ORIGINAL CONTRIBUTION

EXPERIMENTAL ONCOLOGY

https://doi.org/10.15407/exp-oncology.2025.03.347

A. Burlaka [1, 2, *], V. Bezverkhnyi [3], N. Bankovska [1], V. Zvirych [1], V. Skyba [2], A. Beznosenko [1], I. Lisnyy [1], B. Sorokin [4], O. Yatsyna [1]

[1] State Non-commercial Enterprise "National Cancer Institute", Kyiv, Ukraine
[2] Institute of Postgraduate Education of the Bogomolets National Medical University, Kyiv, Ukraine
[3] Military Hospital, Irpin, Ukraine
[4] Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine
* Correspondence: Email: anton.burlaka@unci.org.ua

SIMULTANEOUS VS STAGED RESECTIONS IN COLON CANCER PATIENTS WITH SYNCHRONOUS LIVER METASTASES: PROGNOSTIC IMPACT OF LYMPH NODE RATIO AND TUMOR BURDEN SCORE

Background. Synchronous metastatic liver disease (SLM) in colon cancer (CC) patients is an extremely unfavorable prognostic factor. The impact of lymph node ratio (LNR) and tumor burden score (TBS) on prognosis in this subset of patients remains incompletely understood. **Aim.** To assess the impact of LNR and TBS on survival in CC patients with synchronous LM who underwent staged or simultaneous surgery. **Materials and Methods**. A retrospective analysis of 365 patients with CC and SLM who underwent either staged or simultaneous surgical resection at the National Cancer Institute (Kyiv, Ukraine) between 2010 and 2024 was conducted. The demographic, clinicopathological, and survival data were analyzed. LNR was defined as the proportion of metastatic lymph nodes to total harvested lymph nodes, with a cutoff of 0.25. TBS was calculated using the Sasaki formula and categorized into three risk groups. **Results.** A mathematical model identified TBS clusters ($p < 0.04$, HR = 1.8, 95% CI 1.1—2.3), the number of LM ($p = 0.02$, HR = 0.8, 95% CI 0.3—1.4), pN stage ($p = 0.03$, HR = 0.6, 95% CI 0.3—0.9), LNR ($p = 0.005$, HR = 3.1, 95% CI 2.2—4.2), and KRAS gene status ($p = 0.01$, HR = 1.1, 95% CI 1.1—1.3) as independent risk factors for overall survival. **Conclusion**. Lymph node ratio and tumor burden score allow us to argue the surgical strategy choice for CC patients with synchronous liver metastases who are candidates for surgical resection. The staged surgical strategy provided better oncological outcomes in CC patients with both high LNR and TBS.

Keywords: colon cancer, synchronous liver metastases, lymph node ratio, tumor burden score, staged and simultaneous resections.

Colon cancer (CC) has one of the highest prevalence in the world, while remaining a preventable malignancy [1]. According to the Ukrainian Cancer Register, one in 20 people will be diagnosed with CC throughout life [2]. Approximately half of CC patients die from metastatic disease; however, there are reports on cancer-specific mortality decrease in screening groups [3]. Roughly

Citation: Burlaka A, Bezverkhnyi V, Bankovska N, Zvirych V, Skyba V, Beznosenko A, Lisnyy I, Sorokin B, Yatsyna O. Simultaneous vs staged resections in colon cancer patients with synchronous liver metastases: prognostic impact of lymph node ratio and tumor burden score. *Exp Oncol.* 2025; 47(3): 347-355. https://doi.org/10.15407/exp-oncology.2025.03.347

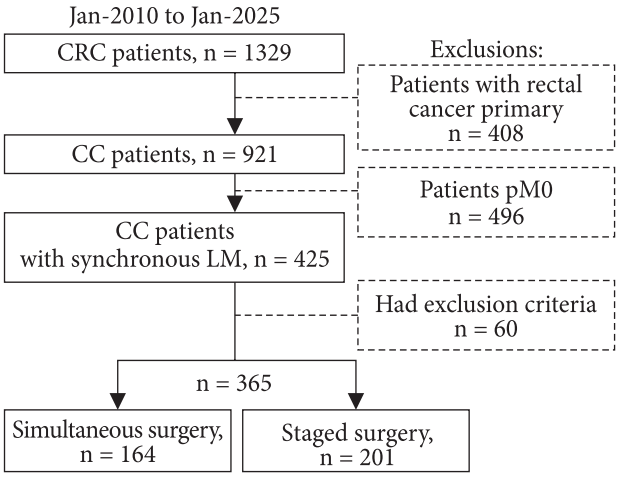

Fig. 1. Schematic representation of the study design.

20% of CC patients are diagnosed with synchronous liver metastases (SLM). Among them, 70% survive beyond 1 year and less than 30% beyond 5 years after initial diagnosis, and up to 50% develop metachronous liver lesions and 33% demonstrate peritoneal involvement [4].

