Current Colorectal Cancer Reports (2018) 14:64–68
https://doi.org/10.1007/s11888-018-0402-0

SURGERY AND SURGICAL INNOVATIONS IN COLORECTAL CANCER (S HUERTA, SECTION EDITOR)

Current Trends on the Treatment Sequence for Colorectal Cancer with Liver Metastases

Petros Bangeas[1,2] · Angeliki Chorti[1] · Theodossis Papavramidis[1] · Georgios Tsoulfas[2]

Published online: 26 February 2018

Abstract

Purpose of Review Colorectal cancer liver metastases (CRCLM) are a significant clinical problem, with different treatment options, depending on the patient's health status and the extent of the disease. With the ideal treatment sequence between resection of the primary cancer, the hepatic metastases and chemotherapy being a matter of debate, the goal of this paper is to evaluate and analyze the current trends regarding the treatment sequence of metastatic colorectal cancer (CRC).

Recent Findings The standard sequence of resecting the primary first, followed by chemotherapy, and then dealing with the metastatic disease has evolved over time, owing to better chemotherapy regimens and improved surgical technique. As a result, there are now the options of simultaneous resection or that of the "liver first technique" where the patient first undergoes chemotherapy, followed by hepatectomy for the metastatic lesions, and finally colectomy for the primary lesion. Advances in the locoregional management of hepatic metastases, such as radiofrequency ablation (RFA), transarterial chemoembolization (TACE), and microwave ablation, have also added significantly to the surgical armamentarium.

Summary The key observation is that no method is ideal for every patient. It is necessary to identify the advantages and disadvantages of the different strategies, so as to find the "right" therapeutic strategy for the "right" patient.

Keywords Colorectal cancer liver metastasis (CRCLM) · Synchronous colorectal cancer · Colorectal cancer (CRC) · Liver-first approach · Radiofrequency ablation · Transarterial chemoembolization (TACE)

Introduction

Colorectal cancer (CRC) is the second leading cause of cancer-related deaths in men and women in the USA, accounting for over 9% of all cancer incidence [1••]. On the other hand, liver is the most common metastatic site of gastrointestinal tumors, including CRC. Contrast-enhancing magnetic resonance imaging (MRI) is the gold standard for the diagnosis of colorectal cancer liver metastases (CRCLM), with better identification of metastatic hepatic lesions compared to computed tomography (CT) imaging [2]. PET scan can play a role in cases where the diagnosis is uncertain. Laparoscopic diagnosis is an alternative, yet more invasive, and thus could play a role in cases where the resectability may be uncertain [3]. Hepatic metastatic disease is a clinical problem with a number of different clinical therapeutic approaches, depending on the tumor load and the overall health status of the patient. Additionally, there is a variety of locoregional therapies, such as percutaneous alcohol injection (PEI), radiofrequency ablation (RFA), microwave ablation (MWA), transarterial chemoembolization (TACE), and radiation therapy (RT), just to name a few. With a patient presenting with a primary CRC and hepatic metastases, the team is faced with the following three strategies: (a) the traditional one of resecting the primary, followed by chemotherapy and the re-evaluation of the hepatic metastatic disease, (b) simultaneous resection of both the

This article is part of the Topical Collection on *Surgery and Surgical Innovations in Colorectal Cancer*

✉ Georgios Tsoulfas
tsoulfasg@gmail.com

[1] 1st Propedeutic Department of Surgery, AHEPA University Hospital of Thessaloniki, Aristotle University of Thessaloniki, Thessaloniki, Greece

[2] 1st Department of Surgery, Papageorgiou University Hospital of Thessaloniki, Aristotle University of Thessaloniki, 66 Tsimiski Street, 54622 Thessaloniki, Greece

primary and the metastatic disease, and (c) chemotherapy, followed by resection of the hepatic metastatic disease, followed by chemotherapy for those patients with rectal lesions and finally resection of the primary. The challenge is in deciding which strategy should be applied in which case, which is an area of active debate [1••, 2, 3].

In order to evaluate the current trends on the treatment strategies for colorectal cancer liver metastases (CRCLM), a bibliographic research was conducted using PubMed, Scopus, and Embase. The search terms employed were "colorectal cancer" AND "synchronous" OR "simultaneous" AND "liver" OR "hepatic" AND "metastases" or "metastasis." We collected the latest articles (published in the last decade), including reviews, clinical trials, meta-analysis, and systematic reviews and excluding case reports. In total, 44 articles were considered eligible for our review.

