



저작자표시-비영리-변경금지 2.0 대한민국

이용자는 아래의 조건을 따르는 경우에 한하여 자유롭게

- 이 저작물을 복제, 배포, 전송, 전시, 공연 및 방송할 수 있습니다.

다음과 같은 조건을 따라야 합니다:



저작자표시. 귀하는 원저작자를 표시하여야 합니다.



비영리. 귀하는 이 저작물을 영리 목적으로 이용할 수 없습니다.



변경금지. 귀하는 이 저작물을 개작, 변형 또는 가공할 수 없습니다.

- 귀하는, 이 저작물의 재이용이나 배포의 경우, 이 저작물에 적용된 이용허락조건을 명확하게 나타내어야 합니다.
- 저작권자로부터 별도의 허가를 받으면 이러한 조건들은 적용되지 않습니다.

저작권법에 따른 이용자의 권리는 위의 내용에 의하여 영향을 받지 않습니다.

이것은 [이용허락규약\(Legal Code\)](#)을 이해하기 쉽게 요약한 것입니다.

[Disclaimer](#)

Role and benefit of minimal invasive
colorectal resection with open
hepatectomy in treatment of synchronous
colorectal cancer with
liver metastases

Jong Min Lee

Department of medicine

The Graduate School, Yonsei University



Role and benefit of minimal invasive
colorectal resection with open
hepatectomy in treatment of synchronous
colorectal cancer with
liver metastases

Jong Min Lee

Department of medicine

The Graduate School, Yonsei University

Role and benefit of minimal invasive
colorectal resection with open
hepatectomy in treatment of synchronous
colorectal cancer with
liver metastases

Directed by Professor Kang Young Lee

The Master's Thesis submitted to the Department of
Medicine, the Graduate School of Yonsei University in
partial fulfillment of the requirements for the degree of
Master of Medical science

Jong Min Lee

June 2019

This certifies that the Master's Thesis of
Jong Min Lee is approved.

Thesis Supervisor: Gi Hong Choi

Thesis Committe Member #1: Kang Young Lee

Thesis Committe Member #2: Sang Joon Shin

The Graduate School
Yonsei University

June 2019

Acknowledgements

First of all, I would like to thank my dissertation advisor Professor Kang Young Lee, who has been my great mentor. His conceptualization, enduring encouragement, and scientific advice have been an inestimable source of support for me during this course. Also, I give my appreciation to professor Gi Hong Choi and professor Sang Joon Shin who reviewed this research and gave valuable comment to improve the quality of work.

Nobody has been support to me in the pursuit of this research than the members of my family. I will keep my wife's dedication deep in my heart.

Table of contents

ABSTRCT	1
I. INTRODUCTION.....	3
II. MATERIALS AND METHODS.....	4
1. PATIENTS AND STUDY DESIGN.....	5
2. SURGICAL TECHNIQUE.....	6
3. POSTOPERATIVE MANAGEMENT.....	7
4. POSTOPERATIVE COMPLICATION.....	7
5. STATISTICAL ANLYSIS.....	7
III RESULTS.....	8
1. CLINICAL CHARACTERISTICS.....	8
2. PATHOLOGIC CHARACTERISTICS.....	9
3. PERIOPERATIVE OUTCOME.....	11
4. ONCOLOGIC OUTCOME.....	13
IV. DISCUSSION.....	16
V. CONCLUSION.....	19
REFERENCES.....	20
ABSTRACT(IN KOREAN).....	25

LIST OF FIGURES

Figure 1. Figure. 1. Comparison of overall- and diseases free survival between Open, Hybrid and MIS groups-----14

Figure 2. Comparison of overall- and diseases free survivals adjusted by Fong score between Open, Hybrid and MIS groups-----15

LIST OF TABLES

Table 1. Clinical characteristics -----9

Table 2. Pathologic characteristics -----10

Table 3. Perioperative outcomes -----12

ABSTRACT

Role and benefit of minimal invasive colorectal resection with open hepatectomy in treatment of synchronous colorectal cancer with liver metastases

Jong Min Lee

*Department of Medicine
The Graduate School, Yonsei University*

(Directed by Professor Kang Young Lee)

Minimal invasive surgery (MIS) for colorectal cancer with liver metastases (CRLM) has expanded border of eligibility, but characteristics of hepatic tumor and surgeon's skills still limit for applying MIS to all patients. Theoretically, combination of minimal invasive colorectal resection with open hepatectomy (Hybrid) could be applied to liver metastases is not amenable to MIS, maintaining advantage of faster postoperative recovery compared to conventional open surgery (Open). This study was aimed to investigate whether there is difference in the patient's characteristics and surgical outcomes of patients who underwent Hybrid surgery compared with Open and MIS.

From February 2006 to May 2017, 477 consecutive patients underwent curative resection for synchronous CRLM at a tertiary referral center were identified. All eligible patients were divided by surgical treatments they received: Conventional open surgery (Open, n=351), Minimal invasive

colorectal resection with open hepatectomy (Hybrid, n=55), Minimal invasive colorectal and liver resection (MIS, n=71).