Complete resection of the primary tumor and regional lymph nodes (LN) has a higher impact on survival improvements and is accepted as the leading strategy in the treatment of CC [5]. At the same time, routine management of CC with SLM involves induction chemotherapy with two surgical strategies implementation options: simultaneous and two-stage resections [6]. Until recently, the traditional surgical approach to CC or CC with SLM encompassed a two-stage surgical strategy (the first stage was the removal of the primary colon tumor, the second one— resection of liver metastases or reverse) [7]. Over the last two decades, we have seen a series of publications on the successful realization of simultaneous resections, including minimally invasive surgical access [8—11]. However, the randomized trials and meta-analysis did not favor one or another surgical strategy of treating CC with SLM, due to the absence of long-term outcome differences [6, 12].

Nowadays, the shifted technical limits of liver surgery have made it possible to offer surgical treatment to patients with a significant metastatic spread (tumor burden) [13, 14]. However, we must question ourselves about the biological rationale for surgical treatment in CC patients with high tumor burden of SLM [15]. The resectability of the primary tumor and metastases must be assessed both from a technical point of view [16] and from the perspective of tumor biology [17]. However, what period or percentage of improvement in cancer prognosis should be considered the cut-off point? That is why we must justify our decisions at a multidisciplinary commission applying prognostic scales [18].

Various prognostic factors have been proposed to predict survival following the resection of CC with SLM [19]. Among them, lymph node ratio (LNR), which is defined as the proportion of metastatic lymph nodes identified on pathological examination to the total number of harvested lymph nodes [20, 21]. However, a standardized reference value for LNR as a prognostic indicator for CC patients with SLM has not yet been established. As well, the tumor burden score (TBS) is another widely accepted prognostic model that converts the size and number of liver lesions into one variable by using the Pythagorean theorem and demonstrates more precise prognostic power than traditional tumor morphologic categorization [19, 22].

The aim of this study was to assess the impact of LNR and TBS on survival in CC patients with synchronous LM who underwent staged or simultaneous surgery.

Materials and Methods

1329 consecutive patients who underwent liver resections for CC with SLM between January 2010 and January 2024 were identified from the National Cancer Institute (Kyiv, Ukraine) prospective database. Of these, 365 patients with CC and SLM who underwent staged or simultaneous surgery were included in the retrospective analysis (Fig. 1). The demographic and clinicopathological data were collected, including age, gender, comorbidities, chemotherapy (CTx), primary tumor location, *KRAS* gene mutation status, surgery characteristics, the number of lesions, and the maximum diameter of the largest lesion (Table 1).

Inclusion criteria: patients with CC and SLM, and morphologically confirmed adenocarcinoma who completed simultaneous or staged surgery.

Exclusion criteria: primary rectal cancer, absence of liver metastases, less than 12 harvested lymph nodes in the surgical sample, disease progression under the induction or neoadjuvant CTx, R2 surgical margin resection status of LM or primary tumor, radiofrequency ablation of LM, unresectable intra/extra-abdominal metastases, and patients with missing data on treatment outcomes.

The LNR was defined as a proportion of the number of positive lymph nodes to the total harvested lymph nodes. We used a cutoff of ≤ 0.25 to define patients with a low LNR (l-LNR), and > 0.25 — with a high LNR (h-LNR), as previously reported [23]. The TBS was calculated according to the K. Sasaki et al. formula, which takes into account the maximum diameter of liver metastases and the number of LM (TBS^2 = (maximum lesion diameter)^2 + + (number of liver lesions) ^{2}). Using the TBS score, all patients were divided into three clusters: TBS < 3, ≥ 3 to < 9 and ≥ 9 [24]. TBS was calculated based on pathological and/or radiological data. The liver resections were classified as 'major' and 'minor' (resection of ≥ 3 and ≤ 2 segments, respectively) [25]. The local Ethical Committee of the National Cancer Institute (Kyiv) approved the study (Project ID 2011/25). The primary outcome was measured by

Table 1. **Baseline demographic, clinical, and morphological characteristics of the patients**

Variables	Groups			*p*
	Simultaneous, n = 164	Staged, n = 201	Total, n = 365	
Age, mean (min-max)	60.4 (37—75)	63.9 (34—81)	61.5 (34—81)	0.85
Gender (female)	75 (45.7)	88 (43.8)	163 (44.6)	0.69
Left-sided primary tumor localization	133 (81.2)	146 (72.6)	279(76.4)	0.86
Bilobar SLM	69 (42.2)	94 (46.7)	163 (44.6)	0.68
Primary tumor stage:				
pT1-pT3	107 (65.3)	118 (58.7)	225 (61.6)	0.72
pT4	57 (34.7)	83 (41.3)	140 (38.4)	0.44
Lymph node status:				
pN0	45 (27.4)	74 (36.8)	119 (32.6)	0.45
pN1	83 (50.6)	89 (44.3)	172 (47.2)	0.54
pN2	36 (22)	38 (18.9)	74 (20.3)	0.65
Conducted CTx:				
Neoadjuvant	130 (79.3)	176 (87.6)	306 (83.8)	0.87
Adjuvant	155 (94.5)	194 (96.5)	349 (95.6)	1.1
CTx cycles (overall)*	2.6 (0—19)	5 (0—30)	4 (0—28)	1.0
Resected SLM	3.7 ± 3.3	3.3 ± 2.9	3.5 ± 3.1	0.32
Size of largest SLM*	3 (2—4)	4.4 (1—12)	4.2 (1—10)	0.51
TBS*,§	4.4 (3.2—6.5)	5.3 (2.0—8.5)	4.6 (2.6—8.0)	0.31
TBS <3	27 (16.5)	33 (16.4)	60 (16.4)	0.94
TBS ≥3 to <9	122 (74.4)	143 (71.2)	265 (72.6)	0.87
TBS ≥ 9	15 (9.2)	25 (12.4)	40 (11)	0.67
LNs harvested	14.3 ± 2.6	14.4 ± 3.24	14.4 ± 3.06	0.32
LNR	0.24 ± 0.17	0.21 ± 0.15	0.22 ± 0.16	0.06
h-LNR	49 (29.8)	72 (35.8)	121 (33.2)	0.29
KRAS gene status, mutated	49 (29.9)	67 (33.3)	116 (31.7)	0.56
Resection of ≥3 anatomical liver segments	21 (12.8)	63 (31.3)	74 (23.1)	<0.0001
Liver-first strategy	-	26 (12.9)	26 (7.1)	<0.0001
CEA level (ng/mL)*	17.4 (2.1—63.5)	24 (1.8—75)	19.2 (2.0—68)	0.78

