Critiquing A Research Paper A Practical Example

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Critiquing
A Research Paper

A Practical Example

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Long-term Outcomes of a Randomized Controlled Trial of Single-incision Versus Multi-port Laparoscopic Colectomy for Colon Cancer

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Objective: The aim of this study was to evaluate the long-term outcomes that were the secondary endpoints of a RCT of multi-port laparoscopic colectomy (MPC) versus SILC in colon cancer surgery.

Summary of Background Data: The actual long-term outcomes, such as the 5-year RFS, OS, and recurrence patterns after surgery, have not been evaluated by a RCT.

Methods: Patients with histologically proven colon carcinoma located in the cecum, ascending, sigmoid or rectosigmoid colon clinically diagnosed as stage 0-III were eligible for this study. Patients were preoperatively randomized and underwent complete mesocolic excision. The 5-year RFS, OS, and recurrence patterns were analyzed (UMIN-CTR 000007220).

Results: Between March 1, 2012, and March 31, 2015, a total of 200 patients were randomly assigned to either the MPC arm (n = 100) or SILC arm (n = 100). The median follow-up for all patients was 61.0 months. An intention-to-treat analysis showed that the 5-year RFS was 91.0% [95% confidence interval (CI) 85.1%–96.9%] in the MPC arm and 88.0% (95% CI 82.1%–93.9%) in the SILC arm (hazard ratio: 1.37; 95% CI 0.58–3.24; $P = 0.479$). The 5-year OS was 95.0% (95% CI 91.1%–98.9%) in the MPC arm and 93.0% (87.1%–98.9%) in the SILC arm (hazard ratio: 1.39; 95% CI 0.44–4.39; $P = 0.568$). There were no significant differences in the recurrence patterns between the 2 arms.

Conclusions: Even though the results of the 5-year OS and RFS in this trial were exploratory and underpowered, there were no statistically significant differences between the SILC and MPC arms. SILC may be an acceptable treatment option for select patients with colon cancer.

Keywords: colorectal cancer, laparoscopic colorectal surgery, long-term outcome, single incision laparoscopic colectomy, single-port laparoscopic colectomy

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Many retrospective studies and 7 randomized clinical trials (RCTs) have reported that single-incision laparoscopic colectomy (SILC) is feasible without any marked difference in short-term outcomes, such as surgical outcomes and postoperative complications, compared with multi-port laparoscopic colectomy (MPC).[1–20]

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Furthermore, meta-analyses have shown that SILC is safe and feasible when skilled laparoscopic surgeons perform it with respect to its short-term results compared with those of MPC.[21–26]

Regarding the long-term results of SILC for colon cancer, however, only a few results have been reported by retrospective propensity score matching analyses.[17,18,27,28] Furthermore, what few SILC data are available are subject to significant biases because the reported studies are nonrandomized and retrospective design, and regarding the indications for surgery and use of instruments, significant heterogeneity in the study population has been reported. Therefore, in the absence of RCT results, there is weak clinical evidence supporting the long-term outcomes of SILC.[29] The oncological outcomes previously reported by RCTs are "surrogate" outcomes, such as the resection margin, specimen length and number of lymph nodes harvested. However, the actual long-term outcomes, such as the 5-year relapse-free survival (RFS), overall survival (OS), and recurrence patterns after surgery, have not been evaluated.

We performed an RCT of MPC versus SILC in colon cancer surgery and reported the short-term results.[3] The aim of this study was this to compare the 5-year RFS, OS, and recurrence patterns that were the secondary endpoints of this RCT after SILC with those after MLC for colon cancer.

METHODS

Patients

This open-label multi-institutional RCT was conducted from March 1, 2012, to March 31, 2015, as has been previously described. This was a parallel group trial with a 1:1 allocation ratio. Patients were enrolled at 3 institutions of the Yokohama Clinical Oncology Group in Japan. The study was approved by the institutional review board for studies in humans of each participating hospital. This study was registered with the Japanese Clinical Trials Registry (UMIN-CTR 000007220 [http://www.umin.ac.jp/ctr/index.htm]). Before enrolling in this study, all patients provided their written informed consent.

