e-CliniC 2025; Vol. 13, No. 2: 261-267
DOI: https://doi.org/10.35790/ecl.v13i2.59701
URL Homepage: https://ejournal.unsrat.ac.id/index.php/eclinic

Delayed Staged Hepatectomy for Metastatic Colorectal Cancer: A Single Case Report

Michael Tendean,[1] Steven Paparang,[2] Ferdinand Tjandra,[1] Toar Mambu,[1] Jimmy Panelewen,[1] Billy Salem[1]

[1]Division of Digestive Surgery, Department of Surgery, Faculty of Medicine, Universitas Sam Ratulangi - Prof. Dr. R. D. Kandou Hospital, Manado, Indonesia
[2]Department of Surgery, Faculty of Medicine, Universitas Sam Ratulangi, Manado, Indonesia
Email: michaeltendean@yahoo.com; steven_paparang@yahoo.co.id
Received: January 5, 2025; Accepted: April 10, 2025; Published online: April 12, 2025

Abstract: Liver metastases are common in patients with colorectal cancer; almost 70% will develop liver metastases during the course. The recommended treatment for colorectal liver metastasis (CRLM) is multidisciplinary, including liver resection and chemotherapy. We reported a 52-year-old female with stage 3B distal third rectal adenocarcinoma which eight months earlier underwent Mile's procedure plus total mesorectal excision (TME) followed by adjuvant radiotherapy (50gy). During surveillance, liver metastases was found at segments 4B-5. A delayed anatomical staged hepatectomy segments 4B-5 was performed. Intraoperative USG findings suggested liver metastases at segments 7, 8, and 3, and non-anatomical liver resection was performed in accordance with parenchymal liver sparing principles. No post-hepatectomy liver failure (PHLF) was detected, but billoma occured at 1-month post hepatectomy. USG guided percutaneous drainage was performed to resolve the billoma. Colorectal metastasis (CRLM) was detected at six months post-hepatectomy, and the patient underwent adjuvant chemotherapy with improvement in survival rate. In conclusion, delayed staged hepatectomy for CRLM is a safe and beneficial procedure, though there is still no guideline regarding the sequence of resection.
Keywords: hepatectomy; colorectal metastasis; billoma; colorectal cancer

INTRODUCTION

Globally, colorectal cancer is the third most frequent cancer[1] and second for the leading cause of cancer death, after lung cancer.[2] Approximately 70% of colorectal cancer patients will experience liver metastasis,[3] 15% and 25% of patients already present with liver metastasis at the initial diagnosis of primary colorectal cancer (synchronous liver metastases).[4] Mortality rates steadily declined from 1999 to 2020. Contributing factors to this decline include advances in screening techniques like fecal occult blood tests, computed tomographic colonography, sigmoidoscopy, and colonoscopy.[5]

The North American Association of Central Cancer Registries (NAACCR) categorizes Multiple Primary Malignancies (MPM) into two main types: 1) Synchronous, where the cancers occur simultaneously, and 2) Metachronous, in which the cancers develop sequentially, with more than six months between their occurrence.[6] In colorectal cancer (CRC), treatment options encompass addressing underlying infections, surgical intervention, cryosurgery, chemotherapy, radiation therapy, and targeted therapy. Albeit, surgery serves as the primary curative approach, often complemented by chemotherapy.[7] In the context of colorectal metastasis (CRLM), there are three surgical strategies: 1) Sequential Resection (SeR); 2) Delayed Resection (DeR); and 3) Simultaneous Resection (SiR). There is still no guideline as a standard resection approach in managing liver metastasis within colorectal cancer treatment.

A recent approach to the treatment of CRLM involves the concept of parenchymal-sparing liver surgery (PSLS) to minimize the removal of normal liver tissue while effectively addressing the metastases. Despite progress in preoperative patient selection, surgical methods, and perioperative care, post-hepatectomy liver failure (PHLF) remains a significant contributor to morbidity and mortality after liver resection[8] that occurs in about 10% of patients undergoing major liver surgery.[9] Balzan et al[10] introduced the "50-50" criteria for PHLF definition, which involves serum bilirubin exceeding 50 μmol/L and prothrombin time falling below 50% of normal on post-operative day 5. Mullen et al[11] also proposed another criterion for postoperative hepatic insufficiency (PHI) based on a peak bilirubin level >7.0 mg/dL. In 2011, the International Study Group of Liver Surgery (ISGLS) reached a consensus on defining PHLF using both laboratory and clinical parameters.[12] An international survey identified post-hepatectomy liver failure (PHLF), ascites, bile leakage, infection, and bleeding as the five crucial components. Li et al[13] proposed a scoring system using the acronym FABIB to enhance its practical applicability. Due to the many criteria stated in the bakground, we present a case of delayed staged hepatectomy for metastatic colorectal cancer.