Notes: * median, (interquartile range). § — TBS <3 — cluster-1; TBS ≥3 to <9 — cluster-2; TBS ≥ 9, cluster-3.

analyzing the overall survival (OS) after the first curative surgery. The liver surgical techniques included an anatomical-oriented parenchymal-sparing liver resection. The colon surgery was performed in accordance with the international and local protocols [26]. Afollow-up was done every 4 months for the first 3 years, every 6 months for the following 2 years, and then every 12 months. Laparoscopic liver interventions were performed by two surgeons who had completed a laparoscopic and open HPB training program and performed more than 25 laparoscopic liver resections.

The data were analyzed using the statistical package Prism 10.0. Statistics. The normality of the distribution was analyzed by the Shapiro — Wilk test. Summary statistics were presented as whole numbers and percentages for categorical variables, medians with interquartile ranges for continuous variables, and means with deviations from the standard error for interval data with a normal distribution. OS was assessed using the Kaplan — Meier method and calculated from the day of liver surgery. The Cox proportional hazards regression model was used to assess the association of relevant clinical and pathological factors with prognosis.

Results

A total of 365 CC patients with SLM who underwent curative simultaneous (n = 164) or staged (n = 201) surgery were included in the retrospective cohort analysis. Both groups exhibited a relatively balanced distribution of demographic, clinical, and morphological parameters (Table 1). The average age of patients was 61.5 years, with no difference between the comparison groups. The female gender was registered less frequently than the male. In both groups, the left-sided primary tumor localization was predominant. A bilobar LM was diagnosed in less than half cases in both groups. The regional lymph node status was mostly pN1. In the same comparison groups, primary tumors had grown through the visceral peritoneum or other adjacent organs in 34.7% and 41.3% of CC patients, respectively. The majority of patients (n = 306) received neoadjuvant and adjuvant CTx (n = 349) with no statistical difference between the groups. The oxaliplatin and irinotecan-based 'doublets' with anti-EGFR therapy were the predominant treatment regimens in the wild-type *KRAS* gene cohort in both groups. About 15% of patients received a combined cytotoxic regimen with anti-VEGF antibodies. The median of received CTx cycles was 2.6 (0—19) and 5 (0–30) in simultaneous and staged strategies, respectively. The groups were homogeneous in the amount of surgically removed SLM, 3.7 ± 3.3 and 3.3 ± 2.9 in simultaneous and staged groups, respectively ($p = 0.32$). In the staged group, the estimated median size of the largest SLM tended to be larger in diameter, 4.4 cm vs 3 cm in the simultaneous surgery group, $p = 0.51$. Median of TBS was similar in the staged group (5.3) and the simultaneous group (4.4), $p = 0.31$. In particular, the comparison groups were homogeneous in TBS clusters: <3, ≥3 to <9, and TBS ≥ 9.

CC patients were stratified by the number of harvested LNs and LNR in simultaneous vs staged groups. The cohorts of 49 and 72 patients in simultaneous and staged groups, respectively, demonstrated h-LNR, $p = 0.29$.

There was no difference in *KRAS* gene mutation between the groups, $p = 0.56$. Major liver resections were frequently performed in the staged group (31.3%), in contrast to the simultaneous strategy (12.8%), $p < 0.0001$. In the group of staged resection, the liver-first strategy was adopted in 12.9% cases. The median CEA levels did not differ significantly between the groups, $p = 0.78$.

Median follow-up for enrolled 365 CC patients with SLM was 30.5 months (range, 12—129 months). Survival distributions were similar according to simultaneous (45.3%) and staged (42.8%) groups, $p = 0.33$. The median of survival was 56.4 and 53.9 months in simultaneous and staged groups, respectively, $p = 0.33$ (Fig. 2, *a*).

The OS median in the cohorts with high-LNR and low-LNR who underwent simultaneous surgery was 31.9 and 83.9 months, respectively, $p < 0.001$, whereas the staged surgery group with high-LNR and low-LNR demonstrated median OS of 45.6 and 51.05 months, respectively, $p = 0.2$ (Fig. 2, *b*). In the cohorts with h-LNR and TBS cluster ≥2, OS median was 24.2 and 54 months for simultaneous and staged strategies, respectively, $p = 0.03$ (Fig. 2, *c*). Note that in the same cohort, liver-first strategy was implemented in 18 (78.3%) patients.

