The Italian Consensus on minimally invasive simultaneous resections for synchronous liver metastasis and primary colorectal cancer: A Delphi methodology

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ORIGINAL ARTICLE

The Italian Consensus on minimally invasive simultaneous resections for synchronous liver metastasis and primary colorectal cancer: A Delphi methodology

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Abstract

At the time of diagnosis synchronous colorectal cancer, liver metastases (SCRLM) account for 15–25% of patients. If primary tumour and synchronous liver metastases are resectable, good results may be achieved performing surgical treatment incorporated into the chemotherapy regimen. So far, the possibility of simultaneous minimally invasive (MI) surgery for SCRLM has not been extensively investigated. The Italian surgical community has captured the need and undertaken the effort to establish a National Consensus on this topic. Four main areas of interest have been analysed: patients' selection, procedures, techniques, and implementations. To establish consensus, an adapted Delphi method was used through as many reiterative rounds were needed. Systematic literature reviews were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses instructions. The Consensus took place between February 2019 and July 2020. Twenty-six Italian centres participated. Eighteen clinically relevant items were identified. After a total of three Delphi rounds, 30-tree recommendations reached expert consensus establishing the herein presented guidelines. The Italian Consensus on MI surgery for SCRLM indicates possible pathways to optimise the treatment for these patients as consensus papers express a trend that is likely to become shortly a standard procedure for clinical pictures still on debate. As matter of fact, no RCT or relevant case series on simultaneous treatment of SCRLM are available in the literature to suggest guidelines. It remains to be investigated whether the MI technique for the simultaneous treatment of SCRLM maintain the already documented benefit of the two separate surgeries.

Keywords Colorectal cancer · Synchronous colorectal liver metastases · Minimally invasive surgery · Consensus

Introduction

At the time of diagnosis, synchronous colorectal cancer liver metastases (SCRLM) account for 15–25% of patients, thus representing a significant, but challenging, clinical picture in terms of strategy of management [1–6]. If primary tumour and synchronous liver metastases are—or become—resectable, good results may be achieved performing surgical treatment well incorporated into the chemotherapy regimen [7–9].

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There is a wide range of feasibility for simultaneous resections, but caution has been raised for major liver resections or colorectal cancer (CRC) complicated tumour considering that delayed surgery might be beneficial for patients in terms of post-operative risk and outcomes [10, 11].

Minimally invasive (MI) approach has changed the surgical scenario, since colorectal resection is routinely performed laparoscopically [12–15] and all liver segments may be now approached trough MI liver surgery [16]. The international position on the role of MI liver surgery has been extensively discussed and defined in the two expert consensus held in Louisville 2008 and Morioka 2014, and as dedicated guidelines in Southampton 2017 [17–19].

So far, the possibility of simultaneous MI surgery for SCRLM has not been extensively investigated. The Italian surgical community has, therefore, captured the need and undertaken the effort to establish a National Consensus on this topic using a modified Delphi method [20], currently the most available tool to analyse gross data in a large context.

Four main areas of interest have been analysed: patients' selection, procedures, techniques, and implementations.

Methods

The Consensus development process was endorsed by the Italian Society of Surgical Oncology (SICO), the Italian Group Of Minimally Invasive Surgery (IGOMILS), the Association of Italian Hospital Surgeons (ACOI), the Italian Society of Surgery (SIC) and the Italian Association of Hepato–Biliary and Pancreatic Surgery (AICEP).

To establish consensus, an adapted Delphi method was used through as many reiterative rounds were needed [20]. Systematic literature reviews were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses instructions [21]. The Oxford Centre for Evidence-Based Medicine method was adopted to assess the study quality, the level of evidence and to assign the grade of recommendations [22].

The Consensus took place between February 2019 and July 2020. The project was conceived by three expert liver surgeons and two expert colorectal surgeons and led by two younger surgeons.

They covered the role of Project Coordinators during the whole period establishing the development methodology and involvement of expert professionals (Online Appendix 1).

The consensus coordinators were FC, LA, PD, MDG, RP, AR, and FeC.

Roles:

- Conception of the project.
- Establishment of the global methodology at the base of the process.
- Identification of experts to cover roles and develop tasks.
- Identification of relevant clinical topics.
- Approval of proposed clinical queries (CQs).
- Amalgamation of proposed statements, summary of voting agreement.

The Steering Committee (SC) and Review Committee (RC) were composed by surgeons of seven main centres devoted to MI surgery (Online Appendix 1).

Roles:

- Formulation of CQs.
- Literature review.
- Assessment of study quality and level of evidence.
- Formulation of recommendations.

The expert panel (EP) was composed by 15 senior surgeons (Online Appendix 1).

Role:

- Voting agreement to proposed recommendations.
- Highlighting critical issues of proposed recommendations.

Selection of members of the steering committee and the expert panel was made according to the case contribution from centres applying to the IGOMILS Registry.

More in detail, clinically relevant items were identified and grouped into four main areas of interest (Table 1). Each item was assigned to the SC to formulate the specific CQs. After approval of the CQs by the Project Coordinators, the SC and RC worked on the production of recommendations. Comprehensive systematic literature reviews were performed in PubMed, Scopus, EMBASE and Cochrane databases (until January 2020) using pertinent key searches (Online Appendix 2).

Considering the high specificity of topics and the low volume of available literature, no time frame was identified. Exclusion criteria were non-English articles and unavailable full-text. Each group produced evidence-based statements from the available literature, assigning the grade of recommendations.

Statements by the SC were addressed to the coordinators who built a questionnaire to get consensus by the EP. Based on an on-line survey platform, members of the EP individually expressed their level of agreement to each statement, thus providing a blinded evaluation. A voting scale from 1 (total disagreement) to 9 (total agreement) was adopted. Based on a selected published cutoff [23], < 3 points were considered as disagreement, 5 points as neuter opinion, > 7 points as agreement.

