(59.075 $\pm$ 9.097)	
Gender			0.6747
Male	132	35	
Female	102	31	
Primary			0.0245
Colon	154	53	
Rectum	80	13	
T stage*			1
T1-T3	187	42	
T4	31	6	
N stage**			0.0383
N0	63	6	
N1	58	19	
N2	77	19	
Extent of LR			0.0025
Minor	203	46	
Major	31	20	
No of SCLMs			0.0600
1	137	28	
2-3	70	26	
≥ 4	27	12	
SCLMs diameter			0.0519
< 5 cm	168	39	
> 5 cm	66	27	
Distribution			0.0169
Unilobar	181	41	
Bilobar	53	25	
Preoperative chemo			< 0.0001
Yes	31	51	
No	203	15	
Operative time (min)	200	320	< 0.0001
Median (mean $\pm$ SD)	(229.414 $\pm$ 100.47)	(315.405 $\pm$ 76.634)	
Blood loss (ml)	300	225	0.3498
Median (mean $\pm$ SD)	(557.547 $\pm$ 731.66)	(308.333 $\pm$ 178.16)	
Incomplete resections (R1/R2)	9	2	1
Patients receiving RBP	46	11	0.7227
Length of hospital stay (days)	12	18	< 0.0001
Median (mean $\pm$ SD)	(15.111 $\pm$ 8.604)	(19.421 $\pm$ 7.363)	

* Missing data in 34 patients; ** Missing data in 58 patients

SgR group, than in the SR group (77.2% vs. 13.2%, p value = 0.0245).

Morbidity Rates

In the SR group, the morbidity rate was 41% (96/234 patients), while in SgR group, 21 patients (31.8%) developed complications. The difference was not statistically significant (p value = 0.1997).

Among the patients with rectal tumors undergoing SR, the morbidity rate was, not statistically significant higher than those observed in patients with rectal tumors who underwent SgR (45% vs. 30.7%, respectively; p value = 0.3825).

As well, in patients undergoing major hepatectomy and simultaneous resection of the primary tumor, the morbidity rate was similar to that observed in patients undergoing major

hepatectomy as part of a staged procedure (45.1% vs. 45%, respectively; p value = 1).

Similarly, the presence of multiple SCLMs, the bilobar distribution of metastases, neo-adjuvant chemotherapy or other characteristics of tumors and therapy did not significantly increase the morbidity rates in SR group vs. SgR group (p value > 0.05) (Table 2).

Mortality Rates

In the SR group, 9 patients deceased post-operatively (3.8%), while in the SgR group, the mortality rate was 3% (2/66 patients). The difference was not statistically significant (p value = 1).

One patient with rectal tumor deceased after SR (1.2%), whereas no death occurred among patients with rectal cancer and SCLMs who underwent a staged procedure. The mortality rates of patients with primary tumors confined to the rectum were similar in the SR group and SgR group (p value = 1).

In patients requiring major hepatectomies for their SCLMs, the mortality rate in SR group was similar to those achieved in SgR group (6.4% vs. 5%, respectively; p value = 1).

Mortality rates of patients with multiple SCLMs were similar among the two groups of patients (p value = 1); in SR group the mortality rate was 6.4% (5/97 patients), while in the SgR group it was 5.2% (2/38 patients).

When bilobar SCLMs were present, the mortality rates were similar in the SR group and SgR group (1.8% vs. 0%, respectively; p value = 1).

In patients undergoing neo-adjuvant chemotherapy, SR was associated with similar mortality as SgR (0% vs. 1.9%, respectively; p value = 1).

Also in the other subgroups of patients the mortality rates were similar after SR and SgR, respectively (p value > 0.05) (Table 3).