Univariate and multivariate logistic regression analyses were used to find out independent predictors for OS (Table 2). A mathematical model identified TBS clusters ($p < 0.04$, HR = 1.8, 95% CI 1.1—2.3), the number of LM ($p = 0.02$, HR = 0.8, 95% CI 0.3—1.4), pN stage ($p = 0.03$, HR = 0.6, 95% CI

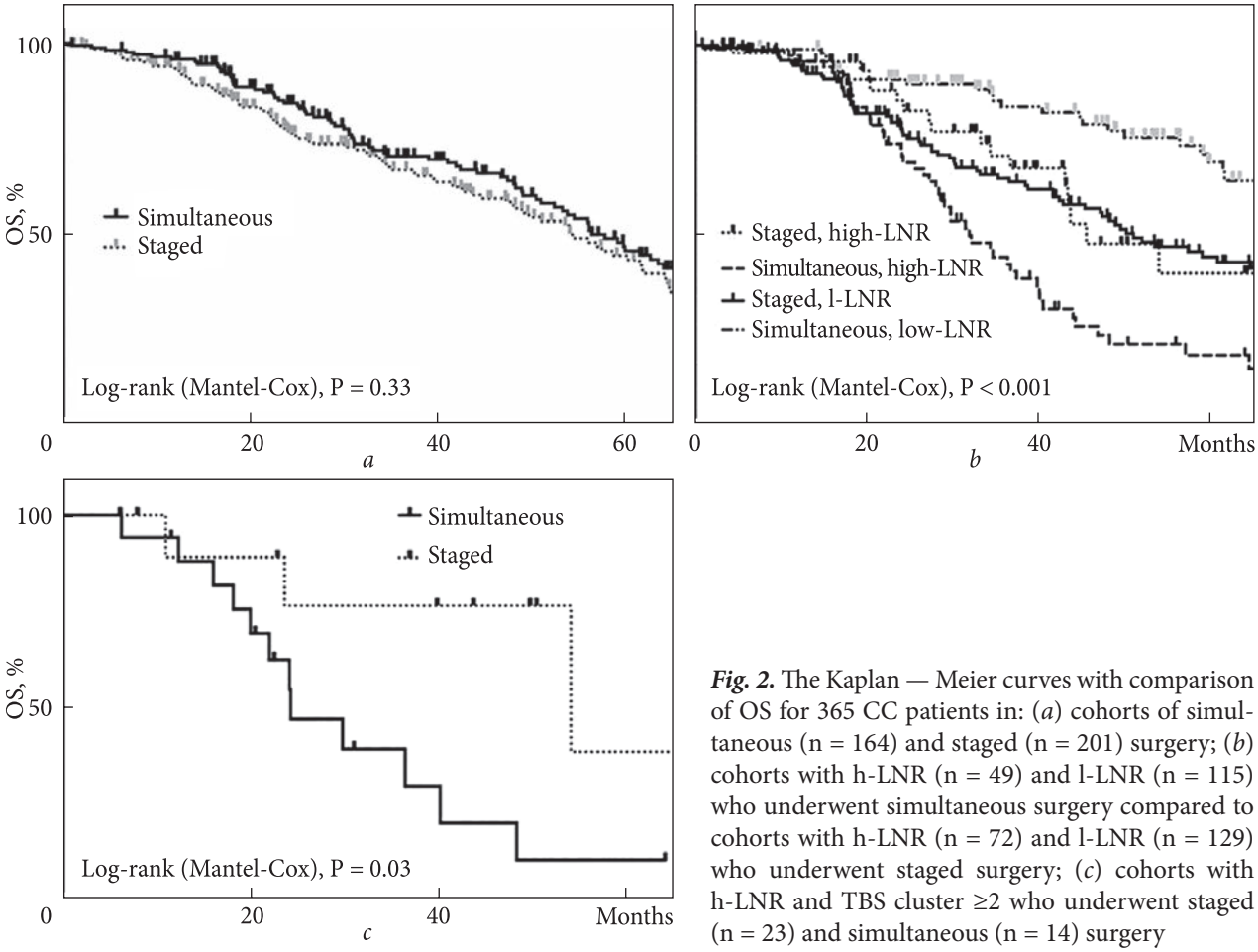

Fig. 2. The Kaplan — Meier curves with comparison of OS for 365 CC patients in: (*a*) cohorts of simultaneous (n = 164) and staged (n = 201) surgery; (*b*) cohorts with h-LNR (n = 49) and l-LNR (n = 115) who underwent simultaneous surgery compared to cohorts with h-LNR (n = 72) and l-LNR (n = 129) who underwent staged surgery; (*c*) cohorts with h-LNR and TBS cluster ≥2 who underwent staged (n = 23) and simultaneous (n = 14) surgery