Review

Resectability Criteria

Even though a plethora of articles have been published in the international literature reporting or reviewing several retrospective studies concerning the treatment of synchronous colorectal liver metastases, the sequence of their surgical management is still controversial. Many aspects should be taken into consideration when patients are selected for a certain treatment sequence. The European Society of Medical Oncology consensus guidelines for the treatment of metastatic colorectal cancer suggest the categorization of patients according to technical and oncological criteria to assess their eligibility for liver metastases resection. These criteria include the type of resection that can be achieved (R0 or R1 resection), the size of the healthy liver remnant, the extrahepatic disease, the tumor progression, and the number of lesions in the liver [1••]. According to the French criteria, the resectability of liver metastases could be defined by <4 liver segments, <1 hepatic vein, vena cava free of disease, $>40\%$ healthy liver remnant, and contra-lateral portal pedicle, while a more risky procedure could be done when >5 segments are involved with major vascular structures [4]. However, the overall thinking has changed significantly over time concerning resectability of hepatic metastatic disease; currently, the key question is not the number or location of lesions, but rather the hepatic remnant after the resection and if it will have sufficient liver function to support the patient's life. The majority of manuscripts provided a comparison of the morbidity and mortality rates between simultaneous and staged management with interesting results.

Comparing the Different Strategies

A meta-analysis in 2015 by Kelly et al. showed no difference in the 5-year overall survival rate and 30-day mortality rate between the three approaches (simultaneous, colon first, liver first), but noted the need for more randomized controlled trials to better evaluate these methods [5••]. When the simultaneous curative resection of CRC with liver metastases is selected, a shorter postoperative hospitalization is achieved, but the percentage of complications is still high (25–76%), also including major complications such as anastomotic leakage, liver failure, bile leak, bowel obstruction, or surgical site infection [6, 7]. Nevertheless, four meta-analyses describe a decrease in complication rates after simultaneous resection, possibly owing to a better understanding and management of the hepatic disease [6, 8–12]. Lower mortality, morbidity, and complication rates after a simultaneous approach have been reported by Ito et al., when the liver is resected first and the colon excision follows in the same operation [13]. The simultaneous approach has been characterized as safe as the staged approach, in addition to benefiting the health care system with the decreased length of hospital stay [7]. On the other hand, Inoue et al. reported that the simultaneous approach is an independent factor for anastomotic leakage [14••]. Muangkaew et al. reported no difference in major complications between simultaneous and staged operations, but an increase in colon complications such as anastomotic leakage has been observed and was attributed to hepatic pedicle clamping.

Furthermore, in the case of the simultaneous approach, potential risk factors include concurrent pulmonary disease, locally advanced primary disease, prolonged pre-operative chemotherapy, and patient's age > 70 years old [15]. The anastomotic leakage has been also attributed to prolonged operation time (> 8 h) or high blood loss, thus making a staged approach less appealing for high-risk patients [16]. A new study published in 2017 that analyzed the short-term outcomes after the simultaneous approach resulted in a higher rectal and hepatic complication rate and advocated for a staged approach [17••]. On the other hand, there seems to be no difference regarding the long-term oncological outcomes between the two approaches, while the extent of liver resection may be a significant risk factor for decreased survival [6, 18•]. Moreover, the extent of the hepatectomy has a direct correlation with morbidity and mortality, which is even more pronounced in high-risk categories of patients. When a synchronous minor hepatectomy and a high- or low-risk colorectal cancer resection is performed, there is a statistical significant decrease in mortality in comparison to the staged procedure. With regard to morbidity, there is no difference between the two surgical approaches [19, 20••]. The overall mortality rate for a synchronous approach is 1.7% and the morbidity rate is 29% [20••]. The same study concluded that there is a statistically significant decrease in mortality after high- or low-risk colorectal cancer excision and minor hepatectomy, compared to colorectal cancer excision combined with

major hepatectomy [20••]. Mayo et al. reported that major or minor hepatectomy could be safely combined with a simultaneous approach, but cautiously due to higher post-operative mortality rates [19]. A meta-analysis that included seven case-control studies reported a lower mortality rate for the staged approach (1.1 vs. 2.4% for the simultaneous approach) and no statistically significant difference for the morbidity between these two approaches [21]. According to Veereman et al., a lower complication rate has been observed in the simultaneous approach [22]. As far as the survival is concerned, no difference has been observed between simultaneous and staged approaches [6, 19, 22, 23]. A 5-year overall survival of 46% and disease-free survival of 35% has been reported by Wei et al., while positive lymph nodes, the number of metastasis, bilobar liver lesions, and no R0 resection have been considered as risk factors of poor prognosis [24]. Pre-operative carcinoembryonic antigen and metastases to other organs have been described as independent prognostic factors [23].