There were no differences in clinicopathological characteristics between Open and Hybrid group. MIS group was associated with significantly lesser extent of hepatic metastases, compared to other two groups. Hybrid group was associated with less severe postoperative day 3 pain ($P=.001$) and faster bowel movement ($P=.016$) and initiation of soft diet ($P<.001$) than Open method. Hepatectomy related complications were more often in Open than MIS group, but not differ between Open and Hybrid group (Open vs. Hybrid; $P=.417$, Hybrid vs. MIS; $P=.032$, MIS vs. Open; $P=.002$). Neither overall- nor disease free survival were not different between Open and Hybrid group.

Hybrid technique is associated with faster recovery of bowel function and similar oncologic outcomes, compared to conventional open surgery. This surgical access could be a feasible option to patients with extensive hepatic metastases.

Key Words: Colorectal cancer; Synchronous liver metastases; Minimal invasive surgery; Minimal invasive colorectal resection with open hepatectomy; conventional open surgery

Role and benefit of minimal invasive colorectal resection with open hepatectomy in treatment of synchronous colorectal cancer with liver metastases

Jong Min Lee

*Department of Medicine
The Graduate School, Yonsei University*

(Directed by Professor Kang Young Lee)

I. Introduction

Colorectal cancer (CRC) is the second and third leading causes of cancer-related deaths in the western countries and South Korea, respectively.¹⁻² The most common metastatic site of CRC is liver with reported 18.9% of synchronous metastases and surgical resection of tumor plays a central role for CRC treatment.³

Simultaneous resection by minimal invasive surgery for both the primary tumor and hepatic metastases has been known to have short term benefit including less amount of blood loss and shorter hospital stay, compared to conventional open surgery.⁴⁻⁷ However, metastatic tumor size, location, proximity to major vessels, underlying liver cirrhosis and surgical skill are still considered as limiting factors for surgical resection with minimal invasive surgery.

In contrast, only the major vessel invasion and insufficient remnant liver volume are considered as the contraindications for conventional open hepatectomy.⁸⁻⁹ However,

conventional open surgery for CRLM usually entails a big incision. Because the two target organs locate at the opposite site of abdominal cavity, long midline incision — from xiphoid process to symphysis pubis — was mandatory, especially in cases of rectal cancer. A large incision accompanies with greater tissue injury and postoperative pain, which could be factors that retards recovery pace after surgery.

Therefore, combination of minimal invasive colorectal resection with open hepatectomy (Hybrid) could be a proper alternative for both conventional open surgery and minimal invasive surgery. This technique could share same selection criteria for CRLM with conventional open hepatectomy. Possible merit of the Hybrid technique over the conventional open surgery is the enhanced immediate postoperative recovery and Hybrid technique is expected to have benefit of faster postoperative recovery without compromising oncologic outcome.

Thus, this study was aimed to investigate the tumor characteristics and surgical outcomes of Hybrid technique in comparison with conventional open- and minimal invasive surgery.

II. Materials & methods

1. Patients and study design

During February 2006 to May 2017, data of consecutive patients underwent simultaneous resection with curative aim for synchronous CRLM at Severance hospital, Seoul, South Korea were drawn from a prospective colorectal cancer registry. Synchronous metastases was defined as metastatic tumors identified at the time of initial work-up. Patients with extra-hepatic metastases or patients underwent radiofrequency ablation (RFA) without liver resection or who underwent staged liver resection were excluded from the study. All eligible patients were grouped based on access technique for surgical resection. Patients who underwent laparoscopic or robotic colorectal resection with open hepatectomy were defined as Hybrid group. Patients who received conventional open surgery for the resection of primary and metastatic tumor were defined as Open group. Patients whose primary and metastatic tumor resection was completed only by laparoscopy or robot were defined as MIS group. Open, MIS and Hybrid were compared each other, from baseline characteristics to short- and long term outcomes. The study protocol was approved by the Institutional Review Board of the Human Research Protection Center, Severance Hospital, Seoul, South Korea (4-2018-1191). The informed consent was waived due to the retrospective analysis of this study.

2. Surgical technique

Surgical resection was conducted under the principle of achieving the complete resection of tumor while preserving resected organ function. Accessing methods for each patients were chosen at the discretion of surgeons. Multidisciplinary team meeting before surgery was held to discuss patient's treatment strategy on the attending of colorectal- and hepato-biliary surgeon. All surgical resections were performed under cooperation of colorectal and hepato-biliary surgeons. Minimal invasive colorectal resection was usually not limited, but if the complete resection was not guaranteed due to invasion of adjacent organ, open method was considered. Preoperative liver status and tumor characteristics were the considered in choosing eligible patient for laparoscopic or robotic hepatectomy.