Table 2. **Risk factors associated with overall survival**

Variables	Univariate and Multivariate logistic regression analyses of OS			
	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*	HR (95% CI)	*p*
TBS (clusters 1, 2, 3)	2.1 (1.4—2.6)	0.01	1.8 (1.1—2.3)	0.04
Bilobar LM (yes, no)	ns	ns	ns	ns
Number of LM (mean)	0.7 (0.2—1.2)	0.04	0.8 (0.3—1.4)	0.02
SLM size (mean)	ns	ns	ns	ns
CTx courses number (<6, ≥6)	0.9 (0.5—1.4)	0.02	ns	ns
pN stage (0, 1, 2)	1.5 (0.8—2.1)	0.01	0.6 (0.3—0.9)	0.03
LNR (low, high)	3.4 (2.1—4.5)	<0.001	3.1 (2.2—4.2)	0.005
pT stage (1, 2, 3, 4)	ns	ns	ns	ns
Liver re-resection (yes, no)	0,55 (0.31—0.90)	0,03	ns	ns
Liver major resection (yes, no)	1,3 (0.75—2.2)	0,04	ns	ns
KRAS gene status (wild type, mutation)	0.8 (0.7—1.1)	0.03	1.1 (1.1—1.3)	0.01
Surgical strategy (simultaneous, staged)	ns	ns	ns	ns

Note: ns — statistically insignificant.

0.3—0.9), LNR ($p = 0.005$, HR = 3.1, 95% CI 2.2—4.2), and *KRAS* gene status ($p = 0.01$, HR = 1.1, 95% CI 1.1—1.3) as independent risk factors for OS. The other factors, including bilobar LM, LM size, CTx courses number, pT stage, liver re-resection, liver major resection, or surgical strategy had no predictive value for OS.

Discussion

SLM in CC is an extremely unfavorable prognostic factor, since the median overall survival in such patients without surgical treatment is 6—12 months [27]. The role of chemotherapy (with or without biologic agents) has been evaluated in large randomized trials, and still surgical treatment remains the most effective method that significantly prolongs the life of such patients [28, 29]. A complete resection of the primary tumor and metastatic burden is the golden standard in the current management of CC patients with SLM [30]. At the same time, preserving adequate liver function and safe colon surgery are equally important for R0 resection [31]. The traditional surgical strategy to CC with SLM involves two-stage or staged resections [32—34]. However, the modern paradigm of surgical tactics for CC with SLM is changing. The evolution of surgical and anesthesiologic technologies and the development of more effective biologic agents are contributing to a revision of the treatment standards. Nowadays, most authors believe that simultaneous resection offers several potential advantages, including the complete removal of tumor burden in a single stage, a shorter overall procedure time, and a reduced hospital stay [6, 35]. These factors may also contribute to quality of life and are expected to decrease the reliance on healthcare resources compared to staged procedures [36]. At the same time, it was shown that synchronous resections that include major hepatectomies are associated with a higher rate of postoperative morbidity [37]. At the same time, LN dissection at the primary tumor area is still being debated [38]. The significance of regional LN metastases is still studied, especially in the context of hematogenous metastases [39]. Randomized trials have not proven the benefit of D3 lymph node dissection in synchronous LM; however, in the settings of pT2 stage, D3 LN dissection has shown a significant survival advantage [40]. Furthermore, the latest publications demonstrate a significant impact of LNR on cancer prognosis rather than TBS in this cohort of CC patients with SLM [41]. Molecular research reports that in 65% of cases, lymphatic and distant metastases originate from independent subclones within the primary tumor, while in 35% of cases, they share a common subclonal origin [42]. The latest molecular and immunological studies summarize that tumor cell invasion leads to immune dysfunction in tumor-draining LN, with further reciprocal inhibition of the antitumor immune function at the primary tumor site and alteration of the growth pattern of liver metastases [43].

In this analysis, we looked for the answers to rather controversial decisions of treatment planning in CC patients with SLM, since the heterogeneity of scientific literature and changes in international guidelines had initiated the problem of choosing the optimal surgical strategy.

As a result, in univariate and multivariate analyses, we found no differences in OS between the two surgical strategies, which is consistent with the global data. Nevertheless, this study demonstrates the tendency of better oncological outcome of staged surgical strategy in the cohort with h-LNR and TBS cluster 2 and higher. We believe that liver-first strategies provide better oncological outcomes in such patients due to better control of the liver disease and an assessment of the tumor response to neoadjuvant chemotherapy. Moreover, we were able to confirm the prognostic significance of LNR, which demonstrated at least the same impact on OS compared to the standard pN status. At the same time, a simultaneous surgical strategy was significantly more efficient in patients with low-LNR and TBS cluster 1. This study included patients who underwent simultaneous resections using a laparoscopic surgical access, which requires additional analysis. However, it is important to note the poor OS in patients undergoing simultaneous resection with major morbidity. Otherwise, simultaneous resections should be recommended for patients with low-LNR and limited TBS. At the same time, a staged strategy is a better approach to uncover the tumor biology and allow a better systemic control with CTx [44].

To sum up, LNR and TBS allow us to argue the surgical strategy choice for CC patients with SLM who are candidates for surgical resection. The staged

surgical strategy provided better oncological outcomes in CC patients with both high LNR and TBS.

Statements and Declarations

Ethical approval. Ethical approval for this study was obtained from the NCI Ethics Service committee (Project ID 2011/25).

Consent to participate. Informed consent was obtained from all individual participants included in the study.

Data availability. The datasets generated during and/or analyzed during the study are available from the corresponding author on reasonable request.

Competing interests

The authors have no competing interests to disclose.