Consensus was reached if 75% of participants rated ≥ 7 or ≤ 3 [23].

Table 1 Main areas of interest

Patients' selection	Procedures	Techniques	Implementation
Items	Items	Items	Items
1. High-risk patients	3. Non-complex ColoRectal Cancer procedures	10. Outcomes: resection margins, harvested lymph nodes, mean hospital stay and complications	15. Training
2. Previous abdominal surgery	4. Complex ColoRectal Cancer procedures	11. Intra-operative staging techniques for liver resections	16. Registries and learned societies
	5. Right colon cancer anastomosis	12. Trocar placement	17. Surgeons
	6. Minor liver resections/left lateral sectionectomy	13. Bleeding and conversion	18. Centres
	7. Major liver resection/posterosuperior segments	14. Minimally invasive approaches and devices	
	8. Two-stage hepatectomies including ALPPS		
	9. Emergency and technically complex disease		

Statements not reaching consensus at the first Delphi round were readdressed to the members of the EP for comments on specific critical issues and consequent reformulation of statements by the SC. The modified statements entered a second Delphi round as previously stated. Statements failing to reach agreement after more than three rounds were removed, to provide only clear and shared recommendations.

Results

Twenty-six Italian centres participated in the consensus.

Four main areas of interests and 18 clinically relevant items were identified.

Thirty-six statements were produced. After a total of 3 Delphi rounds, 33 recommendations initially formulated reached expert consensus establishing the herein presented guidelines. Three statements were removed as failed to reach agreement.

Topic 1 patient selection

- High-risk patients

Q1: Is simultaneous colon and major/minor liver laparoscopic resection indicated in patients ≥ 75 years?

Age ≥ 75 years should not be considered an absolute contraindication to combined colon and liver laparoscopic resection. Minimally Invasive Simultaneous Colon/Rectal and Minor Liver Resection is safe and feasible in patients ≥ 75 year of age without major comorbidities. Simultaneous Major liver resection should be reserved to highly selected cases.

Level of evidence 4.

Grade of recommendation C.

Q2: Is simultaneous colon and minor liver laparoscopic resection indicated in fragile patients (ASA 4 and/or PS > 2)?

In fragile patients (i.e. ASA 4 and/or PS > 2), Colon and Minor Liver Resection should be preferably deferred, and simultaneous surgery indicated only in cases of low surgical complexity.

Level of evidence 4.

Grade of recommendation C.

It has long been recognised that advanced age can carry increased operative risk after surgery. However, Ferretti et al. demonstrated that frailty and operative time are better predictors of morbidity after combined MI Simultaneous Colon-Rectal and Liver Resection than chronological age [24]. Indeed, patients of the same age do not all have the same risk. Preoperative identification and assessment of frailty must be more detailed for identification of vulnerable surgical patients to choose the appropriate surgical management. In this context, age ≥ 75 years should not be considered an absolute contraindication to combined colon and liver laparoscopic resection. In real practice, MI Simultaneous Colon/Rectal and Minor Liver Resection is safe and feasible in patients ≥ 75 years of age without major comorbidities. However, minor hepatectomies encompass a wide range of procedures [25]. Therefore, evaluation of the cumulative operative risk of both procedures (liver and colorectal resection) must also be considered when performing pre-operative assessment. Benefits of the MI approach could be nullified by excessive extended operating time. In fragile patients (i.e. ASA 4 and/or PS > 2) Colon and Minor Liver Resection should be preferably deferred, and simultaneous surgery indicated only in cases of very low surgical complexity.

Q3: Is simultaneous colon and major/minor liver laparoscopic resection indicated in patients with BMI > 30 kg/m^2?

The few data available concerning patients with BMI > 30 kg/m^2 do not allow to generate recommendations regarding safety and feasibility of Combined Minimally Invasive Colon and Major/Minor Liver Resection, but it should be not considered a contraindication. Likely robotic-assisted surgery may minimise conversion to laparotomy and complications.

Level of evidence 4.

Grade of recommendation C.

Obesity rates are increasing worldwide as a result of lifestyle changes. Obesity is generally considered to be associated with increased technical difficulties in surgery and increased operative risk. Ferretti et al. showed that BMI is poorly related to post-operative morbidity at univariate analysis, but this result was not confirmed in multivariate analysis where ASA and longer operative time outweigh BMI impact on post-operative morbidity [24]. In both laparoscopic colorectal and hepatic surgery, BMI is a predictor of longer operation times with high conversion rate, but benefits of the laparoscopic approach may overcome these limitations. Analysis of all series on MI Simultaneous Colon-Rectal and Liver Resection showed that less than 5% of patients analysed had a BMI > 30 kg/m^2. Therefore, it is not possible to generate recommendations regarding safety and feasibility of Combined MI Colon and Major/Minor Liver resection, but it should not be considered “per se” a contraindication. At the moment, there is no evidence of an improvement in results with the robotic approach; however, the promising results obtained in obese patients in other surgeries should recommend exploring this field in the context of clinical trials.

Q4: May we indicate a cutoff of severity of the underlying liver disease (metabolic disease, chemotherapy-related liver injury, and cirrhosis) for simultaneous colon and liver laparoscopic resection?

Few available data concerning patients with underlying liver disease do not allow to generate recommendations regarding safety and feasibility of Combined Minimally Invasive Colon and Major/Minor Liver Resection. Few investigations on chemotherapy-associated liver injury (CALI) are related to low liver burden disease of these patients, who do not need intensive neoadjuvant chemotherapy. The proposal recommendation is to adopt the same exclusion criteria recognised for open surgery.

Level of evidence 4.

Grade of recommendation C.