CASE REPORT

We reported a 51-year-old female with colorectal cancer and metachronous liver metastasis (Table 1). In November 2021 at Prof. Dr. R. D. Kandou Hospital, delayed staged hepatectomy was performed on this patient. At the time of surgery, the patient's Child Pugh score was A-5. Previously, the patient had been given chemotherapy and radiotherapy with a dose 28 x 1.8 gy = 50 gy + Capecitabine 2 x 1000 mg. The patient had a delayed resection, involving non-anatomical removal of the liver metastasis, following the principles of liver parenchymal sparing. A thulium-doped fiber laser (TDFL) was used as the energy device (Table 2).

Table 1. Patient perioperative characteristics

Sex	Age	Colorectal cancer	Metachronous metastasis
Female	51 years	Adenocarcinoma recti 1/3 distal (cT4bN2M1), Total number of tumors = 4, Diameter of the largest tumor = 5x6 cm, Sequence = metachronous metastasis, CEA pre op = 14.4, previous liver resection (-), previous abdominal surgery (+) Miles procedure + TME	Liver metastasis segment 4B,5,7,8,3

The patient suffered from adenocarcinoma recti 1/3 distal (cT4bN2M1) and had previously undergone Mile's procedure and total mesorectal excision (TME) surgery. During surveillance, liver metastasis was found at segments 4B-5. After eight months, the patient underwent bisegmentectomy 4B-5 surgery and non-anatomical liver resection segments 7, 8, and 3. Bleeding is mostly from liver resection. After the procedure, we evaluated the morbidities and incidence of PHLF. Post-operative morbidities were evaluated using Clavien-Dindo and FABIB criteria,[14] while PHLF was evaluated using the PHLF criteria by the ISGLS.[12]

Following the surgery, the patient was treated in the Intensive Care Unit for two days, transferred to the regular hospital floor with a total length of stay of seven days, and then discharged. Two months later, the patient was readmitted for biloma, and percutaneous biloma drainage was performed under local anesthesia.

Table 2. Operation characteristics

Method of resection	Open
Duration	Seven hours
Vascular control	Intermittent pringle
Operation	Bisegmentectomy 4B-5. Non anatomical liver resection segment 7,8,3
Exposure	Right lobe mobilization
Energy device parenchymal transection	Thullium laser + Ligasure advanced bipolar
Intra-op and 1st 24 hours post-op bleeding	1000 cc

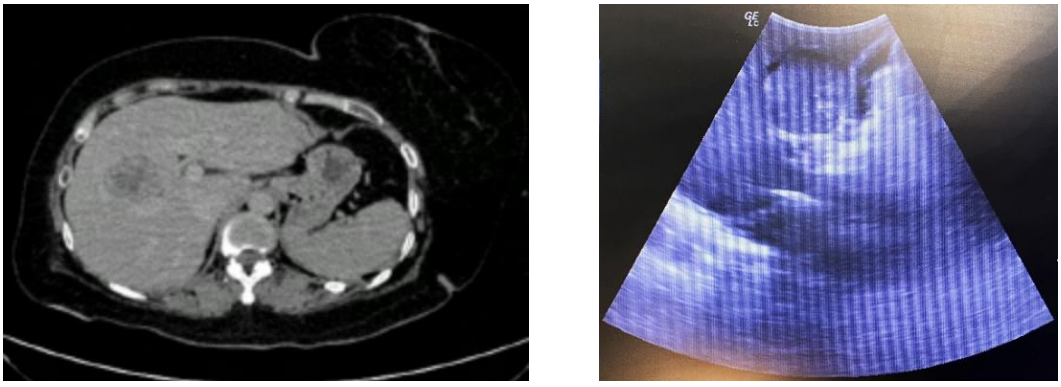

Fig. 1. A, CT scan during surveillance, liver metastases was found at segments 4B-5;
B, Intraoperative sonography for PSLS

DISCUSSION

Metachronous metastasis refers to the development of cancer that arises more than six months after the diagnosis of the first malignancy.[6] Liver metastasis surgical resection in CRC patients have a 5-year survival rate of 24% to 40%, with a median survival ranging from 28 to 46 months. In contrast, those receiving palliative therapy survive only for seven to eight months.[15] Compared to sequential resection, simultaneous resection has a higher incidence of severe complications. However, the prognosis for delayed resection is better when using a staged resection strategy.[4] Combined with preoperative chemotherapy may allow a long-term remission in selected patients[16] and reduce tumor size.[17] This approach allows tumors to shrink, thus simplifying the surgical procedure.