The Role of Chemotherapy and the Challenging Hepatic Remnant

Moreover, pre-operative chemotherapy before liver metastases resection proved to have better disease-free survival outcomes than primary resection of hepatic metastases [25]. Second-line pre-operative chemotherapy for previous unresectable liver metastases could help downsize the lesions and enable their surgical resection in approximately 20% of cases, but overall and disease-free survival seem to be decreased after second-line compared to first-line chemotherapy in terms of outcomes [26•]. Gustavsson et al. reported a different approach on the topic, concerning the liver toxicity after neoadjuvant chemotherapy and suggests that a larger remnant of healthy liver is required when liver resection after chemotherapy is selected. Hepatic complications after chemotherapy include steatohepatitis and sinusoidal injuries [4]. When the remaining liver segments are < 3 or in emergent cases, a two-staged approach is suggested [6, 27, 28]. Hepatectomy should be considered when the tumor is not microscopically detected after neoadjuvant chemotherapy for 3–6 months and a simultaneous excision can be performed [28, 29].

The associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) is a relatively novel surgical method with the goal of increasing the hepatic remnant in a shorter time period, although unfortunately there have been higher recurrence rates observed [30••]. The novelty factor has been critical in promoting the spread of the ALPPS procedure, which is a surgically challenging procedure. As it is being increasingly used, the learning curve effect will lead to wider dissemination over time; however, at this point, portal vein embolization still remains the "golden rule" in terms of dealing with the small hepatic remnant. However, it should be noted that proper portal vein embolization is by itself an intricate procedure as its complete success (which is the only way to ensure the hypertrophy of the remnant) has to do with the completeness of the embolization, the material used, and other factors which require an interventional radiology team with significant expertise.

When the "liver-first" approach is selected, if the primary tumor becomes symptomatic (bleeding or obstruction) during the time interval between the two procedures, this may lead to an emergent operation and inferior patient outcomes [28]. On the other hand, Waisberg et al. have advocated in favor of the "liver-first" approach, as the hepatic metastatic disease can be controlled in a timely manner, while the primary tumor is stable [31]. The combination of adjuvant chemotherapy and radiotherapy makes the liver-first approach feasible, although the appropriate time of primary tumor resection has yet to be decided upon [32]. The median time between neoadjuvant therapy and hepatectomy was 22 days, while the median time until the recurrence was 4.2 months [33]. Neoadjuvant chemotherapy is pivotal in the case of unresectable hepatic metastatic disease. However, its role in resectable hepatic metastasis is questionable as it might delay a potentially curative procedure [34].

Eveno et al. interrogated the genetic pathway affecting metastatic development. As the VEGF pathway is involved in the initiation of the metastatic process and it is overexpressed during operations, antiangiogenic factors have been proposed as supplemental chemotherapeutic agents after primary tumor resection and before the resection of the liver metastatic disease in the case of the staged approach, so as to control metastatic disease [35]. Adjuvant chemotherapy seems to improve overall survival rate, especially in cases of poorly differentiated tumor, > 3 metastases, > 3-cm size of metastasis, and short duration of pre-operative chemotherapy [36]. Pre-operative risk factors for early recurrence after complete liver resection include the size of liver metastases (> 5 cm),> 3 liver segments with metastatic lesions, T3–T4 stage of primary tumors, poorly differentiated colorectal cancer, positive liver margins, radiofrequency ablation during the procedure, and the high-risk surgery alone [37, 38]. In the case of liver recurrence, they could be re-resected, improving patients' survival [29, 38]. Prognostic risk factors for liver recurrence are synchronous disease, resection margins, and the number of metastases [39].

The Future?