On this topic, too few patients have been analysed and this can explain the absence of data regarding the impact of CALI on post-operative outcome in patients undergoing Combined MI Colon and Major/Minor Liver Resection. In the international multicentre series reported by Ferretti et al., neoadjuvant chemotherapy was administered in only 17.6% of patients and among exclusion criteria are reported factors as decompensated cirrhosis, oesophageal varices grade > 1 and platelets count < 80×10^9/L are reported [24]. The strict selection of patients is moreover evident analysing the series reported by Tranchart et al. in which 92% of patients had undergone atypical liver resection or left lateral sectionectomy, and by Shin et al. who reported > 70% of patients with 1 or 2 liver segmental involvement [26, 27]. In a multicentre series comprising 788 patients who underwent hepatectomy for colorectal liver metastases, Zhao et al. (on behalf of the CALI consortium), recently showed an increase in post-operative major morbidity and liver failure in patients with severe sinusoidal dilatation and increase in liver surgery-specific complications in patients with steatohepatitis [28].

- Previous abdominal surgery

Q5: Is simultaneous colon and liver laparoscopic resection indicated in patients already undergone abdominal or pelvic surgery?

Previous abdominal or pelvic surgery should be not considered a contraindication in patients scheduled for Combined Minimally Invasive Colon and Major/Minor Liver Resection.

Level of evidence 4.

Grade of recommendation C.

As for obese patients, as of patients who have already undergone previous abdominal or pelvic surgery, there are no data in the literature that allow to generate recommendations. However, in real practice, previous surgery should not be considered an absolute contraindication in patients scheduled for Combined MI Colon and Major/Minor Liver Resection.

Topic 2 procedures

- Non-complex CRC procedures

Q6: During simultaneous right/left colon and liver minimally invasive resections, is it recommended to perform liver surgery first?

It is recommended to start with the theoretically more difficult procedure based on patient specific characteristics and considering the expertise of the surgical team.

Level of evidence 4.

Grade of recommendation C.

Arguments in favour of liver resection performed before colon resection:

- The low central venous pressure needed to minimise the blood loss and not to interfere with the subsequent fluid resuscitation and colorectal resection;
- The opportunity to change surgical strategy from a simultaneous procedure to a "liver first" resection [29].

However, some authors argued that working first on the healthy colic tissue, avoiding the possible venous congestion of the colonic wall caused by a prolonged Pringle manoeuvre is safer [30].

Furthermore, the evaluation of the primary tumour and its resectability should be assessed before treating liver metastases [31].

In addition, the possibility of a symptomatic colorectal tumour requiring "a colon then liver" approach or a major liver resection requiring "a liver then colon" approach should drive the pre-operative decision [32].

A possible solution suggested by the literature could be to perform the liver resection after the mobilisation of the colon and before the colonic anastomoses (or diversion) [33].

Q7: Is it advisable to minimise the use of Pringle manoeuvre in case of simultaneous non-complex colorectal and liver minimally invasive resection?

A portal triad clamping (Pringle's manoeuvre) should be always prepared but it should be applied selectively, only in case of bleeding.

Level of evidence 4.

Grade of recommendation C.

The portal triad clamping (Pringle's manoeuvre) consists of intermittent cross-clamping of the hepatoduodenal ligament while performing liver transection.

Some authors claimed that the adoption of this manoeuvre during combined colon and liver resection can be cause of transient portal hypertension leading to an increased risk of anastomotic leakage because of the onset of intestinal oedema [34, 35].

The same authors showed in two systematic reviews that the portal triad clamping was frequently prepared but rarely adopted by the majority of surgeons [34, 35].

Furthermore, it was demonstrated that portal triad clamping was associated to increased risk for post-operative complications after combined colon and liver resection [24].

However, no adequate evidence is available to correlate the adoption of portal triad clamping with increased rate of colorectal anastomosis leakage, while a correlation between blood loss and worse clinical outcomes has been clearly demonstrated [36].

- Complex CRC procedures

Q8: Is diverting stoma recommended in simultaneous rectal and liver minimally invasive resection?

There are no evidences supporting an increased risk of intestinal complication during simultaneous MI rectal and minor liver resection. In these cases, the indications to a diverting stoma should be the same than in rectal surgery alone.

Level of evidence 2a.

Grade of recommendation B.

Data from meta-analysis of randomised controlled trials (RCT) showed that stoma may reduce the rate of anastomotic leak and reoperation after surgery for low rectal cancer [37, 38].

As reported by a recent meta-analysis, the rate of abdominal abscess and anastomotic leak after open simultaneous and delayed hepatectomy for synchronous colorectal tumours are similar [39].

In addition, the laparoscopic approach would seem not to increase the rate of intestinal complications as reported by a propensity score-matched study comparing 61 simultaneous laparoscopic colorectal and liver resections and 61 colorectal resections alone [40].

For these reasons, it is reasonable to conclude that there are no evidence supporting an increased risk of intestinal complication during simultaneous MI upper rectal surgery and minor liver resection. In these cases, the indications to a diverting stoma should be the same of rectal surgery alone.

Q9: Is there a role for the laparoscopic approach for simultaneous complex colon-rectal surgery and major/minor liver resections?

Simultaneous laparoscopic resection of upper rectal cancer and low burden liver metastases (requiring minor resection) is safe and associated to shorter hospital stay compared to open approach.

Level of evidence 3a.

Grade of recommendation B.

Numerous cases series showed the feasibility and safety of simultaneous colorectal and liver surgery with both open and laparoscopic approaches [26, 29, 32, 40–43]. However, the rate of rectal surgery in the main series is low/very low.

According to a case-matched series including more than five rectal resections, the advantages of the laparoscopic approach vs open seems to be confirmed in terms of blood loss and length of the hospital stay [29, 41–43].

No difference was reported concerning post-operative morbidity rate [26].

Contraindications to simultaneous mini-invasive rectal and major liver resections have been reported in high-risk patients (according to ASA score and performance status) [8].