The eligibility criteria were as follows: (1) Patients with histologically proven colon carcinoma; (2) Clinically diagnosed as Union for International Cancer Control TMN classification (seventh edition)[29] stage 0–III; (3) Curative resection planned; (4) Tumor located in the cecum, ascending, sigmoid, or rectosigmoid colon; (5) Tumor length ≥4.0 cm; (6) Patient age 20–80 years old; (7) Performance status (Eastern Cooperative Oncology Group) 0–1; (8) No history of gastrointestinal surgery other than appendectomy; and (9) No organ dysfunction or blood abnormality within 14 days before registration (white blood cell count ≥3000/mm^3 and ≤12,000/mm^3, platelet count ≥100,000/mm^3, hemoglobin ≥9.0 g/dL, aspartate aminotransferase and alanine aminotransferase ≤2.5 times standard upper value, serum total bilirubin ≤1.5 mg/dL and serum creatinine ≤1.5 mg/dL.

Summary of the Last Session

- Critiquing a research paper is an important skill
- Helps in evaluation of the available research and application of evidence based medicine
- Requires systematic approach
- Credibility is not an alternative to validity and reliability
- Even credible and authentic studies may not be applied to clinical practice straight away

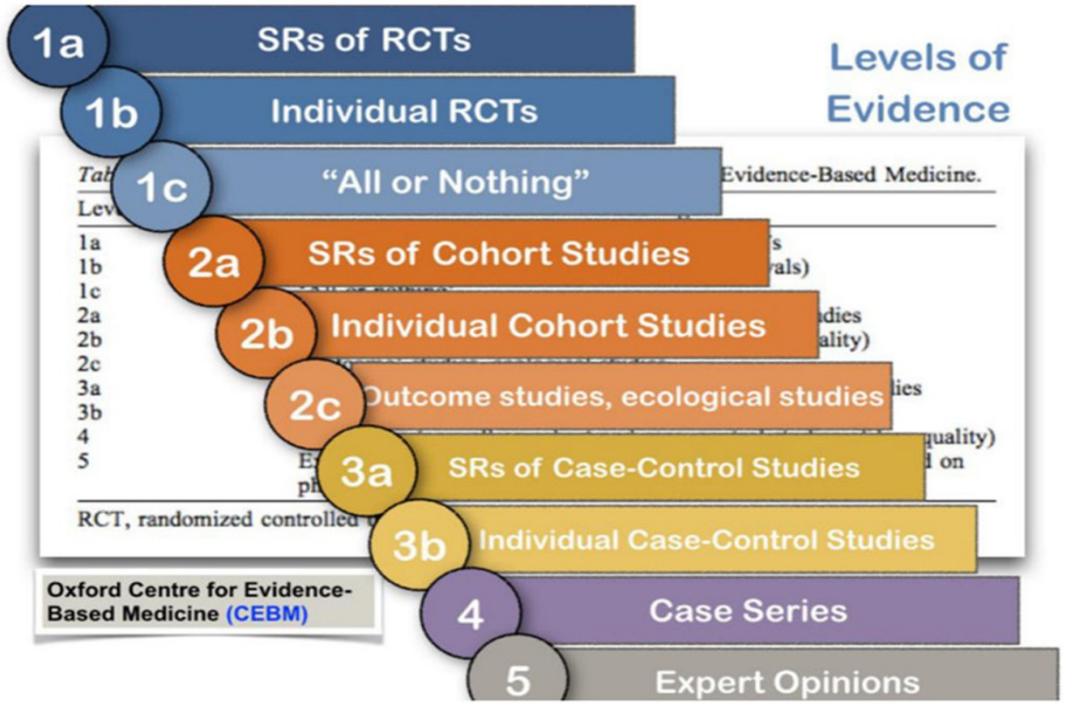
Steps of Critical Appraisal

Step 1: Making sense of Title

- Use of Terminology
- ? Topic of recent interest
- Topic Specialist interest Vs General Interest

Step 2: Assessing Credibility

- Type of Article on Oxford Hierarchy
- Authors and Institute
- Journal and Impact Factor
- Publication Date
- Funding Sources
- References
  - Recent, Balanced, Good Journals
  - minimal information from websites