3. Postoperative management

We routinely urge patients to walk on postoperative day (POD) 1. If any special pre- or intraoperative was not indicated (i.e. high risk of anastomosis leakage or preoperative bowel obstruction), we allow patients to start oral diet on POD 2. Generally, if patients didn't report the passage of flatus, soft diet was not allowed. Removal of abdominal drain was indicated the amount of drainage become less than about 100ml/day, but decision to remove drain was dependent on operator's judgment. Routine check-up on liver was performed with abdomino-pelvic CT scan on POD

5~7.

4. Postoperative complication

Posthepatectomy liver failure was graded according to International study Group of Liver Surgery (ISGLS) definition. Grade A was defined as liver failure that require no change of the patient's clinical management. Patients who needs management which deviates from the regular course including use of diuretics or albumin replacement were graded as B. If the patient needs for invasive treatment, it is defined as grade C liver failure.¹⁰

5. Statistical analysis

All analysis were processed by use of the SPSS version 20.0 (SPSS Institute, Chicago, IL). Frequency testing for categorical variables was conducted by χ^2 test and continuous variables were compared by using ANOVA or Kruskal-Walis test according to the result of the Shapiro Wilk normality test. Then, the Bonferroni corrections for pairwise comparisons were evaluated with the Mann-Whitney U test (significance limit $P < 0.0167$). Univariable analyses for survival and recurrences were carried out by Kaplan-Meier method and log-rank test. The minimum significance

was taken as two-tailed $P < 0.05$.

III. Results

1. Clinical characteristics

The preoperative clinical characteristics are described in Table 1. There were no significant difference in age, sex, body mass index (BMI), proportion of the patients with American Society of Anesthesiologist (ASA) score ≥ 3 and patients submitted to neoadjuvant chemotherapy or preoperative radiotherapy among three groups.

The proportion of primary tumor location among three groups showed significant difference. Rectal cancer was more frequently found in Hybrid group, while right colon cancer was more common in Open group (Open vs Hybrid; $P = .013$, Hybrid vs MIS; $P = .089$, MIS vs Open; $P = .362$).

Table 1. Clinical characteristics

	Open (n=351)	Hybrid (n=55)	MIS (n=71)	P
Age, mean \pm SD, y	58.4 \pm 10.9	60.8 \pm 10.7	58.5 \pm 11.0	.539
Male, n (%)	243 (69.2)	38 (69.1)	45 (63.4)	.622

BMI, median (range), kg/m ²	23.1 ±2.9	23.2 ±3.1	23.8 ±3.1	.149
ASA score≥3, n (%)	54 (15.4)	9 (16.4)	11 (15.5)	.983
CEA at diagnosis, median (range), ng/ml	13.2 (0.5-20000)	13.0 (0.6-6955)	7.1 (0.8-1609)	.171
Preoperative chemotherapy, n (%)				.640
No	170 (48.4)	24 (43.6)	37 (52.1)	
Oxaliplatin or irinotecan	181 (51.6)	31 (56.4)	34 (47.9)	
Target agent, n (%)				.189
No	228 (67.9)	32 (59.3)	39 (58.2)	
Bevacizumab or cetuximab	108 (32.1)	22 (40.7)	28 (41.8)	
Preoperative radiotherapy, n (%)				.811
No	310 (88.3)	50 (90.9)	62 (87.3)	
Yes	41 (11.7)	5 (9.1)	9 (12.7)	
Tumor location, n (%)				.038
Right colon	68 (19.4)	2 (3.6)	11 (15.5)	
Left colon	137 (39.0)	23 (41.8)	24 (33.8)	
Rectum	146 (41.6)	30 (54.5)	36 (50.8)	

Abbreviations: BMI, Body Mass Index; ASA, American Society of Anesthesiologists; CEA, carcinoembryonic antigen.

2. Pathologic characteristics

Pathologic characteristics among groups of three access methods are summarized in Table 2. There was no significant differences in primary tumor characteristics among three groups. On the other hand, all indicators that related to difficulty of curative hepatic resection, including number, size, location of posterior liver segment (S1, 7, 8) showed significant difference between MIS and other two groups. MIS group was associated with fewer number of liver metastases (Open vs Hybrid; $P > .999$, Hybrid vs MIS; $P = .0001$, MIS vs Open; $P < .001$), smaller size of tumor (Open vs Hybrid;

P>.999, Hybrid vs MIS; P=.269, MIS vs Open; P=.002), lower proportion of bilobar involvement (Open vs Hybrid; P=.317, Hybrid vs MIS; P<.001, MIS vs Open; P<.001), and involvement of S1 or 7 or 8 (Open vs Hybrid; P=.859, Hybrid vs MIS; P=.004, MIS vs Open; P<.001). In the comparisons between Open and Hybrid group, extent of hepatic metastases was not different. In line with tumor characteristics of liver, major hepatectomy (≥ 3 segmentectomy) was more frequently performed in Open and Hybrid, when compared with MIS (Open vs Hybrid; P=.232, Hybrid vs MIS; P=.006, MIS vs Open; P<.0001).