Gaëtan-Romain et al[18] give a strong recommendation to optimize nutrition status of patients prior to all hepatic surgery. It provides the opportunity to intervene prior to surgery and potentially improve postoperative outcomes.[19] Staged hepatectomy allows additional time for assessment, and medical teams can gather essential information, optimize patient conditions, and plan surgical approaches with greater precision.

The widely used Clavien-Dindo classification system simplifies the assessment and reporting of postoperative complications.[20] In this case, the Clavien-Dindo grade is 2. The patient was given 2 units of PRC to replace bleeding during resection. While the Clavien-Dindo classification (Table 3) is widely accepted in various surgical fields, a grading system specifically for liver surgery complications has not yet been standardized. Li et al[13] proposed a scoring system to increase the feasibility of routine use with FABIB as the acronym: post-hepatectomy liver failure, ascites, bile leakage, infection, and bleeding. This patient developed a biloma two months after surgery. Percutaneous bile leakage drainage was performed with a local anesthetic.

Bile leakage following hepatectomy is a frequent complication, with a rate of 2.9%–17%. Kimura et al[21] showed that non-surgical treatment, regarded as the first choice in the majority of cases, served as a minimally invasive and effective management approach for postoperative bile leakage. This included percutaneous bile leakage drainage (PBLD).

Balzan et al[10] proposed the "50-50 Criteria" on postoperative day 5 as an accurate predictor of liver failure and death after hepatectomy. These criteria can be detected before clinical signs of complications emerge, allowing timely interventions. However, the study by Rahbari et al[12] stated that the 50-50 criteria, when tested, demonstrated lower accuracy in predicting liver failure (sensitivity 50% and specificity 97%) compared to using peak serum bilirubin >7 mg/dL alone (sensitivity 93% and specificity 94%). Mullen et al[11] proposed another criterion for postoperative hepatic insufficiency (PHI) based on a peak bilirubin level >7.0 mg/dL reliably predicting liver-related mortality and adverse outcomes following major hepatectomy.

The International Study Group on Liver Surgery (ISGLS) proposes a definition and grading of the severity of posthepatectomy liver failure (PHLF), characterized by an increased INR (or need of clotting factors to maintain normal INR) and hyperbilirubinemia (according to the normal cut-off levels defined by the local laboratory) on or after postoperative day 5. After postoperative day 5, the value is compared with the previous day's values. It is also important to exclude other potential causes for the observed biochemical and clinical changes, such as biliary obstruction.[12] This grading can be seen in Table 4-5.

In this case, we consider PHLF by ISGLS as grade A. INR preoperative 0.97 increases to 1.20 in POD 5. Our patient exhibits no clinical symptoms beyond the expected postoperative course and can be managed on the regular ward without additional diagnostic evaluation. The ICU postoperatively in this case is only for observation purposes regarding intraoperative bleeding without any cardiovascular drug support or invasive ventilation (Table 6).

To reduce blood loss and manage bleeding during liver resection, we performed the intermittent Pringle maneuver. Despite concerns about ischemia/reperfusion injury, this technique remains widely used because it has been shown to reduce blood loss with high efficacy.[22] According to Al-Saeedi et al,[23] a Pringle maneuver lasting less than 20 minutes does not lead to increased posthepatectomy liver failure and does not impact the recurrence rate after three years.

At the author's hospital, we utilize a thulium-doped fiber laser (TDFL) emitting at 1940 nm, integrated with a 1470 nm Raman laser within the same fiber optic (Jenna surgery Multipulse TM+1470). This device is a safe and effective tool for liver surgery, provides reliable hemostasis, and facilitates the safe exposure of vascular and biliary structures. A cross-sectional study by Tendean et al[24] confirmed its efficacy without increasing bile leak or PHLF rates.

CONCLUSION

Delayed staged hepatectomy for CRLM is a safe and beneficial procedure, though there is still no guideline regarding the sequence of resection. However, these results require confirmation through future studies.

Conflict of Interest

The authors affirm no conflict of interest in this study.