Step 3: Read the Abstract

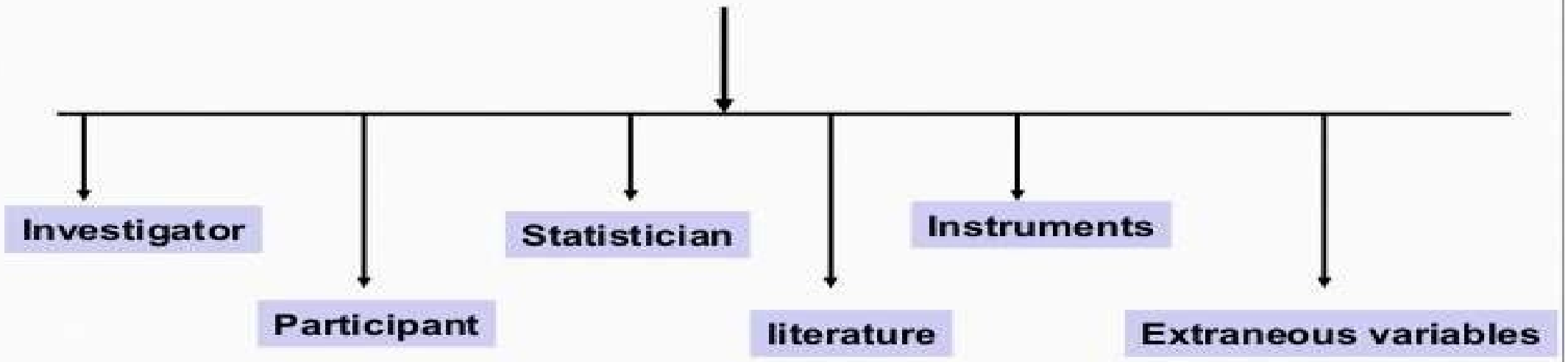
- To get **general Idea** of the Article
- To Assess it **Structure**
  - Background, Methods, Results, Conclusion
- To Assess the **authenticity of the Abstract**
  - Is it the true representative of actual article

Step 4: Assess the validity and Reliability of study (Reading the whole Paper)

- Validity
  - The results produced are the **true representative of reality**.
    - *Absolute Wight is not the true representative of Obesity, BMI may be*
- Reliability
  - The design of the study **will produce similar results over and over** again
    - *An out of order BP machine may report different reading for the same BP*

- A valid and Reliable study will have alignment
  1. **Problem identified** in the introduction was a **real problem**
  2. **Aim** of the study **was to provide solution** for that problem
  3. **Objectives** of the study were clearly defined and were **reflective of the aim** (Measureable)
  4. Study was designed to **measure the objectives-** Appropriate Study Design
  5. **Participants (Sample)** were the true representative of the population under investigation- **No Bias was introduced** at any stage of the study

Sources of bias



6. **Instruments used (Questionnaires)** for data collection are the **valid** instruments (Measure what they intend to measure

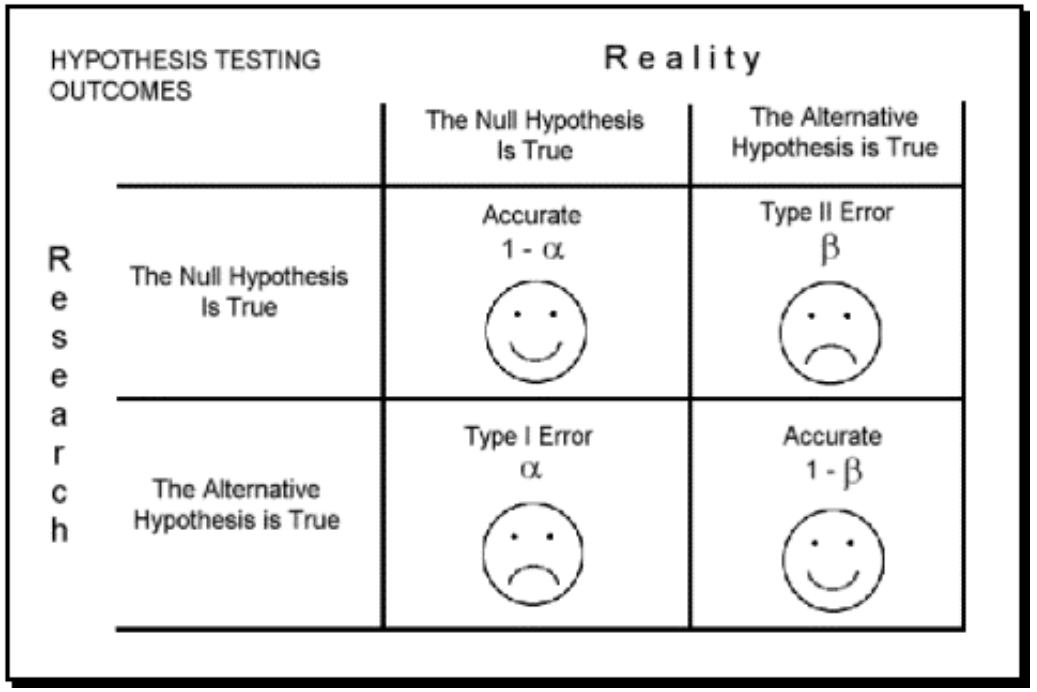
7. Statistical Methods were **aligned with Study design and Objectives**