Overall Survival

In patients undergoing SR the 1-, 3-, 5- and 10-year OS rates were 85.8%, 51.3%, 30% and 15.3%, respectively. The median survival

Table 2. Comparative morbidity rates between SR and SgR (for the entire groups and subgroups)

	SR n=234	SgR n=66	<i>p</i> value
Total number	96	21	0.1997
Gender			
Female	37/102	7/31	0.193
Male	59/132	14/35	0.7030
Location			
Colon	60/154	17/53	0.4130
Rectum	36/80	4/13	0.3825
T stage			
T1-T3	79/187	12/42	0.1179
T4	6/31	2/6	0.5913
N-stage			
N0	27/63	1/6	0.3894
N1	20/58	8/19	0.5900
N2	37/77	5/19	0.1218
Extent of liver resection			
Minor	82/203	12/46	0.0916
Major	14/31	9/20	1
Nr of SCLMs			
1	51/137	8/28	0.5169
2-3	35/70	8/26	0.1098
>=4	10/27	5/12	1
SCLMs diameter			
< 5 cm	67/168	12/39	0.3613
> 5cm	29/66	9/27	0.3654
Distribution			
Unilobar	75/181	14/41	0.4809
Bilobar	21/53	7/25	0.4487
Preoperative chemo			
Yes	13/31	16/51	0.3512
No	83/203	5/15	0.7860

following SR was 39 months. In SgR group, the OS rates at 1-, 3-, 5- and 10-year were 87%, 49.6%, 22.5% and 12.5%, respectively, with a median survival of 35 months. The difference between OS achieved by SR and SgR, respectively, was not statistically significantly different (p value = 0.386). Comparative survival curves are displayed in Fig. 1.

In patients with rectal tumors and SCLMs who underwent SR, the 1-, 3- and 5-year OS rates were not significantly lower than those achieved by SgR (91.2%, 50% and 28.2%, vs. 76.9%, 56.1% and 28%, respectively; p value = 0.317).

The OS rates achieved by SR in patients

Table 3. Comparative mortality rates between SR and SgR (for the entire groups and subgroups)

	SR n=234	SgR n=66	p value
Total number	9	2	1
Location			
Colon	8/154	2/53	1
Rectum	1/80	0/13	1
Extent of liver resection			
Minor	7/203	1/46	1
Major	2/31	1/20	1
Nr of SCLMs			
1	4/137	0/28	1
≥2	5/97	2/38	1
SCLMs diameter			
< 5 cm	6/168	1/39	1
> 5cm	3/66	1/27	1
Distribution			
Unilobar	8/181	2/41	1
Bilobar	1/53	0/25	1
Preoperative chemo			
Yes	0/31	1/51	1
No	9/203	1/15	0.5535

with SCLMs and lymph nodes metastases (N1, N2) were not lower than those achieved by SgR (p value > 0.05). In patients presenting metastases in 1-3 lymph nodes (N1), the 1-, 3-

and 5-year OS rates achieved by SR and SgR (87.7%, 47.1% and 31% vs. 94.4%, 63.6% and 28.3%, respectively) were not significantly different (p value = 0.559). As well, in SR group, the 1-, 3- and 5-year OS rates achieved by patients presenting at least 4 metastatic lymph nodes (N2) were not lower than those observed in similar patients undergoing SgR (81.5%, 42.3% and 21.2% vs. 87.8%, 36.9% and 12.3%, respectively; p value = 0.447).

When bilobar metastases were present, the performance of SgR did not improve OS comparative with SR (81%, 27.8% and 13.9% vs. 80%, 36.1% and 20%, at 1-, 3- and 5-year, respectively; p value = 0.380).

In patients with multiple SCLMs, the OS rates achieved by SR were also similar to those achieved by SgR (p value > 0.05).

For each subgroup of patients that was analyzed, SR provided OS rates comparable to SgR (Table 4).

Discussion

Historically, the first surgical approach to SCLMs was DR, whose initial results were published in the late '80s (4). In this procedure, after resection of primary tumor, the patients