Funding

The study was supported by grant of the Ministry of Health of Ukraine, state registration number: 0121U110087.

Author Contributions

A.B. — conception and design, manuscript writing; V.R. — material preparation, manuscript submission; D.M. and A.S. — conception and design; A.B., A.L., and I.L. — collection and assembly of data; V.S. — administrative support.

REFERENCES

1. Tonini V, Zanni M. Why is early detection of colon cancer still not possible in 2023? *World J Gastroenterol*. 202421;30(3):211-224. https://doi.org/10.3748/wjg.v30.i3.211
2. Burlaka A, Ryzhov A, Ostapenko Y, et al. Twenty-year experience in liver surgery in metastatic colorectal patients: a case series study in Ukraine. *Ann Med Surg (Lond)*. 2023;85(5):1413-1419. https://doi.org/10.1097/MS9.0000000000000619
3. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. *CA Cancer J Clin*. 2021 Jan;71(1):7-33. https://doi.org/10.3322/caac.21654
4. Rahbari NN, Biondo S, Frago R… SYNCHRONOUS and CCRe-IV Trial Groups. Primary tumor resection before systemic therapy in patients with colon cancer and unresectable metastases: combined results of the SYNCHRONOUS and CCRe-IV Trials. *J Clin Oncol*. 2024;42(13):1531-1541. https://doi.org/10.1200/JCO.23.01540
5. Benson AB, Venook AP, Adam M, et al. Colon Cancer, Version 3.2024, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2024;22(2D):e240029. https://doi.org/10.6004/jnccn.2024.0029
6. Sijberden JP, Alvarez Escribano MS, Kasai M, et al. Perioperative safety and oncological efficacy of simultaneous versus colorectal and liver first two-staged resections in patients with synchronous colorectal liver metastases: a systematic review and network meta-analysis. *HPB (Oxford)*. 2025;27(2):135-149. https://doi.org/10.1016/j.hpb.2024.10.010
7. Ghiasloo M, Pavlenko D, Verhaeghe M, et al. Surgical treatment of stage IV colorectal cancer with synchronous liver metastases: A systematic review and network meta-analysis. *Eur J Surg Oncol*. 2020;46(7):1203-1213. https://doi.org/10.1016/j.ejso.2020.02.040.
8. Minagawa M, Yamamoto J, Miwa S, et al. Selection criteria for simultaneous resection in patients with synchronous liver metastasis. *Arch Surg*. 2006;141(10):1006-1012; discussion 1013. https://doi.org/10.1001/archsurg.141.10.1006
9. Hajibandeh S, Hajibandeh S, Sultana A, et al. Simultaneous versus staged colorectal and hepatic resections for colorectal cancer with synchronous hepatic metastases: a meta-analysis of outcomes and clinical characteristics. *Int J Colorectal Dis*. 2020;35(9):1629-1650. https://doi.org/10.1007/s00384-020-03694-9
10. Reddy SK, Pawlik TM, Zorzi D, et al. Simultaneous resections of colorectal cancer and synchronous liver metastases: a multi-institutional analysis. *Ann Surg Oncol*. 2007;14(12):3481-3491. https://doi.org/10.1245/s10434-007-9522-5
11. Guerra F, Giuliani G, Saccucci G, Coratti A. Simultaneous, single-docking robotic resection for right colon cancer with synchronous liver metastases. *Surg Oncol*. 2022;43:101816. https://doi.org/10.1016/j.suronc.2022.101816
12. Boudjema K, Locher C, Sabbagh C, … METASYNC Study group. Simultaneous versus delayed resection for initially resectable synchronous colorectal cancer liver metastases: A prospective, open-label, randomized, controlled trial. *Ann Surg*. 2021;273(1):49-56. https://doi.org/10.1097/SLA.0000000000003848. PMID: 32209911
13. Nassar A, Tzedakis S, Dhote A, et al. Multiple laparoscopic liver resection for colorectal liver metastases. *Cancers (Basel)*. 2023;15(2):435. https://doi.org/10.3390/cancers15020435
14. Burlaka A, Rozhkova V, Pavliuk R, et al. Laennec's approach for central liver resection of colorectal cancer liver metastasis adjacent to the hepatic hilum that occurred 10 years after colectomy: A case report. *Int J Surg Case Rep*. 2024;116:109327. https://doi.org/10.1016/j.ijscr.2024.109327
15. Paro A, Hyer MJ, Tsilimigras DI, et al. Machine learning approach to stratifying prognosis relative to tumor burden after resection of colorectal liver metastases: an international cohort analysis. *J Am Coll Surg*. 2022;234(4):504-513. https://doi.org/10.1097/XCS.0000000000000094