1. Must have good knowledge of different statistical test

Statistical tests overview

Type of Variable	Two Groups		More Groups	
	Paired Data	Unpaired Data	Paired Data	Unpaired Data
Proportion	McNemar test	Fisher's test or Chi-square test	Cochran's Q-test	Chi-square test
Rank Data	Wilcoxon test	Mann-Whitney test	Friedman test	Kruskal-Wallis test
Quantitative Data	t-test for paired data	t-test for unpaired data	Analysis of Variance (ANOVA)	Analysis of Variance (ANOVA)

9. **No errors** in the results, All the results were reported – **Nothing was hidden**

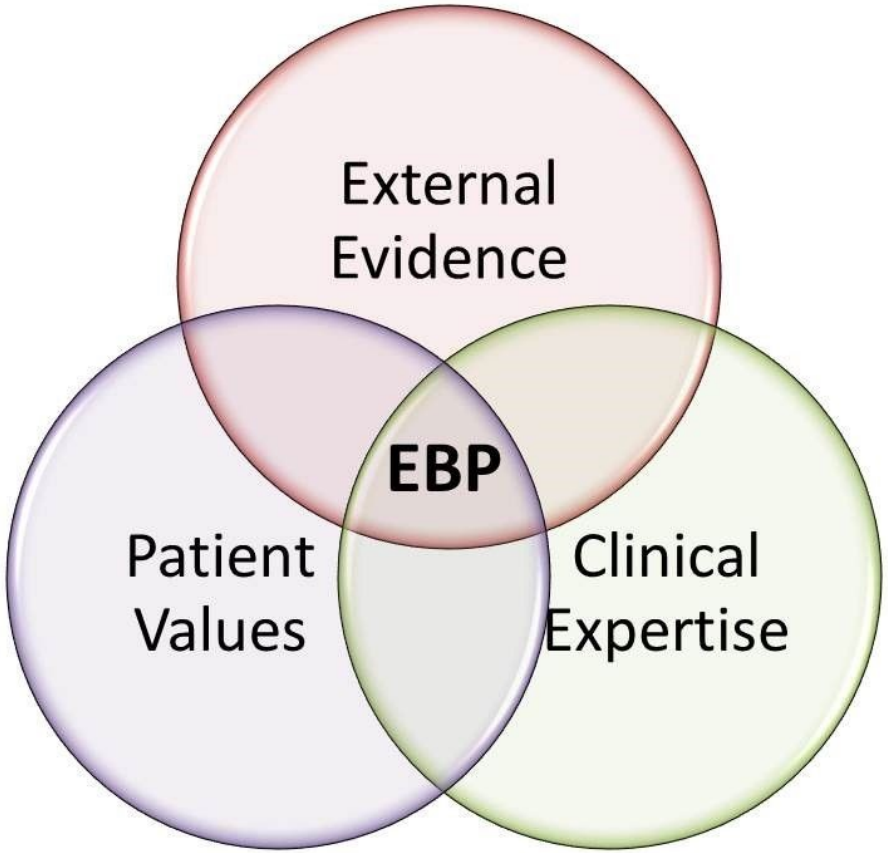


10. The results were discussed appropriately- **No misinterpretation**
11. Strengths motioned are the **true strengths**
12. Limitations are reported do not affect the **applicability of the study-**
13. There is **no issue of the generalizability** of results.
14. Conclusion drawn **are true representative of the results**.