Table 2. Pathologic characteristics

	Open (n=351)	Hybrid (n=55)	MIS (n=71)	P
pT stage, n (%)				.336
Complete response	13 (3.7)	1 (1.8)	3 (4.2)	
1	5 (1.4)	1 (1.8)	2 (2.8)	
2	16 (4.6)	5 (9.1)	7 (9.9)	
3	260 (74.1)	34 (61.8)	49 (69.0)	
4	57 (16.2)	14 (25.5)	10 (14.1)	
pN stage, n (%)				.157
0	90 (25.6)	17 (30.9)	28 (39.4)	
1	146 (41.6)	24 (43.6)	25 (35.2)	
2	115 (32.8)	14 (25.5)	18 (25.4)	
No. of metastatic tumor, median (range)	3 (0-27)	3 (1-17)	1 (1-6)	<.001
Size of the metastatic tumor, median (range), cm	2.2 (0.0-17.0)	2.0 (0.2-10.0)	1.4 (0.1-6.0)	.003
Bilobar involvement, n (%)				<.001
No	185 (52.7)	25 (45.5)	64 (90.1)	
Yes	166 (47.3)	30 (54.5)	7 (9.9)	
Involvement of S1 or 7 or 8, n (%)				<.001
No	117 (33.3)	19 (34.5)	43 (60.6)	
Yes	234 (66.7)	36 (65.5)	28 (39.4)	

Extent of liver resection, n (%)				<.001
Wedge resection	138 (39.3)	19 (34.5)	44 (62.0)	
≤2 segmentectomy	95 (27.1)	21 (38.2)	19 (26.8)	
≥3 segmentectomy	118 (33.6)	15 (27.3)	8 (11.3)	

Abbreviations: p, pathologic; No, number;

3. Perioperative outcome

Operation time of Hybrid group was significantly longer (Open vs Hybrid; $P<.001$, Hybrid vs MIS; $P=.038$, MIS vs Open; $P>.999$) but the amount of blood loss was not different, compared with Open (Open vs Hybrid; $P>.999$, Hybrid vs MIS; $P<.001$, MIS vs Open; $P<.001$). Rate of R1 resections both in primary and metastatic tumor didn't show significant differences.

Hybrid group showed earlier recovery of bowel function which was composed by bowel movement (Open vs Hybrid; $P=.012$, Hybrid vs MIS; $P=.063$, MIS vs Open; $P<.001$) and initiation of soft diet (Open vs Hybrid; $P<.001$, Hybrid vs MIS; $P=.005$, MIS vs Open; $P<.0001$) than Open. Hybrid group showed better result in postoperative day (POD) 3 pain intensity (Open vs Hybrid; $P<.001$, Hybrid vs MIS; $P=.407$, MIS vs Open; $P<.001$) than Open group. However, significant difference in POD 5 pain intensity only demonstrated in comparison between MIS and Open groups (Open vs Hybrid; $P=.624$, Hybrid vs MIS; $P=.048$, MIS vs Open; $P<.001$).

Any significant difference was not observed in primary tumor related surgical

complication among groups. Hepatectomy related complications were commonly found in Open group, when compared with MIS group (Open vs Hybrid; P=.417, Hybrid vs MIS; P=.032, MIS vs Open; P=.002). The significant difference in ISGLS grade B liver failure (Open vs Hybrid; P=.390, Hybrid vs MIS; P=.021, MIS vs Open; P=.003) may contribute to this result. MIS showed the shortest length of hospital stay in comparison with other two groups (Open vs Hybrid; P=.797, Hybrid vs MIS; P<.001, MIS vs Open; P<.001) (Table 3).

Table 3. Perioperative outcome

	Open (n=351)	Hybrid (n=55)	MIS (n=71)	P
Operation time, median (range), min	409 (216-914)	507 (226-952)	426 (154-884)	.001
Blood loss, median (range), ml	550 (0-3950)	500 (50-3500)	200 (0-1200)	<.001
R1 resection of primary tumor, n (%)	18 (5.1)	5 (9.1)	2 (2.8)	.586
R1 resection of liver metastases, n (%)	19 (5.4)	2 (3.6)	2 (2.8)	.122
POD 3 NPIS, median (range)	6 (1-9)	5 (1-8)	3 (1-7)	<.001
POD 5 NPIS, median (range)	4 (1-9)	3 (2-8)	3 (2-8)	<.001
Passage of flatus, median (range), d	4 (1-19)	3 (2-7)	3 (1-7)	<.001
Return to soft diet, median (range), d	5 (3-17)	4 (3-8)	4 (2-8)	<.001
Surgical complication, n (%)	118 (33.6)	18 (32.7)	13 (18.3)	.039
Primary tumor resection related, n (%)	93 (26.5)	15 (27.3)	13 (18.3)	.331
Wound infection, n (%)	16 (4.6)	2 (3.6)	2 (2.8)	.781
Ileus, n (%)	36 (10.3)	3 (5.5)	2 (2.8)	.085
Acute urinary retention, n (%)	19 (5.4)	5 (9.1)	5 (7.0)	.532