16. Torzilli G, Adam R, Viganò L, et al. Surgery of colorectal liver metastases: pushing the limits. *Liver Cancer*. 2016;6(1):80-89. https://doi.org/10.1159/000449495
17. Zhou H, Liu Z, Wang Y, et al. Colorectal liver metastasis: molecular mechanism and interventional therapy. *Signal Transduct Target Ther*. 2022;7(1):70. https://doi.org/10.1038/s41392-022-00922-2
18. Cotan HT, Emilescu RA, Iaciu CI,et al. Prognostic and predictive determinants of colorectal cancer: a comprehensive review. *Cancers (Basel)*. 2024;16(23):3928. https://doi.org/10.3390/cancers16233928
19. Yonekawa Y, Uehara K, Mizuno T, et al. The survival benefit of neoadjuvant chemotherapy for resectable colorectal liver metastases with high tumor burden score. *Int J Clin Oncol*. 2021;26(1):126-134. https://doi.org/10.1007/s10147-020-01793-9
20. Beirat AF, Amarin JZ, Suradi HH, et al. Lymph node ratio is a more robust predictor of overall survival than N stage in stage III colorectal adenocarcinoma. *Diagn Pathol*. 2024;19(1):44. https://doi.org/10.1186/s13000-024-01449-6
21. Nawras M, Chawla K, DeRiso A, et al. The effect of preoperative endoscopic tattooing on lymph node retrieval in colorectal cancer: a systematic review and meta-analysis. *Int J Colorectal Dis*. 2023;38(1):166. https://doi.org/10.1007/s00384-023-04466-x
22. Sasaki K, Margonis GA, Andreatos N, et al. The prognostic utility of the «Tumor Burden Score» based on preoperative radiographic features of colorectal liver metastases. *J Surg Oncol*. 2017;116(4):515-523. https://doi.org/10.1002/jso.24678
23. Ahmad A, Reha J, Saied A, et al. Association of primary tumor lymph node ratio with burden of liver metastases and survival in stage IV colorectal cancer. *Hepatobiliary Surg Nutr*. 2017;6(3):154-161. https://doi.org/10.21037/hbsn.2016.08.08
24. Sasaki K, Morioka D, Conci S, et al. The tumor burden score: a new «metro-ticket» prognostic tool for colorectal liver metastases based on tumor size and number of tumors. *Ann Surg*. 2018;267(1):132-141. https://doi.org/10.1097/SLA.0000000000002064
25. Nagino M, DeMatteo R, Lang H, et al. Proposal of a new comprehensive notation for hepatectomy: The «new world» terminology. *Ann Surg*. 2021;274(1):1-3. https://doi.org/10.1097/SLA.0000000000004808
26. National Comprehensive Cancer Network. (2025). Colon cancer. Retrieved from https://www.nccn.org/login?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf
27. Stewart CL, Warner S, Ito K, et al. Cytoreduction for colorectal metastases: liver, lung, peritoneum, lymph nodes, bone, brain. When does it palliate, prolong survival, and potentially cure? *Curr Probl Surg*. 2018;55(9):330-379. https://doi.org/10.1067/j.cpsurg.2018.08.004
28. Lin Q, Ding K, Zhao R, et al. Preoperative chemotherapy prior to primary tumour resection for asymptomatic synchronous unresectable colorectal liver-limited metastases: The RECUT multicenter randomised controlled trial. *Eur J Cancer*. 2023;191:112961. https://doi.org/10.1016/j.ejca.2023.112961
29. Tepelenis K, Pappas-Gogos G, Ntellas P, et al. The role of preoperative chemotherapy in the management of synchronous resectable colorectal liver metastases: a meta-analysis. *Curr Oncol*. 2023;30(5):4499-4511. https://doi.org/10.3390/curroncol30050340
30. Colletti G, Ciniselli CM, Sorrentino L, et al. Multimodal treatment of rectal cancer with resectable synchronous liver metastases: A systematic review. *Dig Liver Dis*. 2023;55(12):1602-1610. https://doi.org/10.1016/j.dld.2023.05.023
31. National Comprehensive Cancer Network. NCCN Guidelines Version 6.2024 Colon Cancer. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. 28-jan-2025.
32. Kasai S, Ashida R, Sugiura T, et al. Long-term outcomes of staged liver resection for synchronous liver metastases from colorectal cancer and the clinical impact of early recurrence: A single-center retrospective cohort study. *Ann Gastroenterol Surg*. 2022;7(2):318-325. https://doi.org/10.1002/ags3.12628
33. Kim HH, Nguyen NH, Yang CJ, et al. Outcomes of simultaneous versus staged resection for stage IV colorectal cancer with synchronous liver metastases. *Am Surg*. 2024;90(10):2367-2373. https://doi.org/10.1177/00031348241244632
34. Machairas N, Di Martino M, Primavesi F, et al. Simultaneous resection for colorectal cancer with synchronous liver metastases: current state-of-the-art. *J Gastrointest Surg*. 2024;28(4):577-586. https://doi.org/10.1016/j.gassur.2024.01.034
35. Wang SH, Song L, Tang JY, et al. Safety and long-term prognosis of simultaneous versus staged resection in synchronous colorectal cancer with liver metastasis: a systematic review and meta-analysis. *Eur J Med Res*. 2022;27(1):297. https://doi.org/10.1186/s40001-022-00937-z
36. Conci S, Ruzzenente A, Pedrazzani C, et al. Simultaneous approach for patients with synchronous colon and rectal liver metastases: Impact of site of primary on postoperative and oncological outcomes. *Eur J Surg Oncol*. 2021;47(4):842-849. https://doi.org/10.1016/j.ejso.2020.09.015
37. Serrano PE, Parpia S, Karanicolas P, et al. Simultaneous resection for synchronous colorectal cancer liver metastases: A feasibility clinical trial. *J Surg Oncol*. 2022;125(4):671-677. https://doi.org/10.1002/jso.26764
38. Jiao S, Guan X, Zhang W, et al. Prognostic impact of increased lymph node yield in colorectal cancer patients with synchronous liver metastasis: a population-based retrospective study of the US database and a Chinese registry. *Int J Surg*. 2023;109(7):1932-1940. https://doi.org/10.1097/JS9.0000000000000244