5. Assess the overall structure Research paper

- Randomized controlled trials – CONSORT
- Systematic reviews – PRISMA
- Observational studies – STROBE
- Case reports – CARE
- Qualitative research – COREQ
- Pre-clinical animal studies – ARRIVE

6. Assess the clinical Applicability of the study



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Long-term Outcomes of a Randomized Controlled Trial of Single-incision Versus Multi-port Laparoscopic Colectomy for Colon Cancer

Step 2: Assessing Credibility

- Type of Article on Oxford Hierarchy
- Authors and Institute
- Journal and Impact Factor
- Publication Date
- Funding Sources
- References
  - Recent, Balanced, Good Journals
  - minimal information from websites

- RCT- Level 1B

- Renowned Authors/ Institute
- Very recent – June2021
- No conflict of interest
- Good Recent references (Am J Surg/ BJS/ Surg Endos (2011-2020)

Step 3: Read the Abstract

- To get **general Idea** of the Article
- To Assess it **Structure**
  - Background, Methods, Results, Conclusion
- To Assess the **authenticity of the Abstract**
  - Is it the true representative of actual article

- Publication for the sake of Publication ?? *
- Well Structured
- Used Abbreviations in the Abstract RFS, OS

***Conclusion:** Even though the results of the 5-year OS and RFS in this trial were exploratory and underpowered, there were no statistically significant differences between the SILC and MPC arms. SILC may be an acceptable treatment option for select patients with colon cancer.

Step 4: Assess the validity and Reliability of study (Reading the whole Paper)

- Problems Identified
  - Oncological outcomes of SILC are not patient based outcomes rather surrogate outcomes
  - No RCTS to report long-term outcomes of SILC

Problem identified in the introduction was a **real problem**

- Aim
  - To Report the long-term outcomes of MPC vs SILC by a RCT.

Aim of the study **was to provide solution** for that problem

- The Objective of study
  - To compare the 5-year RFS, OS, and recurrence patterns SILC with those after MLC for colon cancer through RCT

Objectives were **reflective of the aim** (Measurable)

NOT clearly defined

No operational definitions for

- Recurrence free survival
- Overall Survival
- Recurrence Patterns

- Study Design
  - RCT
  - Approved by IRB
  - Registered

Study was designed to **measure the objectives-** Appropriate Study Design

- Sampling
  - Open-label multi-institutional RCT
  - March 1, 2012, to March 31, 2015,
  - 1:1 allocation ratio.
  - Enrolled at 3 institutions of the Yokohama Clinical Oncology Group

- **Participants (Sample)** were the true representative of the population under investigation- with certain inclusion and Exclusion Criteria –
- Can have issues of generalizability
- Randomization- Valid Method

- Were the sources of Bias avoided

- Participants- 200 and then randomized- Where as study duration was 2-3 years
- Blinding was Double as compared to Triple
- Surgeon Bias
- Definition of conversion to MPC from SILC *(if 2 or more additional ports were used)*

Instruments used (Questionnaires) for data collection are the **valid** instruments (Measure what they intend to measure

- Not Documented

- Differences between categorical and continuous variables were tested with **Pearson Chi-square test** and the **Mann-Whitney U-test,**
- The 5-year RFS and OS were evaluated using the **Kaplan-Meier method** with the log-rank test.
- **Cox proportional-hazards** model to perform the subgroup analyses for the RFS.

Statistical Methods were **aligned with Study design and Objectives**

Intention to treat analysis – Analysis also included patient who lost follow up.

- All the results were reported
- Results have been reported honestly though there may be issues with interpretation