REFERENCES

1. Global Cancer Observatory. Available from: https://gco.iarc.who.int/en (accessed 23 Jul2024).
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209–49. Doi: 10.3322/caac.21660.
3. Kow AWC. Hepatic metastasis from colorectal cancer. J Gastrointest Oncol. 2019;10(6):1274–98. Doi: 10.21037/jgo.2019.08.06.
4. Wang LJ, Wang HW, Jin KM, Li J, Xing BC. Comparison of sequential, delayed and simultaneous resection strategies for synchronous colorectal liver metastases. BMC Surgery. 2020;20(1):16. Doi: https://doi.org/10.1186/s12893-020-0681-7
5. Kusnik A, Renjithlal SLM, Chodos A, Shanmukhappa SC, Eid MM, Renjith KM, et al. Trends in colorectal cancer mortality in the United States, 1999 - 2020. Gastroenterology Research. 2023;16(4):217–25. Doi: 10.14740/gr1631
6. Synchronous and Metachronous Cancers: An Update. Available from: https://www.anncaserep.com/full-text/accr-v2-id1388.php# (accessed 23 Jul2024).
7. Adebayo AS, Agbaje K, Adesina SK, Olajubutu O. Colorectal cancer: disease process, current treatment options, and future perspectives. Pharmaceutics. 2023;15(11):2620. Doi: 10.3390/pharmaceutics15112620
8. Merath K, Tiwari A, Court C, Parikh A, Dillhoff M, Cloyd J, et al. Postoperative liver failure: definitions, risk factors, prediction models and prevention strategies. Journal of Gastrointestinal Surgery (JOGS). 2023;27(11):2640–9. Doi: 10.1007/s11605-023-05834-2
9. Ocak İ, Topaloğlu S, Acarli K. Posthepatectomy liver failure. Turkish Journal of Medical Sciences. 2020;50(6):1491–503. Doi: 10.3906/sag-2006-31
10. Balzan S, Belghiti J, Farges O, Ogata S, Sauvanet A, Delefosse D, et al. The "50-50 Criteria" on postoperative day 5. Ann Surg. 2005;242(6):824–9. Doi: 10.1097/01.sla.0000189131.90876.9e
11. Mullen JT, Ribero D, Reddy SK, Donadon M, Zorzi D, Gautam S, et al. Hepatic insufficiency and mortality in 1,059 noncirrhotic patients undergoing major hepatectomy. J Am Coll Surg. 2007;204(5):854–62. Doi: 10.1016/j.jamcollsurg.2006.12.032
12. Rahbari NN, Garden OJ, Padbury R, Brooke-Smith M, Crawford M, Adam R, et al. Posthepatectomy liver failure: A definition and grading by the International Study Group of Liver Surgery (ISGLS). Surgery. 2011;149(5):713–24. Doi: 10.1016/j.surg.2010.10.001
13. Li J, Moustafa M, Freiwald-Bibiza E, Alzudjali A, Fischer L, Nashan B. Is it feasible to standardize a composite postoperative complication reporting system for liver resection? Journal of Gastrointestinal Surgery (JOGS). 2020;24(12):2748–55. Doi: 10.1007/s11605-019-04457-w
14. Dindo D, Demartines N, Clavien PA. Classification of surgical complications. Ann Surg. 2004;240(2):205–13. Doi: 10.1097/01.sla.0000133083.54934.ae
15. Aziz H, Ahmed Z, Lee Y, Drumm G, Saif MW. A comprehensive review of management of colorectal liver mets in the current era. Cancer Medicine Journal. 2022;5(1):46–57. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8849579/
16. Adam R, Laurent A, Azoulay D, Castaing D, Bismuth H. Two-stage hepatectomy: a planned strategy to treat irresectable liver tumors. Ann Surg. 2000;232(6):777–85. Doi: 10.1097/00000658-200012000-00006
17. Blazer DG, Kishi Y, Maru DM, Kopetz S, Chun YS, Overman MJ, et al. Pathologic response to preoperative chemotherapy: a new outcome end point after resection of hepatic colorectal metastases. Journal of Clinical Oncology (JCO). 2008;26(33):5344–51. Doi: 10.1200/JCO.2008.17.5299
18. Gaëtan-Romain J, Kobayashi K, Hasegawa K, Thomson J, Padbury R, Scott M, et al. Guidelines for perioperative care for liver surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations 2022. World J Surg. 2023;47(1):11–34. Doi: 10.1007/s00268-022-06732-5
19. Walcott-Sapp S, Billingsley KG. Preoperative optimization for major hepatic resection. Langenbeck's Archives of Surgery. 2018;403(1):23–35. Doi: 10.1007/s00423-017-1638-x
20. Bolliger M, Kroehnert JA, Molineus F, Kandioler D, Schindl M, Riss P. Experiences with the standardized classification of surgical complications (Clavien-Dindo) in general surgery patients. European Surgery. 2018;50(6):256–61. Doi: 10.1007/s10353-018-0551-z
21. Kimura T, Kawai T, Ohuchi Y, Yata S, Adachi A, Takeda Y, et al. Non-surgical management of bile leakage after hepatectomy: a single-center study. Yonago Acta Medica. 2018;61(4):213–9. Doi: 10.33160/yam.2018.12.004
22. Lee KF, Chong CCN, Cheung SYS, Wong J, Fung AKY, Lok HT, et al. Impact of intermittent Pringle maneuver on long-term survival after hepatectomy for hepatocellular carcinoma: result from two combined randomized controlled trials. World J Surg. 2019;43(12):3101–9. Doi: 10.1007/s00268-019-05130-8