Chylous ascites, n (%)	19 (5.4)	3 (5.5)	3 (4.2)	.917
Anastomosis leakage, n (%)	13 (3.7)	3 (5.5)	2 (2.8)	.737
Hepatectomy related, n (%)	60 (17.1)	7 (12.7)	2 (2.8)	.007
Perihepatic complicated fluid collection, n (%)	23 (6.6)	2 (3.6)	2 (2.8)	.364
ISGLS grade B, n (%)	39 (11.1)	4 (7.3)	0 (0.0)	.010
ISGLS grade C, n (%)	1 (0.3)	1 (1.8)	0 (0.0)	.220
Medical complication, n (%)	44 (12.5)	7 (12.7)	5 (7.0)	.411
Clavien-Dindo grade ≥ 3 , n (%)	51 (14.5)	8 (14.5)	5 (7.0)	.232
Hospital stay, median (range), d	12 (6-96)	11 (6-55)	8 (5-27)	<.001
Mortality, n (%)	2 (0.6)	0 (0.0)	1 (1.4)	.589
Adjuvant chemotherapy, n (%)	305 (86.9)	49 (89.1)	66 (93.0)	.345

All mortality and morbidity were within 1 month.

Abbreviations: ISGLS, International study Group of Liver Surgery; NPIS, Numeric Pain Intensity Scale

4. Oncologic outcomes

Unadjusted survival comparison between groups showed significant difference (Figure 1). Pairwise comparisons of overall survival (OS) and disease free survival (DFS) were not significantly different between Open and Hybrid group. However, MIS group showed better 5-year OS (Open vs Hybrid; $P=.962$, Hybrid vs MIS; $P=.066$, MIS vs Open; $P=.02$) and DFS (Open vs Hybrid; $P=.967$, Hybrid vs MIS; $P=.077$, MIS vs Open; $P=.016$), compared with Open group. To control the heterogeneity in hepatic characteristics among the groups, Fong score based on previously published studies was

calculated for each patients.¹¹ The following risk factors consisted of clinical risk scores: nodal status of primary tumor, number of hepatic tumors > 1, initial CEA level of >200 ng/ml and size of largest hepatic tumor > 5 cm. Each criterion was assigned 1 point. Patients with scores of 0 or 1 were classified as low Fong and patients with scores of 2, 3 or 4 as high Fong. Fong score-adjusted overall survival (OS) and disease free survival (DFS) were not significantly different between the groups (Figure 2).

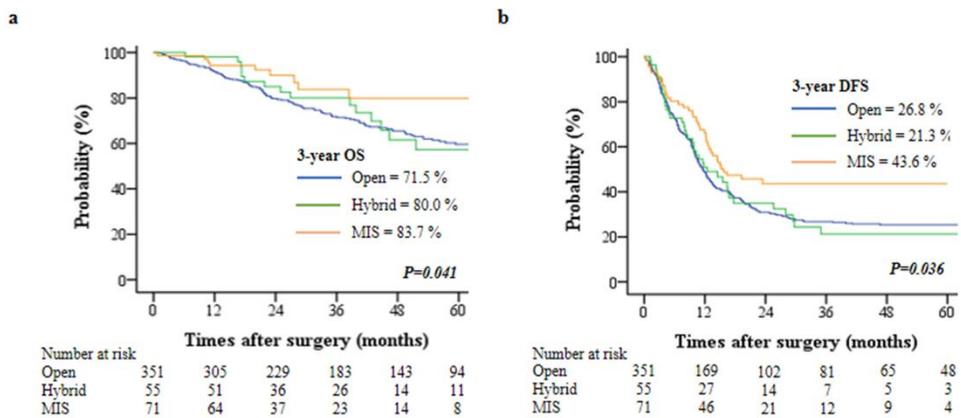


Figure. 1. Comparison of overall- and diseases free survival between Open, Hybrid and MIS groups. (a) Overall survival (Open vs Hybrid; $P=0.962$, Hybrid vs MIS; $P=0.066$, MIS vs Open; $P=0.02$) (b) Diseases free survival (Open vs Hybrid; $P=0.036$, Hybrid vs MIS; $P=0.036$, MIS vs Open; $P=0.036$)

Hybrid; $P=.967$, Hybrid vs MIS; $P=.077$, MIS vs Open; $P=.016$).