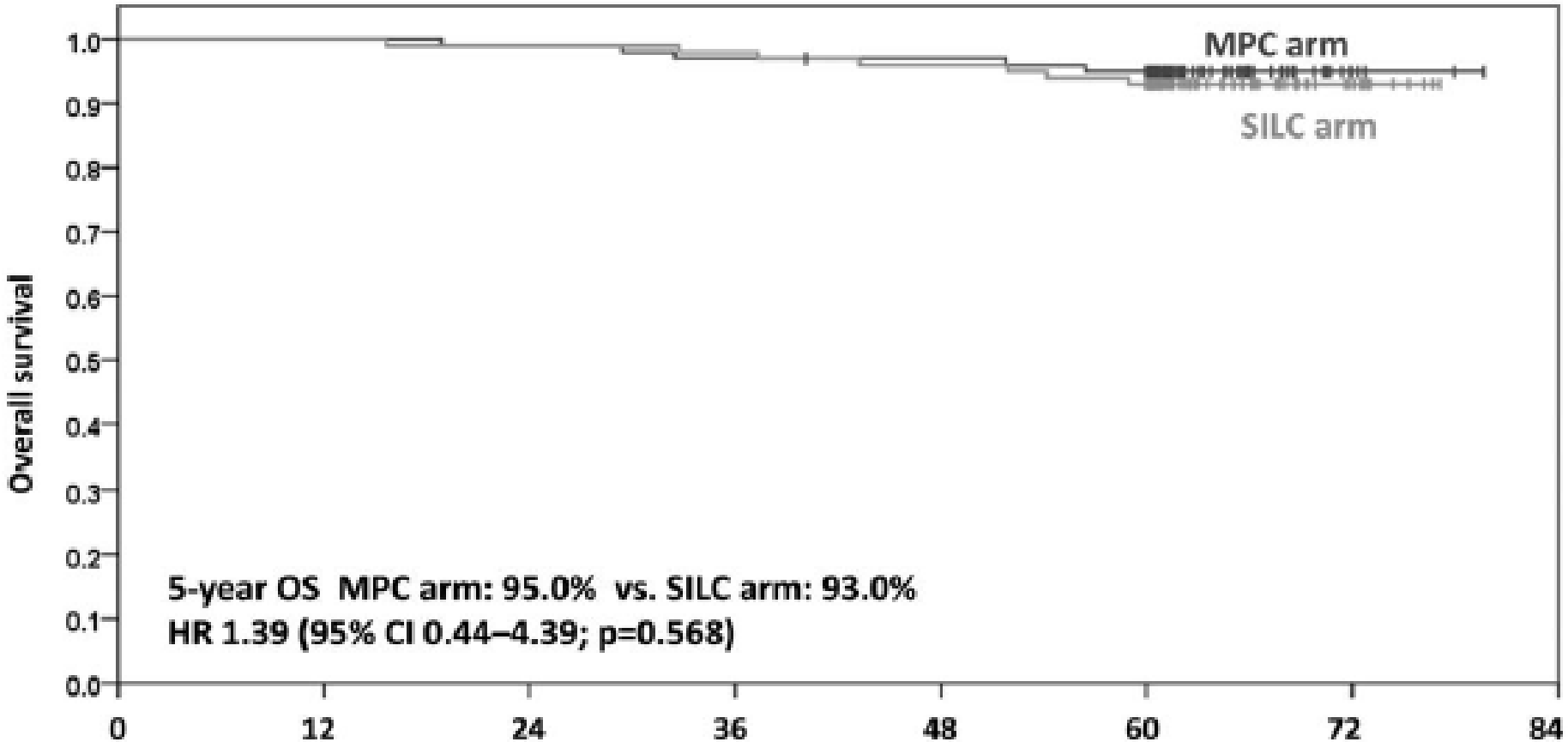
TABLE 1. Clinicopathological Characteristics

Variable	MPC n = 100	SILC n = 100
Age (yr)*	67 (61–74)	68 (61–74)
Sex		
Male	56 (56.0)	56 (56.0)
Female	44 (44.0)	44 (44.0)
BMI (kg/m^2)*	23.1 (21.1–24.8)	22.9 (20.3–25.2)
Location		
Cecum	9 (9.0)	16 (16.0)
Ascending colon	21 (21.0)	21 (21.0)
Sigmoid colon	54 (54.0)	49 (49.0)
Rectosigmoid	16 (16.0)	14 (14.0)

Values in parentheses are percentages, unless indicated otherwise.