- Right colon cancer anastomosis

Q10: Is intracorporeal anastomosis (IA) as safe and effective as extracorporeal anastomosis (EA) during simultaneous right colon and liver minimally invasive resection?

IA is safe as EA when performed by proficient surgeons in isolated right colectomy, IA could also be used in simultaneous laparoscopic resection of right colon cancer and liver metastases.

Level of evidence 4.

Grade of recommendation C.

One of the most debated items in MI right colon resection is certainly the IA versus EA. A total 76 patients are reported in the literature undergoing MI simultaneous IA and liver resections [36, 43–49]. IA is safe and effective in experienced hands and leakage might not be necessarily related to the anastomotic technique. Simultaneous liver procedures did not increase post-operative complication rate [45, 50–54].

- Minor liver resections/left lateral sectionectomy

Q11: Should all minimally invasive resections of anterior liver segments and left lateral sectionectomies combined with CRC resection be considered “easy” procedures? What criteria should be used to stratify their complexity?

The term minor resections of anterior segments and left lateral sectionectomy encompasses heterogeneous procedures at different complexity. To date, the IWATE criteria are the most reliable ones to stratify complexity of laparoscopic liver resections. Minor resections of anterior segments and left lateral sectionectomies with an Iwate score ≤ 3 may be considered as easy procedure in case of associated CRC resection.

Level of evidence 4.

Grade of recommendation C.

Q12: May “easy” minor liver resection/left lateral sectionectomy (IWATE score ≤ 3) combined with CRC resection be considered as a standard laparoscopic procedure?

Simultaneous laparoscopic “easy” minor resection/left lateral sectionectomy (Iwate score ≤ 3) associated with CRC resection is a standard procedure if not contraindicated by patient’s condition and/or by complexity of CRC resection.

Level of evidence 4.

Grade of recommendation C.

Minor hepatectomies are the vast majority of procedures reported in the series of laparoscopic simultaneous resections, but they encompass a wide range of procedures having heterogeneous complexity and outcome [24–26, 36]. No RCT comparing simultaneous open and laparoscopic resections with open is available, but some propensity score matching analyses have been published.

Some classifications and scores have been proposed to stratify laparoscopic minor hepatectomies [55–59], but a difficulty index according to IWATE criteria ≤ 3 identifies the easiest resections [56].

Although no papers have been focusing on easy hepatectomies, we may assume the feasibility, safety, and oncological efficacy and the clinical benefits of easy synchronous laparoscopic resections with a difficulty index ≤ 3 [24, 26, 29, 36, 42, 60].

In all series, patients' characteristics and primary tumour data (staging and complexity of resection) were considered to select candidates for simultaneous laparoscopic resection.

- Major liver resections—posterosuperior segments

Q13: Is there a role for simultaneous minimally invasive liver resection on the posterosuperior segments and colorectal surgery?

Simultaneous colorectal and liver resection in the posterosuperior segments can be feasible with a MI technique. However, the evidence to support that this approach may produce similar or better results of the combined open is insufficient. Therefore, they have to be considered an option in experienced hands and for selected patients.

Level of evidence 4.

Grade of recommendation C.

Q14: Is there a role for simultaneous minimally invasive major hepatectomies and colorectal surgery?

Simultaneous colorectal and major liver resection may be feasible with a MI technique. However, the evidence to support that this approach may produce similar or better results of the combined open is insufficient. Therefore, it is not recommended an expansion of the indications compared to what is currently defined for the open approach.

Level of evidence 4.

Grade of recommendation C.

Major or posterosuperior liver resection combined with colorectal surgery is demanding. Retrospective comparative studies show that combined laparoscopic major liver and colorectal resections are feasible, with perioperative outcomes globally not inferior to open and some benefits [36, 61, 62]. However, the data are based on a limited number of treated patients. Existing oncosurgical consensus on SCRLM judge the evidence still controversial to recommend simultaneous major liver and colorectal resections [7, 8].

In addition, guidelines on laparoscopic liver surgery define insufficient evidence to support similar outcomes between laparoscopic and open combined major liver and colorectal resections [19]. Specific literature on laparoscopic combined posterosuperior liver and colorectal resections is absent: few treated patients have been described in mixed series of synchronous resections [30, 36, 63]. Therefore, the indications derive from the literature on laparoscopic posterosuperior liver resections [64–66]. Theoretically, the two laparoscopic operations should not increase perioperative risks with respect to open.

- Two-stage hepatectomies including ALPPS

Q15: In case of needed two-stage hepatectomy, is there a role for the minimally invasive first step liver treatment and simultaneous colorectal resection?

Simultaneous resection of primary tumour during the first step of a classic two-stage hepatectomy for SCRLM may be considered feasible and safe.

Level of evidence 4.

Grade of recommendation C.

The hepatic burden of disease and the pattern of SCRLM distribution may require two-stage liver resection strategy to achieve a free margin.

In the literature, only two retrospective observational studies have been published describing this subclass of patients [67, 68].

Evidences are LOW (case series, case reports) [69–72]. Collected data showed an acceptable complications rate (12.5%), overall morbidity (35.2%) and mortality rate (2.7%) [51, 73–86].

Q16: Is it safe to perform minimally invasive colorectal surgery and simultaneous ALPPS (first step)?

To date, we cannot recommend to perform combined primary tumour resection and first step of ALPPS for SCRLM.

Level of evidence 4.

Grade of recommendation C.

Data were collected from 1 case series including 31 patients and 4 case reports. Total complication rate was 50% with a 90-day mortality was 8% [68].

To date, associating ALPPS procedures combined with primary tumour resection is not recommendable. Evidences are

LOW (case series, case reports) [69, 71, 78, 80]. Therefore, more data are needed.

- Emergency and technically complex disease

Q17: Is there a role for minimally invasive colorectal surgery and simultaneous minor liver resection in the haemorrhagic patients?