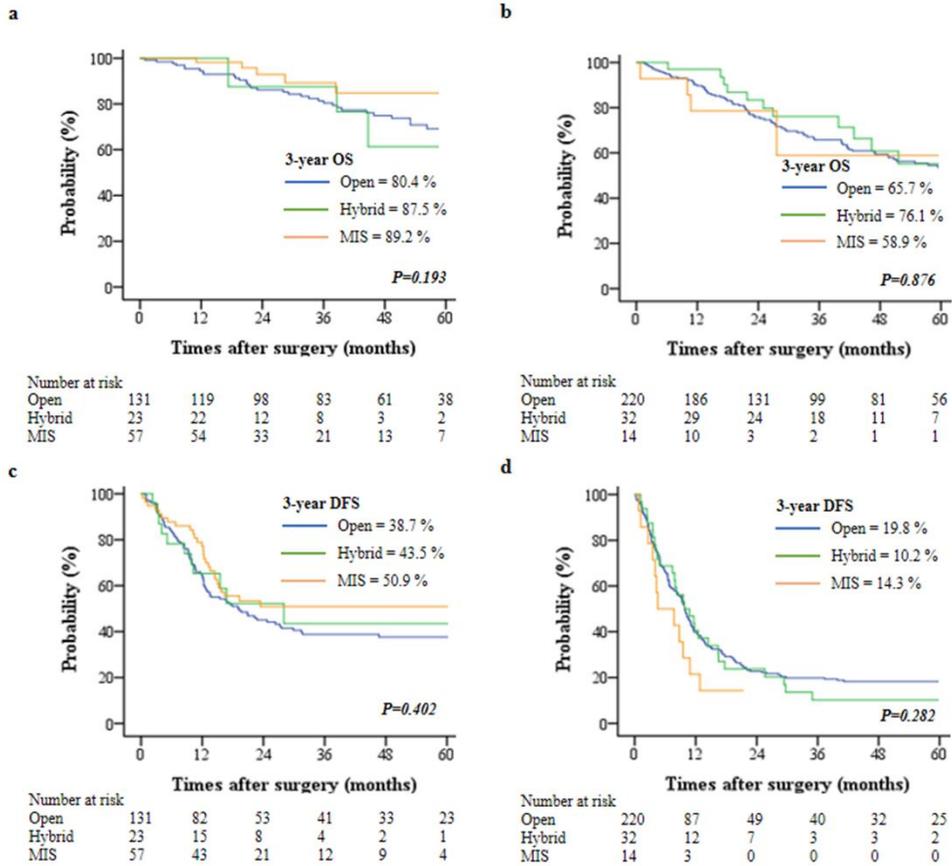


Figure 2. Comparison of overall- and diseases free survivals adjusted by Fong score between Open, Hybrid and MIS groups. (a) Overall survival in patients with Fong score 0-1 (b) Overall survival in patients with Fong score 2-4 (c) Disease free survival in patients with Fong score 0-1 (d) Disease free survival in patients with Fong score 2-4

Diseases free survival in patients with score Fong 0-1 (d) Diseases free survival in patients with Fong score 2-4.

IV. Discussion

As far as we know, this is the first study comparing the surgical outcomes of Hybrid technique with other surgical access methods. There were few studies reporting surgical outcome of combined laparoscopic colorectal resection with open liver resection.¹²⁻¹³ These studies analyzed only 10 patients and combined the Hybrid and MIS as a same group, which prevents to examine the surgical outcome of Hybrid technique.

Our principal finding was that Hybrid technique showed faster immediate postoperative recovery in comparison with Open technique and no significant difference in days of passage of flatus and pain intensity, even when compared with MIS group. Importantly, Hybrid technique did not compromise oncologic outcomes, compared with other methods. These findings suggested that Hybrid technique may be oncologically safe, as well as have strength in immediate postoperative recovery. There are several possible explanations for this results. Laparoscopic surgery have shown that minimize the surgical trauma, which in turn decreased postoperative pain, respiratory distress and rapid discharge from hospital. Even open hepatectomy was

combined with minimal invasive colorectal resection in patients with Hybrid technique, Hybrid group showed lower POD 3 pain intensity than Open group, which support the faster recovery of bowel function. In addition to the issue of incision length, reduced bowel manipulation could be the one reason for better recovery of Hybrid technique.¹⁴⁻¹⁶ Several studies have demonstrated that air exposure of peritoneal cavity can induce the peritoneal, even the systemic inflammatory reaction in laparotomy. Some experimental studies have demonstrated the length of peritoneal air exposure is correlated with the level of systemic and intestinal inflammation.¹⁷⁻²⁰ All these factors are possible contributors for faster postoperative recovery of Hybrid technique.