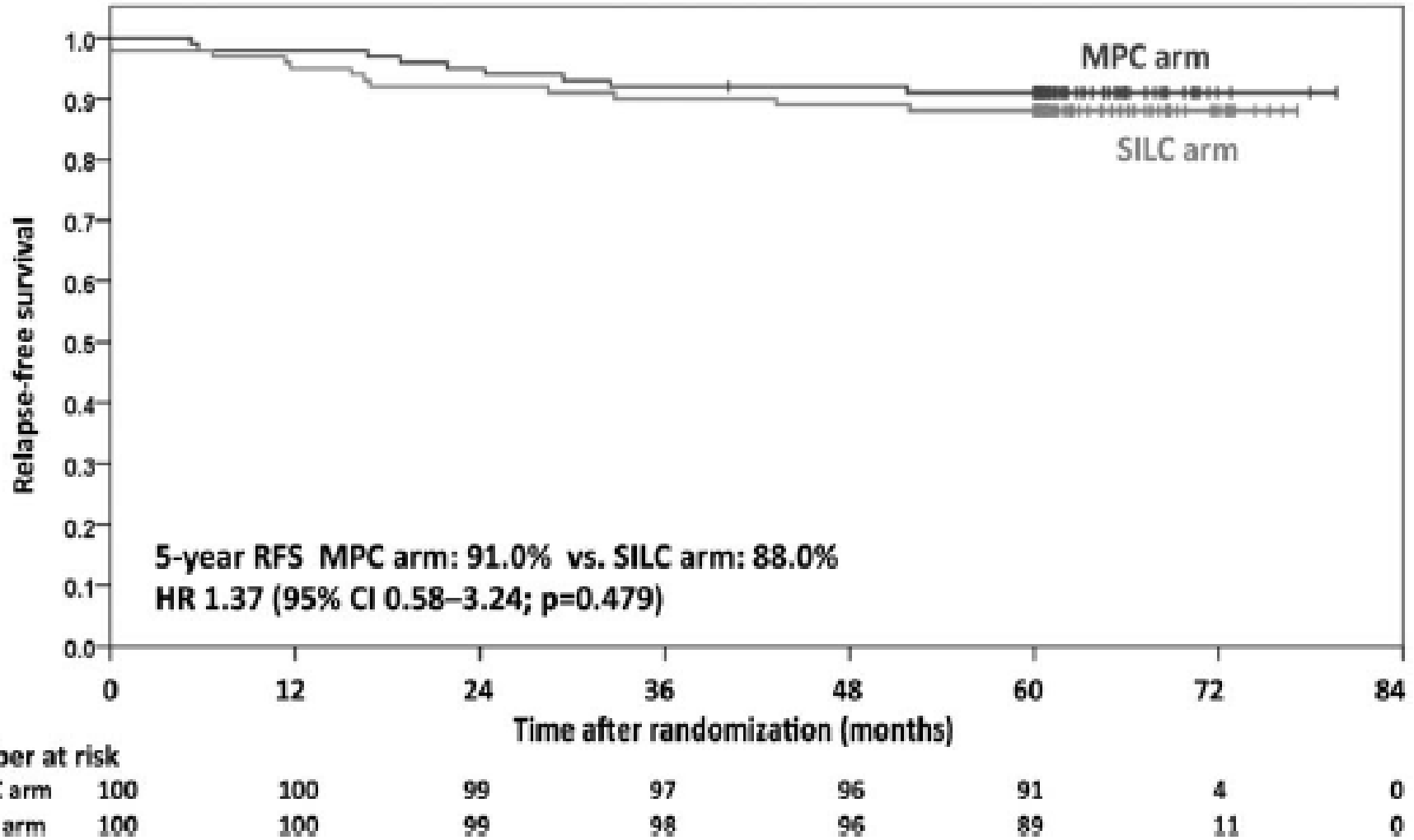
*values are median (IQR).

BMI indicates body mass index; MPC, multi-port laparoscopic colectomy; PS, performance status; SILC, single-incision laparoscopic colectomy.