39. Leong SP, Naxerova K, Keller L, et al. Molecular mechanisms of cancer metastasis via the lymphatic versus the blood vessels. *Clin Exp Metastasis.* 2022;39:159-179. https://doi.org/10.1007/s10585-021-10120-z
40. Wang L, Song B, Chen Y, Hirano Y. D3 lymph node dissection improves the survival outcome in patients with pT2 colorectal cancer. *Int J Colorectal Dis*. 2023;38(1):30. https://doi.org/10.1007/s00384-023-04326-8
41. Naidu K, Chapuis PH, Connell L, et al. Lymph node ratio prognosticates overall survival in patients with stage IV colorectal cancer. *Tech Coloproctol*. 2024;28(1):115. https://doi.org/10.1007/s10151-024-02984-6.
42. Naxerova K, Reiter JG, Brachtel E, et al. Origins of lymphatic and distant metastases in human colorectal cancer. *Science*. 2017;357(6346):55-60. https://doi.org/10.1126/science.aai8515
43. Zhang Y, Wu D, Zhang Z, et al. Impact of lymph node metastasis on immune microenvironment and prognosis in colorectal cancer liver metastasis: insights from multiomics profiling. *Br J Cancer*. 2025;132:513-524. https://doi.org/10.1038/s41416-024-02921-2
44. O'Connell RM, Hoti E. Challenges and opportunities for precision surgery for colorectal liver metastases. *Cancers (Basel)*. 2024;16(13):2379. https://doi.org/10.3390/cancers16132379

Submitted: May 16, 2025

А. Бурлака [1, 2], В. Безверхний [3], Н. Банковська [1], В. Звірич [1], В. Скиба [2], А. Безносенко [1], І. Лісний [1], Б. Сорокін [4], О. Яцина [1]

[1] Державне некомерційне підприємство «Національний інститут раку», Київ, Україна
[2] Інститут післядипломної освіти Національного медичного університету ім. О. Богомольця, Київ, Україна
[3] Військовий госпіталь, Ірпінь, Україна
[4] Національний університет охорони здоров'я України ім. П.Л. Шупика, Київ, Україна

ОДНОЧАСНІ ТА ДВОЕТАПНІ РЕЗЕКЦІЇ ПРИ РАКУ ОБОДОВОЇ КИШКИ ІЗ СИНХРОННИМ УРАЖЕННЯМ ПЕЧІНКИ: ПРОГНОСТИЧНЕ ЗНАЧЕННЯ КОЕФІЦІЄНТА ЛІМФАТИЧНИХ ВУЗЛІВ ТА ІНДЕКСУ ПУХЛИННОГО НАВАНТАЖЕННЯ

Стан питання. Синхронне метастатичне ураження печінки у хворих на рак ободової кишки є вкрай несприятливим прогностичним фактором. Вплив показника частки уражених лімфатичних вузлів та індексу пухлинного навантаження на прогноз у таких хворих вивчений недостатньо. **Мета** роботи полягала у визначенні залежності виживаності хворих на рак ободової кишки із синхронним метастатичним ураженням печінки від показника частки уражених лімфатичних вузлів та індексу пухлинного навантаження в разі одночасної або двоетапної резекції. **Матеріали та методи**. Проведено ретроспективний аналіз 365 хворих на рак ободової кишки із синхронним метастатичним ураженням печінки, яким було виконано одночасну або двоетапну резекцію в період з 2010 по 2024 рр. Проаналізовано демографічні, клініко-патологічні дані та виживаність. Визначаючи відношення між метастатично ураженими лімфовузлами та всіма видаленими лімфовузлами, порогове значення приймали за 0,25. Індекс пухлинного навантаження визначали за формулою Сасакі, і дані відносили до трьох груп ризику. **Результати**. Математична модель виявила такі незалежні фактори ризику загальної виживаності: кластер за індексом пухлинного навантаження ($p < 0.04$, HR = 1.8, 95% CI 1.1—2.3), кількість уражених лімфовузлів ($p = 0.02$, HR = 0.8, 95% CI 0.3—1.4), стадія за pN ($p = 0.03$, HR = 0.6, 95% CI 0.3—0.9), частка уражених лімфовузлів ($p = 0.005$, HR = 3.1, 95% CI 2.2—4.2) та статус гена *KRAS* ($p = 0.01$, HR = 1.1, 95% CI 1.1—1.3). **Висновки**. Показники коефіцієнта лімфатичних вузлів та індексу пухлинного навантаження дозволяють аргументувати вибір хірургічної стратегії для хворих на рак ободової кишки із синхронним метастатичним ураженням печінки. Двоетапна резекція демонструє кращі показники ефективності в онкологічному контексті.

Ключові слова: рак ободової кишки, синхронне метастатичне ураження печінки, коефіцієнт лімфатичних вузлів, індекс пухлинного навантаження, одночасна або двоетапна резекція.