However, why the comparison in hospital stay between Open and hybrid failed to demonstrate the statistical difference is not clear. Previous studies presented that there are various clinical, socioeconomical factors for length of hospital stay in colorectal cancer. Kelly et al. analyzed 8197 colorectal cancer patients identified from National Cancer Registry Ireland and showed age, marital status, smoking history, comorbidity, tumor location, insurance status are associated with length of stay.²¹ Hsia et al. demonstrated that independent factors of prolonged hospital stay after hepatectomy for hepatocellular carcinoma were preoperative prothrombin activity, intraoperative blood transfusion, surgical complication, and the time to abdominal drain removal.²² Because this study was not aimed to analyze the hospital stay after

colorectal surgery, assessment to these factors were limited. One possible explanation based on the perioperative outcome of this study is that hepatectomy related complication diluted the effect from faster recovery in bowel function. Rates of complications related with hepatectomy and ISGLS grade B liver failure were similar in Open and Hybrid and rare in MIS group due to lesser amount of hepatic resection. The analysis of complication in detail leads us to speculated that ISGLS grade B, which was defined as any routine use of diuretics and/or replacement of albumin after postoperative day 5, may impact on length of the hospital stay. The difference of the day between median hospital stay and the day of starting soft diet was 7 days (Soft diet: 5, 4 days; Hospital stay: 12, 11 days in Open and Hybrid, respectively). This means one week of hospital rehabilitation was required to discharge the patients after starting soft diet in patients with Open and Hybrid. Compared to this, only 4 days of additional hospital stay was needed in MIS group. Thus, we can assume the high frequency of hepatic complication in Open and Hybrid group might result in statistical insignificance in hospital stay between two groups.

This study has inherent selection bias due to its retrospective nature. The difference in primary tumor location between Open and Hybrid is one example of selection bias of this study. This clinical feature suggested us one thinking point. The phenomenon that rectal cancer is common in Hybrid group may be reflection that surgeon have avoided the Open technique in cases of rectal cancer, which needs larger incision than

patients with right colon cancer.

Despite the abovementioned limitation of this study, Hybrid seems to be a strong alternative to conventional open surgery in patients who cannot be a candidate for minimal invasive hepatectomy. For patients with CRLM difficult to perform minimal invasive hepatectomy, Hybrid technique offers relatively safe surgical resection for liver metastases, while taking advantage of earlier recovery of bowel function.

V. CONCLUSION

Minimal invasive colorectal resection with open hepatectomy showed lesser postoperative pain and earlier recovery of bowel function without compromising oncologic outcomes, compared to conventional open surgery. These short-term outcomes were also comparable to the result of minimal invasive surgery. Hybrid technique could be an appropriate alternative to conventional open- and minimal invasive surgery for colorectal patients with extensive hepatic metastases.

REFERENCES

- (1) Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin* 2013;63:11–30.
- (2) Hur H, Oh CM, Won YJ, Oh JH, Kim NK. Characteristics and Survival of Korean Patients With Colorectal Cancer Based on Data From the Korea Central Cancer Registry Data. *Ann Coloproctol* 2018;34(4):212-21
- (3) Leporrier J, Maurel J, Chiche L, Bara S, Segol P, Launoy G. A population-based study of the incidence, management and prognosis of hepatic metastases from colorectal cancer. *Br J Surg* 2006;93:465–74
- (4) Chie Takasu, Shimada M, Sato H, Miyatani T, Imura S, Morine Y et al. Benefits of simultaneous laparoscopic resection of primary colorectal cancer and liver metastases. *Asian J Endosc Surg*. 2014;7(1):31-7
- (5) Ferretti S, Tranchart H, Buell JF, Eretta C, Patriti A, Spampinato MG et al. Laparoscopic Simultaneous Resection of Colorectal Primary Tumor and Liver Metastases: Results of a Multicenter International Study. *World J Surg*. 2015;39(8):2052-60
- (6) Untereiner X, Cagniet A, Memeo R, Tzedakis S, Piardi T, Severac F et al.

Laparoscopic hepatectomy versus open hepatectomy for colorectal cancer liver metastases: comparative study with propensity score matching. *HepatoBiliary Surg Nutr* 2016;5(4):290-99

- (7) Beppu T, Wakabayashi G, Hasegawa K, Gotohda N, Mizuguchi T, Takahashi Y et al. Long-term and perioperative outcomes of laparoscopic versus open liver resection for colorectal liver metastases with propensity score matching: a multi-institutional Japanese study. *J Hepatobiliary Pancreat Sci.* 2015;22(10):711-20
- (8) Rees M, Tekkis PP, Welsh FK, O'Rourke T, John TG. Evaluation of long-term survival after hepatic resection for metastatic colorectal cancer: a multifactorial model of 929 patients. *Ann Surg.* 2008;247(1):125-35.
- (9) Rocha FG, Helton WS. Resectability of colorectal liver metastases: an evolving definition. *HPB (Oxford).* 2012;14(5):283-4
- (10) 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;149:713-24.