Figure 1. Comparative overall survival between SR and SgR

Table 4. Comparative overall survival rates between SR and SgR

	Simultaneous resection				Staged resection				p value
	1-yr	3-yr	5-yr	Median	1-yr	3-yr	5-yr	Median	
Entire groups	85.8%	51.3%	30%	39 mo	87%	49.6%	22.5%	35 mo	0.386
Gender									
Female	88.6%	53%	27.7%	41 mo	92.6%	40.2%	26.8%	31 mo	0.688
Male	83.6%	50.1%	33.4%	37 mo	82%	60.5%	16.8%	41 mo	0.390
Location									
Colon	82.7%	52.2%	30.8%	40 mo	89.6%	50.4%	22.5%	37 mo	0.535
Rectum	91.2%	50%	28.2%	35 mo	76.9%	56.1%	28%	47 mo	0.317
T-stage									
T1-T3	85.7%	50.3%	30.1%	37 mo	84.5%	49.4%	21.2%	31 mo	0.363
T4	87.5%	61.7%	31%	46 mo	100%	60%	40%	37 mo	0.596
N-stage									
N0	93.7%	65.7%	42.2%	51 mo	66.7%	22.2%	22.2%	22 mo	0.232
N1	87.7%	47.1%	31%	32 mo	94.4%	63.6%	28.3%	43 mo	0.559
N2	81.5%	42.3%	21.2%	31 mo	87.8%	36.9%	12.3%	24mo	0.447
Extent of liver resection									
Minor	85.3%	51.6%	31.1%	39 mo	92.8%	50.4%	20.2%	37 mo	0.356
Major	89.1%	45%	22.5%	31 mo	72.2%	48.8%	29.3%	35 mo	0.981
Nr. of SCLMs									
1	89.2%	57.6%	35.8%	46 mo	92.9%	56.1%	28.3%	41 mo	0.650
2-3	77.8%	44.8%	24.7%	31 mo	86.7%	58.2%	19.4%	41 mo	0.723
>= 4	88.5%	35.1%	8.8%	28 mo	70%	11.7%	11.7%	17 mo	0.155
SCLMs diameter									
< 5 cm.	88.7%	56.8%	33.4%	46 mo	86.3%	54.7%	25.2%	38 mo	0.348
> 5 cm.	77.9%	37.6%	21.7%	27 mo	87.5%	42.8%	18.3%	31 mo	0.812
Distribution									
Unilobar	87.5%	55.9%	33%	46 mo	90%	60.9%	26.9%	41 mo	0.812
Bilobar	80%	36.1%	20%	29 mo	81%	27.8%	13.9%	20 mo	0.380
Preoperative chemo									
Yes	92.6%	44.7%	38.3%	29 mo	91.3%	50.1%	25.2%	38 mo	0.919
No	85.9%	52.4%	29.1%	40 mo	72%	37%	12.3%	27 mo	0.266

underwent chemotherapy and subsequently, if SCLMs did not progress, liver resection was performed (3). These early reports had a tremendous contribution to the improvement of life-expectancy of patients with SCLMs, because it was revealed that complete resection of synchronous liver metastases from colorectal cancer represents a worthwhile operation which significantly increase survival of these patients (3,4). During the '90s, due to the progresses in liver surgery and anesthetic management of patients undergoing hepatectomies, the safety of liver resection increased (11,12). Thus, some centers decided to proceed with concomitant resection of both primary tumor and SCLMs (13). However, this strategy (called SR) raised many concerns related to the safety of the procedure, as well as to its oncologic benefit. Because these issues were not clearly

elucidated, a novel staged approach to SCLMs was launched in 2006 by Gilles Mentha et al., aiming to avoid the hypothetical higher risks of SR and improve the oncologic outcome of these patients (5). This new onco-surgical strategy called "liver-first" approach consists in neo-adjuvant chemotherapy followed by initial liver resection and subsequent colorectal resection. In present, a consensus regarding the indications of each approach (SR or SgR) has not been reached, especially in patients with rectal tumors or requiring major liver resections.

The present study revealed that the morbidity and mortality rates associated with SR are not significantly higher than those observed after SgR. Although similar results have been reported by our group and other recent studies (13-16), consensus conferences from 2012 and 2015 still recommended the

avoidance of SR in patients with rectal cancer or in those requiring a major hepatectomy (17,18). These recommendations (strength of evidence – level C) are based on the results of retrospective studies and reviews (1,2,19). Moreover, these studies included small number of patients with rectal primaries or major hepatectomies in the SR groups.

In this study, almost one third (80/234) of the patients undergoing SR presented rectal tumors. Because the proportion of patients with rectal tumors was significantly higher in the SR group than in SgR group, a direct comparison between patients with rectal cancer who underwent SR vs. SgR was performed. The morbidity and mortality rates after SR of rectal tumor and liver metastases were not significantly higher than in patients with synchronous liver metastases from rectal cancer who underwent SgR. These results, consistent with similar recent reports on this subject (9,20), confirm that even when the primary tumor is confined to the rectum, the SR could be safely performed in selected patients, treated in high-volume centers.