"According to present evidence, there is no indication for simultaneous resection in the haemorrhagic patients".

Level of evidence 4.

Grade of recommendation C.

There are currently no reports in the literature about synchronous colorectal and liver resection in patients with bleeding CRC and liver metastasis. This may be influenced by several factors: low incidence of surgery for bleeding in patients with CRC (<4%) [87, 88] and the non-optimal anaesthetic setting for simultaneous liver resection (i.e. haemodynamic instability, need of massive intra-venous fluid administration). There are few reports on emergency liver resection for ruptured hepatocellular carcinoma that show an increased mortality and morbidity rate of 12% and 40%, respectively, if compared to planned liver resection [89].

In the paper by the Association Française de Chirurgie, laparoscopic colorectal resection may have a mortality up to 30% when multiple of the following factors are present: emergency setting, synchronous liver metastasis, age > 70 years, vascular-respiratory-neurological comorbidities and malnutrition [90].

Q18: Is there a role for simultaneous colorectal and liver laparoscopic resection for Iwate score ≥ 4?

Synchronous Colorectal and Liver resection are safe and feasible in intermediate Iwate score 4–5–6. Advanced-Expert resections reserved to selected patients and high-volume centres.

Level of evidence 4.

Grade of recommendation C.

Iwate scoring system recognises four different levels of difficulty (low, intermediate, advanced, expert) in laparoscopic liver resections according to the sum of different items which include: tumour location, tumour size, proximity to major vessels, extent of liver resection, Hand Assisted Laparoscopic Surgery/Hybrid and liver function. A score ≥ 4 includes the intermediate, advanced and expert resections [55].

Among 422 synchronous resections reported in the literature, the rate of intermediate-advanced-expert liver resection is 21%, 14% and 0.5%, respectively [29, 30, 32, 33, 36, 44, 49–51, 62, 63, 91–95]. Simultaneous resections are safe and feasible, with a faster recovery and comparable outcomes. However, there are no subgroup analysis, no comparisons of results between Iwate score < 4 (i.e. left lateral sectionectomy) and ≥ 4 with no analysis of different types of Iwate ≥ 4 (i.e. segment 7 resection vs right hepatectomy) [55]. Therefore, synchronous resections (Iwate ≤ 6) are safe and feasible. Iwate > 6 resections are indicated only for highly selected patients and high-volume centres.

Topic 3 techniques

- Outcomes: resection margins, harvested lymph nodes, mean hospital stay and complications

Q19: Is minimally invasive surgical approach as adequate as open for lymphadenectomy during CRC resections and simultaneous liver resection?

Colorectal Lymphadenectomy during Combined Colon and Liver MI Resection is as effective as during open approach.

Level of evidence 3a.

Grade of recommendation B.

Q20: Is minimally invasive surgical approach as adequate as open for liver resection margin during simultaneous colorectal resection?

There are no differences regarding liver resection margin between simultaneous MI and open approach.

Level of evidence 3a.

Grade of recommendation B.

A review including several RCT has supported the effectiveness and similar oncologic outcomes of MI colectomy compared with open surgery in the setting of isolated colon cancer [96]. As of lymphadenectomy, revision of four case-matched studies comparing MI and open approach including a total of 75 matched patients, showed no significant differences regarding adequacy of lymphadenectomy (including harvested lymph nodes) between the two approaches [29, 36, 61, 97].

Recently, in the setting of hepatic surgery, two RCT supported the effectiveness and non-inferior oncologic outcomes of MI resection for colorectal metastasis [98, 99]. However, in both these RCT is evident that included patients had low liver burden disease (one or two metastases). Looking at liver resection margin, 5 case-matched studies including a total of 162 matched patients, showed no significantly differences in R0 resection rate between MI and open approach [26, 29, 32, 36, 61].

Q21: Does laparoscopic approach for simultaneous colon and liver resection reduce complications rate compared to open?

Compared to open approach, combined Colon and Liver Laparoscopic Resection in selected patients reduces post-operative morbidity and severity of the complications whenever occurring.

Level of evidence 2a.

Grade of recommendation B.

Q22: Does laparoscopic approach for simultaneous colon and liver resection reduce post-operative stay compared to open?

Combined Colon and Liver Laparoscopic Resection in selected patients reduces post-operative stay compared to open approach.

Level of evidence 2a.

Grade of recommendation B.

A recent meta-analysis of 10 comparative studies including 502 patients showed that the surgical complications were fewer and post-operative stay shorter in the MI group than in the open one, emphasising safety and efficacy of the MI approach [100]. A lower morbidity rate (20.2% vs 33%) was also showed by Shin et al. in 109 patients after a propensity score matching analysis in a similar group of patients [27]. Interestingly, Ratti et al. showed that post-operative morbidity index was significantly lower in the laparoscopic group [36].

- Intra-operative staging techniques for liver resections

Q23: Intra-operative staging during minimally invasive approach for simultaneous colon and liver surgery: is it mandatory before liver resection?

IOUS should be performed in all patients undergoing surgery for colorectal liver metastases to improve pre-operative staging of hepatic disease.

Level of evidence: 3b.

Grade of recommendation B.

Several surgical series have reported the superiority of intra-operative liver ultrasound (IOUS) to stage hepatic disease in colorectal liver metastases compared with various imaging modalities [101–107]. The improvements of radiological techniques over the years (especially MRI) represent a challenge for the current role of IOUS. As expected, the rate of new metastases found by IOUS decreased in the most recent series but remains noteworthy, ranging from 8 to 21%. A recent paper confirms the superiority of IOUS in a large series of patients all studied with pre-operative MRI [108]. Most of the data on IOUS accuracy come from studies on open liver surgery [101–105]. Nevertheless, some authors suggested that the laparoscopic and open IOUS have a similar performance even if the learning curve of laparoscopic IOUS remains to be clarified [109]. In conclusion, IOUS should be performed in all patients undergoing surgery for colorectal liver metastases to improve pre-operative staging of hepatic disease.