Technological advances have led to the increased use of minimally invasive surgery for the simultaneous excision of primary and metastatic tumors with satisfying results, concerning morbidity (18%) and mortality (1.3%) [40]. A systematic review on laparoscopic simultaneous colorectal cancer and hepatic metastatic lesion excision reported encouraging initial results. Although more studies should be conducted to determine more accurately the recurrence and survival rates of the laparoscopic approach [41]. After a laparoscopic approach, the main complication observed was anastomotic leak, whereas conversion to

an open procedure has not been reported [41]. Wei et al. proposed the use of the laparoscopic approach for the hepatectomy with or without simultaneous colectomy only in carefully selected patients [24]. Furthermore, a recently described technique combines laparoscopic excision of the primary tumor with the radiofrequency ablation of liver metastases [42]. Liver resection and intraoperative radiofrequency ablation of liver metastases have satisfactory results regarding mortality and morbidity rates and seem to be a safe combined approach [43]. Although RFA has been shown to have increased recurrence when used as the first approach for the management of the hepatic metastatic disease, when compared to resection, the overall survival did not differ between the two methods [44]. Siriwardena described the protocol of a new study which aims to compare the long-term outcomes of newly diagnosed patients with colorectal cancer and synchronous liver metastases concerning quality of life, morbidity, and mortality rates [45].

Conclusion

When dealing with synchronous colorectal cancer with hepatic metastases, choosing between the three management strategies can sometimes be more art than science. However, as there is increasing experience and outcomes, some conclusions are being drawn. Specifically, the simultaneous management has significant benefits if the hepatectomy is a limited one (not more than 3 segments), thus not substantially increasing the risk of the procedure. Additionally, the "liver-first" technique is an indication of our improved understanding of the increased risk to the patient from the metastatic disease load. It also offers the ability to evaluate the biological behavior of the disease with the use of the neoadjuvant chemotherapy, so as to determine which patients will actually be responsive to the treatment plan. The variety of locoregional therapies (RFA, MWA, TACE, PEI, among others) that can be used either in the case of patients with poor performance status, or alone, or in combination with resection for a more complete outcome need to be taken into account in the overall treatment. The management of synchronous colorectal cancer with hepatic metastatic disease has been further aided significantly by the use of portal vein embolization and also ALPPS, as ways to increase the hepatic remnant. Finally, the use of minimally invasive procedures is bound to increase, thus opening new frontiers for the management of these patients.

Compliance with Ethical Standards

Conflict of Interest The authors declare they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1.•• Van Cutsem E, et al. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. Ann Oncol. 2016;**27**(8):1386–422. **Most recent ESMO consensus guidelines have been developed based on the current available evidence to provide a series of evidence-based recommendations to assist in the treatment and management of patients with mCRC in this rapidly evolving treatment setting.**
2. Xu L-H, Cai SJ, Cai GX, Peng WJ. Imaging diagnosis of colorectal liver metastases. World J Gastroenterol. 2011;17(42):4654–9.
3. Meriggi F, Bertocchi P, Zaniboni A. Management of potentially resectable colorectal cancer liver metastases. World J Gastrointest Surg. 2013;5(5):138–45.
4. Ismaili N. Treatment of colorectal liver metastases. World J Surg Oncol. 2011;9:154.
5.•• Kelly ME, et al. Synchronous colorectal liver metastasis: a network meta-analysis review comparing classical, combined, and liver-first surgical strategies. J Surg Oncol. 2015;**111**(3):341–51. **This meta-analysis demonstrated no clear statistical surgical outcome or survival advantage between the different strategies used in the management of sunchronous colorectal liver metastases.**
6. Ali SM, Pawlik TM, Rodriguez-Bigas MA, Monson JRT, Chang GJ, Larson DW. Timing of surgical resection for curative colorectal cancer with liver metastasis. Ann Surg Oncol. 2018;25(1):32–7.
7. Abelson JS, Michelassi F, Sun T, Mao J, Milsom J, Samstein B, et al. Simultaneous resection for synchronous colorectal liver metastasis: the new standard of care? J Gastrointest Surg. 2017;21(6):975–82.
8. Capussotti L, et al. Major liver resections synchronous with colorectal surgery. Ann Surg Oncol. 2007;14(1):195–201.
9. Chen J, Li Q, Wang C, Zhu H, Shi Y, Zhao G. Simultaneous vs. staged resection for synchronous colorectal liver metastases: a metaanalysis. Int J Color Dis. 2011;26(2):191–9.
10. Yin Z, Liu C, Chen Y, Bai Y, Shang C, Yin R, et al. Timing of hepatectomy in resectable synchronous colorectal liver metastases (SCRLM): simultaneous or delayed? Hepatology. 2013;57(6):2346–57.
11. Li ZQ, Liu K, Duan JC, Li Z, Su CQ, Yang JH. Meta-analysis of simultaneous versus staged resection for synchronous colorectal liver metastases. Hepatol Res. 2013;43(1):72–83.
12. Feng Q, Wei Y, Zhu D, Ye L, Lin Q, Li W, et al. Timing of hepatectomy for resectable synchronous colorectal liver metastases: for whom simultaneous resection is more suitable—a meta-analysis. PLoS One. 2014;9(8):e104348.
13. Ito K, Govindarajan A, Ito H, Fong Y. Surgical treatment of hepatic colorectal metastasis: evolving role in the setting of improving systemic therapies and ablative treatments in the 21st century. Cancer J. 2010;16(2):103–10.
14.•• Inoue Y, et al. What is the optimal timing for liver surgery of resectable synchronous liver metastases from colorectal cancer? Am Surg. 2017;**83**(1):45–53. **When comparing the different strategies, this paper found that simultaneous surgery was the only independent risk factor for anastomotic leakage and thus advocated for a staged approach.**
15. Muangkaew P, Cho JY, Han HS, Yoon YS, Choi YR, Jang JY, et al. Outcomes of simultaneous major liver resection and colorectal surgery for colorectal liver metastases. J Gastrointest Surg. 2016;20(3):554–63.