Because in this study, major liver resection was more frequently performed in SgR group, it was performed a comparative analysis between patients undergoing major hepatectomy by simultaneous or staged approaches. The morbidity and mortality rates of patients undergoing resection of 3 or more liver segments were similar irrespective the timing of primary tumor resection (simultaneous or staged; p value = 1). Similar short-term outcomes after simultaneous major liver resections were reported in the last decade by other authors (15,21,22), challenging the paradigm that SR should be avoided when major hepatectomies are needed.

Nowadays it is well known that the only predictors of both morbidity and mortality after liver surgery are blood loss and the number of resected liver segments (23). In this study the blood loss was comparable in the SR group and SgR group (557.547 ± 731.66 ml vs. 308.333 ± 178.16 ml, p value = 0.3498), thus explaining the similar morbidity and mortality rates observed in the two groups. Therefore, reduction in blood loss is responsible for the

decrease in morbidity and mortality, despite the performance of concomitant procedures.

Another criticism addressed to the SR is the impossibility to select the patients, due to the lack of observation period before liver resection (3,24,25). It was considered that chemotherapy administered before liver resection (neo-adjuvant chemotherapy) will allow a better understanding of tumor biology. Thus, if SCLMs will progress during chemotherapy, the liver resection is considered futile, because tumor progression before surgery is associated with poor outcomes (5-year OS rates lower than 8%) (6). Therefore, traditionally, SgR used to be considered better than SR in terms of survival rates (3,26).

In this series, the OS rates achieved by SR were higher than those achieved by SgR, although the difference was not statistically significant. In the last years, several series revealed that OS rates achieved by SR were not significantly lower than those achieved by SgR (10,13,27-29). Moreover, in several large series it was observed that neo-adjuvant chemotherapy did not improve OS and disease-free survival in patients with SCLMs (30,31). These results could be explained by the fact that in the era of modern chemotherapy, the progression-free survival rates are longer than 6 months (32). Thus, it is unlikely to assess the tumor biology during an observation interval shorter than 6 months. By these reasons, some authors consider that the traditional paradigms of SCLMs management should be reconsidered, as long as neo-adjuvant chemotherapy did not bring any survival advantage in majority of patients with SCLMs (32,33). In a recent paper, Ayez et al. suggested that neo-adjuvant chemotherapy might be beneficial only in patients whose clinical risk score ranges between 3 and 5 (34). Corroborating this result with the observation presented by Tanaka et al. who reported a survival advantage in patients with multiple and bilobar SCLMs undergoing neo-adjuvant chemotherapy, it seems that SgR could improve survival in high-risk patients (35). However, in the series presented here, the survival rates achieved by SgR were not significantly higher than those achieved by SR,

either in patients with bilobar SCLMs or in those with multiple metastases. Until the results of ongoing randomized clinical trials (36) will be available, the neo-adjuvant chemotherapy could not be considered as therapeutic standard in patients with SCLMs and the superior oncologic outcomes of SgR over SR cannot be sustained.

The results of the present study suggest that SR can be safely performed in most patients with SCLMs and the oncologic outcomes of this approach are not inferior to those achieved by SgR.

The length of hospital stay was also significantly shorter after SR than following SgR, similar results being reported by other authors (1,28,37). By reducing the hospital stay and sparing one hospitalization, it is obvious that comfort of the patient increases and the exposure to pathogens decreases (10). Moreover, the shorter operative time and length of hospitalization associated with SR will lead to a lower cost to health care system, optimizing economic outcomes of surgical therapy for patients with SCLMs (38).

Conclusion

In summary, the results of this study reveal that SR of colorectal cancer and synchronous metastases offers similar short- and long-term outcomes as SgR, in patients treated in a high-volume center, with large expertise in liver and colorectal surgery. In experienced institutions, low morbidity and mortality rates could be achieved by SR, even in patients with rectal primaries or requiring major hepatectomies. The SR enables a shorter hospital stay, improving the comfort of the patient and reducing the costs for the health care system.

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