Q24: Intra-operative staging during minimally invasive approach for simultaneous colon and liver surgery: may it change the combined strategy?

Intra-operative liver ultrasound can change the liver surgical strategy and accordingly the convenience to perform simultaneous colorectal and liver surgery. For this reason, the first step during simultaneous colorectal and liver surgery is supposed to be intraoperative liver ultrasound.

Level of evidence 3b.

Grade of recommendation B.

No studies analysing the need for conversion from a simultaneous to a staged approach due to intraoperative liver findings are available. The impact of IOUS on liver resection planning depends strongly on the attitude of the individual surgeon: the more a parenchyma-sparing policy is adopted, the more the operative strategy can be modified. For this reason, there is a wide variation on change in planned surgical strategy (from 1.4 to 72%). In conclusion, intraoperative liver ultrasound can change the surgical strategy on the liver and accordingly the convenience to perform simultaneous colorectal and liver surgery. For this reason, the first step during simultaneous colorectal and liver surgery is supposed to be IOUS.

- Trocar placement

Q25: What is the optimal trocar setting for a simultaneous colon and liver laparoscopic resection?

Laparoscopic simultaneous colorectal and liver resection can be feasible with a trocar configuration that depends on the laterality of both procedures, the patient's decubitus and the surgeon's position. The principles of triangulation between optical and operating ports should be taken as a general guidance to ensure comfortable instrument ergonomics for both the first operator and assistant, as well as good exposure and adequate view during all the operation steps.

In general, not less than four active accesses for each resection are recommended.

Level of evidence 5.

Grade of recommendation D.

The number and the position of trocars varies depending on: the laterality and type of colorectal resection (left- or right-sided or rectal) and liver resection (left- or right-sided or posterosuperior segments, major or minor), which resection is performed first and the equipe's own technique including the position of both the surgeon and the patient (supine, semi decubitus, semi prone, partial tilting) (Fig. 1 shows an example of trocar placement based on the statement above).

The reported number of trocars varies from 4 to 9 in pure laparoscopic access [110, 111]. Hybrid techniques use a small laparotomy for hand-port placement and specimen extraction [112, 113]. In general, colorectal and liver resections in opposite abdominal quadrants (for example left colectomy and right-sided liver resection) require the highest number of trocars [110].

- Bleeding and conversion

Q26: What are the main causes of conversion during simultaneous colon and liver laparoscopic resections?

Bleeding seems to be the major cause of conversion during synchronous laparoscopic colorectal and liver resection. Accurate patients' selection remains the mainstay to reduce the conversion rate.

Level of evidence 3b.

Grade of recommendation B.

During laparoscopic liver resection, main conversion causes are due to intraoperative findings (i.e. poor access, oncological drawbacks) and unfavourable events (i.e. bleeding, damage to surrounding structures, cardiovascular instability) [59]. Further causes of conversions may be represented by difficult resection [57], previous abdominal surgery especially in upper-abdominal quadrants [114], obesity and tumour diameter > 10 cm [115].

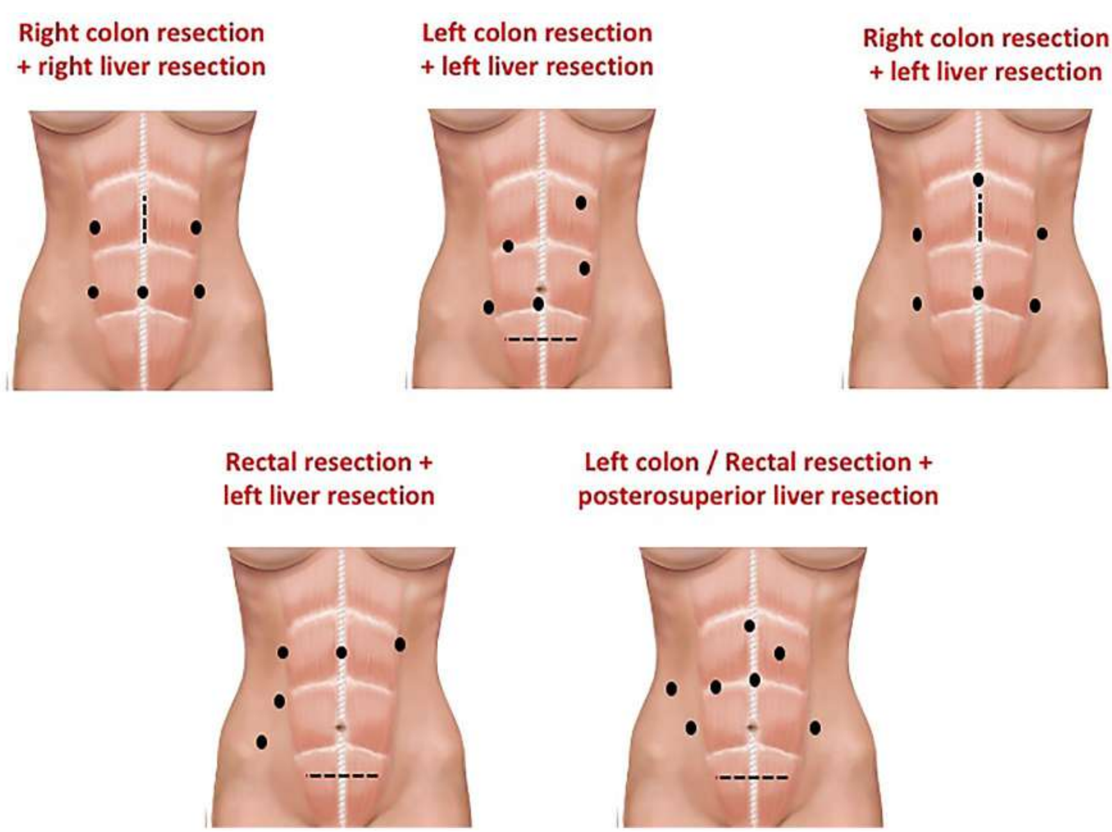

Fig. 1 Example of trocar placement to perform a combined resection

In case of synchronous laparoscopic colorectal liver resections, the conversion rate ranges between 0 and 14% [29, 30, 32, 33, 36, 44, 49–51, 62, 63, 91–95]. Bleeding is the main cause of conversion accounting for 33% of the patients [24, 36, 45, 116].