- (11) Fong Y, Fortner J, Sun RL, Brennan MF, Blumgart LH. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. *Ann Surg.* 1999;230(3):309-18
- (12) Hatwell C, Bretagnol F, Farges O, Belghiti J, Panis Y. Laparoscopic resection of colorectal cancer facilitates simultaneous surgery of synchronous liver metastases. *Colorectal Dis.* 2013;15(1):e21-8
- (13) Akiyoshi T, Kuroyanagi H, Saiura A, Fujimoto Y, Koga R, Konishi T et al. Simultaneous resection of colorectal cancer and synchronous liver metastases: initial experience of laparoscopy for colorectal cancer resection. *Dig Surg.* 2009;26(6):471-5
- (14) Veldkamp R, Kuhry E, Hop WC, Kazemier G, Bonjer HJ, Haglind E et al. Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. *Lancet Oncol* 2005; 6: 477–84
- (15) Bauer AJ, Boeckxstaens GE. Mechanisms of postoperative ileus. *Neurogastroenterol Motil.* 2004;16 (Suppl 2):54-60
- (16) Buunen M, Gholghesaei M, Veldkamp R, Meijer DW, Bonjer HJ, Bouvy

- ND. Stress response to laparoscopic surgery: a review. *Surg Endosc.* 2004;18(7):1022-8
- (17) Novitsky YW, Litwin DE, Callery MP. The net immunologic advantage of laparoscopic surgery. *Surg Endosc.* 2004;18(10):1411-9
- (18) Kalff JC, Schraut WH, Simmons RL, Bauer AJ. Surgical manipulation of the gut elicits an intestinal muscularis inflammatory response resulting in postsurgical ileus. *Ann Surg.* 1998;228(5):652-63.
- (19) Tan S, Yu W, Lin Z, Chen Q, Shi J, Dong Y et al. Peritoneal air exposure elicits an intestinal inflammation resulting in postoperative ileus. *Mediators Inflamm.* 2014;2014:924296
- (20) Watson RW, Redmond HP, McCarthy J, Burke PE, Bouchier-Hayes D. Exposure of the peritoneal cavity to air regulates early inflammatory responses to surgery in a murine model. *Br J Surg.* 1995;82(8):1060-5.
- (21) Kelly M, Sharp L, Dwane F, Kelleher T, Comber H. Factors predicting hospital length-of-stay and readmission after colorectal resection: a population-based study of elective and emergency admissions. *BMC Health Serv Res.* 2012;26:12:77

(22) Hsia CY, Chau GY, King KL, Loong CC, Lui WY, Wu CW. Factors for prolonged length of stay after elective hepatectomy for hepatocellular carcinoma. The surgeon's role in the managed care era. *Hepatogastroenterology*. 2003;50(51):798-804

국문요약

동시성 대장직장암 간 전이 환자에서 최소침습 대장 절제술과 결합된 개복 간 전이 절제의 역할 및 이점

<지도교수 이강영>

연세대학교 대학원 의학과

이종민

동시성 대장직장암 간 전이 환자에서 최소 침습 수술의 적응증은 점차 확장되어 왔지만 간 전이의 특징과 외과의의 수술 기술은 모든 환자에게 최소 침습 수술을 적용하는 데에 있어 한계점이 되고 있다. 이론적으로, 최소 침습 대장직장 절제술과 개복 간 절제의 병합 기법 (하이브리드)은 최소 침습 수술로 절제가 어려운 간 전이에 적용될 수 있고, 전통적 개복 수술 (개복 수술)에 비해 수술 후 회복 속도가 빠르다. 본 연구는 개복 수술 또는 최소 침습 수술과 비교하여 하이브리드 수술을 받은 환자의 특성 및 수술 결과를 비교하고자 한다.

2006 년 2 월부터 2017 년 5 월까지 신촌 세브란스 병원에서 동시성 대장직장암 간 전이에 대한 근치적 절제술을 받은 477 명의 환자가 수술 방법에 따라 개복 수술 군 (351명), 하이브리드 군 (55명), 최소 침습 수술 군(71명) 으로 분류되었다.

개복수술 군과 하이브리드 군간에 임상 병리학 적 특징에는 차이가 없었다. 최소 침습 수술 군은 다른 두 군과 비교하여 간 전이의 범위가 유의하게 적었다. 하이브리드 군은 전통적 개복수술 군에 비하여 수술 후

3 일째 통증이 적었고 ($P = .001$), 가스 배출이 빨랐으며 ($P = .016$), 연식 섭취가 빨리 시작되었다 ($P < .001$). 간 절제 관련 합병증은 최소 침습 수술 군보다 개복 수술 군에서 더 많았지만 개복 수술 군과 하이브리드 군에서는 차이가 없었다 (개복 대 하이브리드; $P = .417$, 하이브리드 대 최소 침습 수술; $P = .032$, 최소 침습 수술 대 개복, $P = .002$). 전체 및 무병 생존율은 개복 수술 하이브리드 군간에 차이가 없었다.

하이브리드 수술은 기존의 개복 수술과 비교하여 빠른 장 기능 회복과 유사한 종양학적 결과를 보인다. 이 수술 기법은 광범위한 간 전이가 있는 환자에서 개복 수술이나 최소 침습 수술을 대체할 적절한 하나의 방법으로 보인다.

핵심되는 말: 대장암, 직장암, 동시성 간 전이, 최소 침습 수술, 개복 수술, 최소 침습 대장 절제 및 개복 간 절제