23. Al-Saeedi M, Ghamarnejad O, Khajeh E, Shafiei S, Salehpour R, Golriz M, et al. Pringle maneuver in extended liver resection: a propensity score analysis. Sci Rep. 2020;10(1):8847. Doi: 10.1038/s41598-020-64596-y
24. Tendean M, Mambu TDB, Tjandra F, Panelewen J. The use of Thulium-Doped Fiber Laser (TDFL) 1940 nm as an energy device in liver parenchyma resection, a-pilot-study in Indonesia. Ann Med Surg (Lond). 2020;60:491–7. Doi: 10.1016/j.amsu.2020.11.039

Table 3. Clavien-Dindo according to Dindo et al[21]

Grade	Definition
I	Any deviation from the normal postoperative course without the need for pharmacological treatment, or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics and electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included
III	Requiring surgical, endoscopic, or radiological intervention
IIIa	Intervention not under general anesthesia
IIIb	Intervention under general anesthesia
IV	Life-threatening complication (including central nervous system complications) requiring IC/ICU management
IVa	Single organ dysfunction (including dialysis)
IVb	Multiorgan dysfunction
V	Death of a patient

Table 4. Criteria grading for PHLF[12]

PHLF	Grade A	Grade B	Grade C
Specific treatment	Not required	Fresh-frozen plasma albumin Daily diuretics Noninvasive ventilation Transfer to intermediate/ intensive care unit	Transfer to the ICU Circulatory support (vasoactive drugs) Need for glucose infusion Hemodialysis Intubation and mechanical ventilation Extracorporeal liver support Rescue hepatectomy/liver transplantation
Hepatic function	Adequate coagulation (INR<1.5) No neurological symptoms	Inadequate coagulation (INR >1.5 <2.0) Beginning of neurologic symptoms (ie, somnolence and confusion)	Inadequate coagulation (INR >2.0) Severe neurologic symptoms/ hepatic encephalopathy
Renal function	Adequate urine output (>0.5 mL/kg/h) BUN <150 mg/dL No symptoms of uremia	Inadequate urine output (<0.5 ml/kg/h) BUN <150 mg/dL No symptoms of uremia	Renal dysfunction not manageable with diuretics BUN >150 mg/dL Symptoms of uremia
Pulmonary function	Arterial oxygen saturation >90% May have oxygen supply via nasal cannula or oxygen mask	Arterial oxygen saturation <90% despite oxygen supply via nasal cannula or oxygen mask	Severe refractory hypoxemia (arterial oxygen saturation <85% with high fraction of inspired oxygen)
Additional evaluation	Not required	Abdominal ultrasonography/CT Chest radiography Sputum, blood, urine cultures Brain CT	Abdominal USG/CT chest radiography/CT Sputum, blood, urine cultures Brain CT ICP monitoring device

Table 5. Consensus definition and severity grading of post hepatectomy liver failure (PHLF) by the International Study Group of Liver Surgery (ISGLS)[12]

Grade	PHLF by ISGLS
A	PHLF resulting in abnormal laboratory parameters but requiring no change in the clinical management of the patient.
B	PHLF resulting in a deviation from the regular clinical management but manageable without invasive treatment.
C	PHLF resulting in a deviation from the regular clinical management and requiring invasive treatment.

Table 6. Postoperative complications

PHLF -ISGLS	Clavien-Dindo	FABIB
Grade A	Grade 2 =1 (transfusion)	Bile leakage