Accurate patient's selection remains the mainstay to reduce the conversion rate.

Q27: Is there an increased risk of bleeding during simultaneous colon and liver laparoscopic resection if compared to open?

Laparoscopic synchronous colorectal and liver resection is associated to an equal/reduced blood loss if compared to open surgery.

Level of evidence 3b.

Grade of recommendation B.

In a recent systematic review of the literature, the short-term outcomes between synchronous open and laparoscopic resection were analysed and compared in eight different studies. Four studies showed a non-statistically difference of estimated blood loss between the two different approaches ($p > 0.05$), while the remaining four ones showed a statistically significant reduction in estimated blood loss in the laparoscopic group ($p < 0.05$) [117].

- Minimally invasive approaches and devices

Q28: What is the best device for parenchymal transection in minimally invasive liver resections and simultaneous colorectal surgery?

Bipolar cautery may offer advantages in terms of blood loss during MI liver resection for combined CRC and hepatic metastases.

Level of evidence 2a.

Grade of recommendation B.

The use of Argon beam during laparoscopic haemostasis of liver's transection areas requires caution because of the risk of embolism.

Level of evidence 4.

Grade of recommendation C.

In the literature, there are seven case reports of embolism during coagulation with argon plasma systems [19, 136–143]. Two patients died [144]. Although no evidence of RCT is provided, the use of Argon Beam should cautiously avoided [144–146]. Looking at other energy devices, to date there are no comparative studies using different devices during combined colon and liver surgery [118–122]. Almost every laparoscopic liver resection is conducted using a dissection device [123–127]. Regarding haemostasis during liver transection, again the use of several devices is described [128–135]. A network meta-analysis of RCT showed the advantages of using bipolar cautery [136].

Topic 4 implementation

- Training, registries and learned societies

Q29: What should be the role of surgical societies in the development and implementation of minimally invasive approaches for simultaneous colon and liver surgery?

The importance of specific training programs and a stepwise learning is essential and should be promoted by learned societies.

Level of evidence 4.

Grade of recommendation D.

One of the aims of the surgical societies is to improve the progress of the surgical science [147]. Societies should help surgeons to build an ideal curriculum in both colorectal and liver surgery; or alternatively in either one of the field learning to work together. In addition, the learned societies should encourage to promote fellowships, courses and master classes on this specific ITEM; encourage certification system aimed to assess surgeons' proficiency; sustain registries on this specific matter [148].

Q30: Is it advisable, for simultaneous colon and liver minimally invasive surgery, to establish a specific public registry to guarantee data retrieval and analysis?

Registries for laparoscopic combined colon and liver surgery should be established to collect data over time and guarantee data analysis.

Level of evidence 4.

Grade of recommendation C.

Clinical registries collecting data on combined colon and liver resections could be useful to produce scientific evidence, to define outcomes and to advance surgical quality. The adoption of a registry guarantees that all the actions for quality improvements are properly addressed [149]. It also may improve the quality of care thus providing a feedback to the surgeon on the surgical outcomes [150].

When compared to trials on a specific ITEM, registries require fewer resources, have stronger external validity and provide longer term outcome data [151]. The condition for a high-quality registry is the inclusion of the totality of patients as well as its completeness and correctness [152].

- Surgeons and centres

Q31: Is it advisable to reach a proper training in both colorectal and liver surgery before performing simultaneous colon and liver minimally invasive resections?

How many minor and major resections are necessary to complete training in minimally invasive liver surgery?

How many CRC resections are necessary to complete training in minimally invasive colorectal surgery?

Training in both colonic and liver surgery should be obtained before attempting a combined approach.

Level of evidence 4.

Grade of recommendation C.

Several definitions of the proper learning phase in both liver and colorectal surgery have been proposed. The advisable process consists of a step-up approach which starts from basic training followed by training on specific models (animal or cadaveric). Then, the surgeon should advance from simple to complex procedures, under the supervision of a mentor [153].

In a recent systematic review, it was suggested that the number of minor liver resection should be around 60 followed by 50 major resections [154]. Concerning colorectal resections, if considering multiple outcomes, the overall number of procedures to guarantee surgeon proficiency should be more than 200 [153].

To perform a combined resection, proficiency in both colorectal and liver surgery should be obtained. The exception is represented by the availability of two different surgical teams which should be present simultaneously at the operative table to design a proper operative plan.

Q32: Which centres should perform simultaneous colorectal and liver laparoscopic resections?

Centres performing simultaneous laparoscopic colorectal and hepatic resection should have the following requirements:

– A program of advanced laparoscopic surgery;
– A program of open liver surgery with an expertise in intraoperative hepatic ultrasonography;
– A multidisciplinary team for the management of these patients.

Low-volume centres can perform simultaneous laparoscopic resections when both colorectal and liver resection could be defined as easy procedures.

Complex procedures, either colorectal or hepatic or both, should be performed in high-volume centres as long as their outcome is associated with case volume.

Level of evidence 4.

Grade of recommendation C.

The outcome of complex surgical procedures is associated with the hospital volume [155–160]. One study demonstrated that low-volume centres (≤ 2 laparoscopic liver resections/month) perform laparoscopic easy hepatectomies with results similar to high-volume centres (> 2), achieving a worse outcome after complex resections [161]. A Delphi consensus-based position paper mentioned that hospital volume and standardised training are crucial to assure quality to laparoscopic colorectal surgery [12].