16. Nakajima K, Takahashi S, Saito N, Sugito M, Konishi M, Kinoshita T, et al. Efficacy of the predicted operation time (POT) strategy for synchronous colorectal liver metastasis (SCLM): feasibility study for staged resection in patients with a long pot. J Gastrointest Surg. 2013;17(4):688–95.
17.•• Ono Y, Saiura A, Arita J, Takahashi Y, Takahashi M, Inoue Y. Short-term outcomes after simultaneous colorectal and major hepatic resection for synchronous colorectal liver metastases. Dig Surg. 2017;34(6):447–54. **This study showed that simultaneous major hepatectomy and colorectal resection led to increased morbidity.**
18.• Silberhumer GR, et al. Long-term oncological outcomes for simultaneous resection of synchronous metastatic liver and primary colorectal cancer. Surgery. 2016;160(1):67–73. **This paper from a major cancer center showed similar long-term outcomes between simultaneous and staged approaches.**
19. Mayo SC, Pulitano C, Marques H, Lamelas J, Wolfgang CL, de Saussure W, et al. Surgical management of patients with synchronous colorectal liver metastasis: a multicenter international analysis. J Am Coll Surg. 2013;216(4):707–16. discussion 716-8
20.•• Shubert CR, et al. A NSQIP review of major morbidity and mortality of synchronous liver resection for colorectal metastasis stratified by extent of liver resection and type of colorectal resection. J Gastrointest Surg. 2015;**19**(11):1982–94. **This review of a large database states that what makes a difference in whether a simultaneous approach can be followed is the extent of the colorectal or the hepatic resection, with the data being in favor of such an approach when the hepatectomy is minor.**
21. Chen GQ, Li J, Ding KF. A meta-analysis of the safety of simultaneous versus staged resection for synchronous liver metastasis from colorectal cancer. Zhonghua Wei Chang Wai Ke Za Zhi. 2010;13(5):337–41.
22. Veereman G, Robays J, Verleye L, Leroy R, Rolfo C, van Cutsem E, et al. Pooled analysis of the surgical treatment for colorectal cancer liver metastases. Crit Rev Oncol Hematol. 2015;94(1):122–35.
23. Bigourdan JM, Faber B, Rayar M, Chirpaz E, Boucher E, Boudjema K. Disease-free survival after simultaneous or delayed resection of synchronous colorectal liver metastasis and primary cancer. Hepato-Gastroenterology. 2014;61(132):1074–81.
24. Wei M, He YZ, Wang JR, Chen N, Zhou ZG, Wang ZQ. Laparoscopic versus open hepatectomy with or without synchronous colectomy for colorectal liver metastasis: a meta-analysis. PLoS One. 2014;9(1):e87461.
25. Kim CW, Lee JL, Yoon YS, Park IJ, Lim SB, Yu CS, et al. Resection after preoperative chemotherapy versus synchronous liver resection of colorectal cancer liver metastases: a propensity score matching analysis. Medicine. 2017;96(7):e6174.
26.• Adam R, et al. Resection of colorectal liver metastases after second-line chemotherapy: is it worthwhile? A LiverMetSurvey analysis of 6415 patients. Eur J Cancer. 2017;**78**:7–15. **This paper from a large European database shows that for appropriately selected patients, resection after second-line chemotherapy can have similar results as that after first-line chemotherapy.**
27. Gustavsson B. Simultaneous surgery for primary colorectal cancer and metastatic lesions? Scand J Gastroenterol. 2012;47(3):269–76.
28. Osada S, Imai H, Sasaki Y, Tanaka Y, Matsuhashi N, Okumura N, et al. Therapeutic strategies for synchronous and multiple liver metastases from colorectal cancer. Oncol Rev. 2012;6(1):e9.
29. Popescu I, Alexandrescu S. Hepatic metastasis of colorectal cancer—current therapeutic possibilities. Chirurgia (Bucur). 2010;105(2):155–69.