International consensus conferences about laparoscopic liver surgery stated that: centres must have expertise in both liver and laparoscopic surgery [17]; indications should be adapted to the local level of proficiency [19]. The Japanese Society for Cancer of the Colon and Rectum stated that, while training in standard laparoscopic colonic resections is introduced since surgical residency programs, advanced training is needed to face complex procedures [162].

Additional requirements to perform liver surgery are: an expertise in intraoperative hepatic ultrasonography and a multidisciplinary team for perioperative management [158].

Q33: Should simultaneous colorectal and liver minimally invasive resections be performed by a single surgical team or by two teams (one colorectal and one hepatic)?

The level of proficiency of a surgical team facing simultaneous resection should be evaluated separately considering laparoscopic colorectal and hepatic resections.

The choice between one-team or two-team surgery should rely on the technical complexity and the surgeons' expertise evaluating each surgical procedure (colorectal and hepatic surgery).

A single team with adequate expertise to face both the resections may perform the whole intervention. Whenever complex and long operations are scheduled, the alternation of two teams is suggested.

Level of evidence 4.

Grade of recommendation C.

No study compared the outcome of procedures performed by one or two teams together. In only 14 of the 31 papers considered for the present analysis, the authors stated whether the surgical procedure was performed by one team ($n=6$) [44, 91, 112, 163–165]; two teams ($n=6$) [36, 41, 43, 94, 166, 167]; or by both ($n=2$, multi-institutional studies) [24, 26]. All series reported favourable outcome, independently of the adoption of one-team or two-team policy. The choice depends on the local organisation and team level of proficiency. The level of proficiency must be evaluated considering the two procedures separately. Laparoscopic major hepatectomies and complex minor hepatectomies should be performed by teams having high-volume laparoscopic liver surgery activity [19, 161]. Complex laparoscopic colorectal procedures, i.e. resection of transverse colon cancer or rectal cancer, resection of bulky tumours, and surgery in severely obese patients or patients with severe adhesions, should be performed by teams with advanced dedicated training [162].

Discussion

This consensus has involved all major Italian Centers dedicated to MI liver and colorectal surgery. Nearly 50% of the engaged centres have specific surgical teams dedicated to each specialty. As a consequence, SCRLM is performed synergistically in the operating theatre. It also means that hospitals are progressively adapting their organisation to the specialties run by teams working in an integrated way.

Regarding patient's selection, age, fragile patients, BMI ≥ 30 and previous surgery do not represent a formal contraindication to synchronous surgery, but attention should be paid to major comorbidities and underlying liver disease as in the open approach.

With regard to procedures, the question of sequence of surgical steps has been widely discussed: prepare always the Pringle manoeuvre and go for liver first in case of difficult/posterior resections.

In case of right colectomy, IA may be equally performed safely as EA if carried on by proficient surgeons. Interestingly, there is no evidence of increased risk of intestinal complication during simultaneous MI rectal and minor liver resection. In addition, indications to stoma diversion for rectal cancer should be the same as in open surgery.

Complex hepatic procedures, as major hepatectomies or resections for posteriorly located lesions, should be performed only by experienced hands and in selected patients.

Conversely, minor resections of anterior segments and left lateral sectionectomies with an Iwate score ≤ 3 may be considered easier and even standard procedures to associate with CRC resection.

Alternatively, no indications were found to operate with a simultaneous approach haemorrhagic colorectal patients.

In the classical two-stage procedures, it is possible to perform safely the first step together with the resection of the primary, but to date, no evidence exists to support the first step of ALPPS.

In the third area of interest "Techniques", no contraindication was found to achieve a correct lymphadenectomy and resection margin R0 in the synchronous approach. There is a reduced rate of post-operative complications in simultaneous procedures and less intraoperative bleeding and shorter hospital stay are found. Particularly intraoperative bleeding seems to be the most frequent cause of conversion to open surgery. In this respect, bipolar forceps seem to be the best device to achieve haemostasis during transection, whereas the use of argon beam should be forbidden to avoid possible embolic complications.

An intraoperative ultrasound exploration should be routinely performed before starting resections: in many studies [109, 110], laparoscopic IOUS has a performance similar to the open one, even if the learning curve of laparoscopic IOUS remains to be clarified.

Figure 1 shows an example of trocar placement, based on the statement above, to perform a combined resection.

In the implementation area of interests, the Consensus underlines that to get credits to perform such complex procedures training, registry of patients and education should be continuously carried on in a context of advanced MI approaches.

Conclusion

In the last 20 years, liver surgery has undergone a real revolution in the technical approaches and surgeons are more confident in MI liver surgery even when simultaneous resections are needed, as the consensus held in Louisville, Morioka and the guidelines in Southampton have clearly assessed.

The birth of the IGOMILS registry in 2014 is the result of this increased activity. Proctoring between Units with different expertise has been one of the crucial ways of spreading of competences and techniques setting a unique strategy to implement technical capacities of dedicated centres.

The Italian Consensus on MI surgery for SCRLM indicates possible pathways to optimise the treatment for these patients as consensus papers express a trend that is likely to become shortly a standard procedure for clinical pictures still on debate. As matter of fact, no RCT or relevant case series on simultaneous treatment of SCRLM are available in the literature to suggest guidelines. Moreover, it remains to be investigated whether the MI technique for the simultaneous treatment of SCRLM maintain the already documented benefit of the two separate surgeries.

The use of Delphi method has indeed allowed strong cooperation and exchange among different centres. Five official multicentre meeting have been carried on in one and a half year to seal the recommendations presented in this paper. The level of evidence is generally not too high because of lack of literature indications and they often reflect the personal experience of surgeons. This the major limitation of this consensus, but it may represent a main stream for the years to come.

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