30.•• Bjornsson B, et al. Associating liver partition and portal vein ligation for primary hepatobiliary malignancies and non-colorectal liver metastases. Scand J Surg. 2016;**105**(3):158–62. **This paper presents the feasibility of using ALPPS in the case of colorectal liver metastases with good results.**
31. Waisberg J, Ivankovics IG. Liver-first approach of colorectal cancer with synchronous hepatic metastases: a reverse strategy. World J Hepatol. 2015;7(11):1444–9.
32. Pudil J, Batko S, Menclová K, Bláha M, Ryska M. "Liver fist approach" in the management of synchronous liver metastases from colorectal cancer: preliminary non-randomized study results. Rozhl Chir. 2015;94(12):522–5.
33. D'Hondt M, Lucidi V, Vermeiren K, van den Bossche B, Donckier V, Sergeant G. The interval approach: an adaptation of the liver-first approach to treat synchronous liver metastases from rectal cancer. World J Surg Oncol. 2017;15:54.
34. Bonney GK, Coldham C, Adam R, Kaiser G, Barroso E, Capussotti L, et al. Role of neoadjuvant chemotherapy in resectable synchronous colorectal liver metastasis; an international multi-center data analysis using LiverMetSurvey. J Surg Oncol. 2015;111(6):716–24.
35. Eveno C, Pocard M. VEGF levels and the angiogenic potential of the microenvironment can affect surgical strategy for colorectal liver metastasis. Cell Adhes Migr. 2012;6(6):569–73.
36. Wang Y, Wang ZQ, Wang FH, Yuan YF, Li BK, Ding PR, et al. The role of adjuvant chemotherapy for colorectal liver metastasectomy after pre-operative chemotherapy: is the treatment worthwhile? J Cancer. 2017;8(7):1179–86.
37. Jung SW, Kim DS, Yu YD, Han JH, Suh SO. Risk factors for cancer recurrence or death within 6 months after liver resection in patients with colorectal cancer liver metastasis. Ann Surg Treat Res. 2016;90(5):257–64.
38. Vigano L, et al. Early recurrence after liver resection for colorectal metastases: risk factors, prognosis, and treatment. A LiverMetSurvey-based study of 6,025 patients. Ann Surg Oncol. 2014;21(4):1276–86.
39. Angelsen JH, Viste A, Løes IM, Eide GE, Hoem D, Sorbye H, et al. Predictive factors for time to recurrence, treatment and post-recurrence survival in patients with initially resected colorectal liver metastases. World J Surg Oncol. 2015;13:328.
40. Garritano S, Selvaggi F, Spampinato MG. Simultaneous minimally invasive treatment of colorectal neoplasm with synchronous liver metastasis. Biomed Res Int. 2016;2016:7.
41. Lupinacci RM, Andraus W, de Paiva Haddad LB, Carneiro D′ Albuquerque LA, Herman P. Simultaneous laparoscopic resection of primary colorectal cancer and associated liver metastases: a systematic review. Tech Coloproctol. 2014;18(2):129–35.
42. Yigitbas H, et al. A new technique of radiofrequency-assisted ultrasound-guided needle-localized laparoscopic resection of disappearing colorectal liver metastases. Surg Laparosc Endosc Percutan Tech. 2017;27(1):e1–5.
43. van Amerongen MJ, van der Stok EP, Fütterer JJ, Jenniskens SFM, Moelker A, Grünhagen DJ, et al. Short term and long term results of patients with colorectal liver metastases undergoing surgery with or without radiofrequency ablation. Eur J Surg Oncol. 2016;42(4):523–30.
44. Hof J, Wertenbroek MWJLAE, Peeters PMJG, Widder J, Sieders E, de Jong KP. Outcomes after resection and/or radiofrequency ablation for recurrence after treatment of colorectal liver metastases. Br J Surg. 2016;103(8):1055–62.
45. Siriwardena AK, Chan AKC, Ignatowicz AM, Mason JM, CoSMIC study collaborators. Colorectal cancer with synchronous liver-limited metastases: the protocol of an inception cohort study (CoSMIC). BMJ Open. 2017;7(6):e015018.