Number at risk

MPC arm	100	98	95	92	91	87	3	0
SILC arm	100	95	92	90	89	84	10	0



Number at risk

MPC arm	100	100	99	97	96	91	4	0
SILC arm	100	100	99	98	96	89	11	0

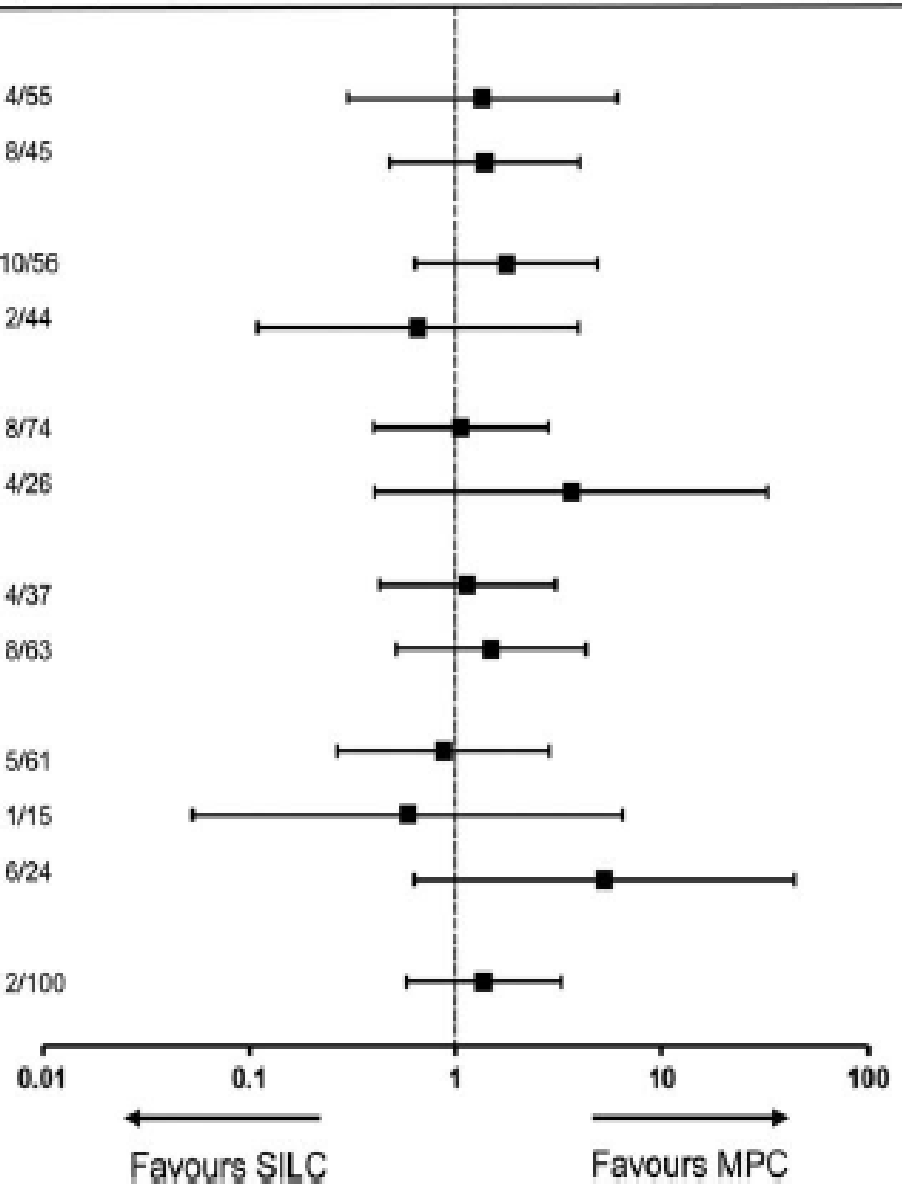
TABLE 3. Recurrence Patterns

Variable	MPC n = 100	SILC n = 100	*P* value
Total	5 (5.0)	7 (7.0)	0.767
Liver	3 (3.0)	5 (5.0)	
Lung	1 (1.0)	2 (2.0)	
Peritoneal dissemination	1 (1.0)	0 (0.0)	

Values in parentheses are percentages.

MPC indicates multi-port laparoscopic colectomy; SILC, single-incision laparoscopic colectomy.

Subgroup	MPC (event/n)	SILC (event/n)	HR (95% CI)
Age (years)			
<70	3/55	4/55	1.34 (0.30-6.01)
≥70	6/45	8/45	1.38 (0.48-3.96)
Sex			
Male	6/56	10/56	1.75 (0.64-4.83)
Female	3/44	2/44	0.65 (0.11-3.92)
Body mass index (kg/m2)			
<25	8/78	8/74	1.06 (0.40-2.83)
≥25	1/22	4/26	3.61 (0.40-32.30)
Tumor location			
Right sided (Cecum/Ascending)	3/32	4/37	1.14 (0.43-3.04)
Left sided (Sigmoid/Rectosigmoid)	6/68	8/63	1.48 (0.51-4.26)
Clinical stage			
I	6/64	5/61	0.87 (0.27-2.86)
II	2/17	1/15	0.58 (0.05-6.41)
III	1/19	6/24	5.25 (0.63-43.65)
Overall	9/100	12/100	1.37 (0.58-3.24)



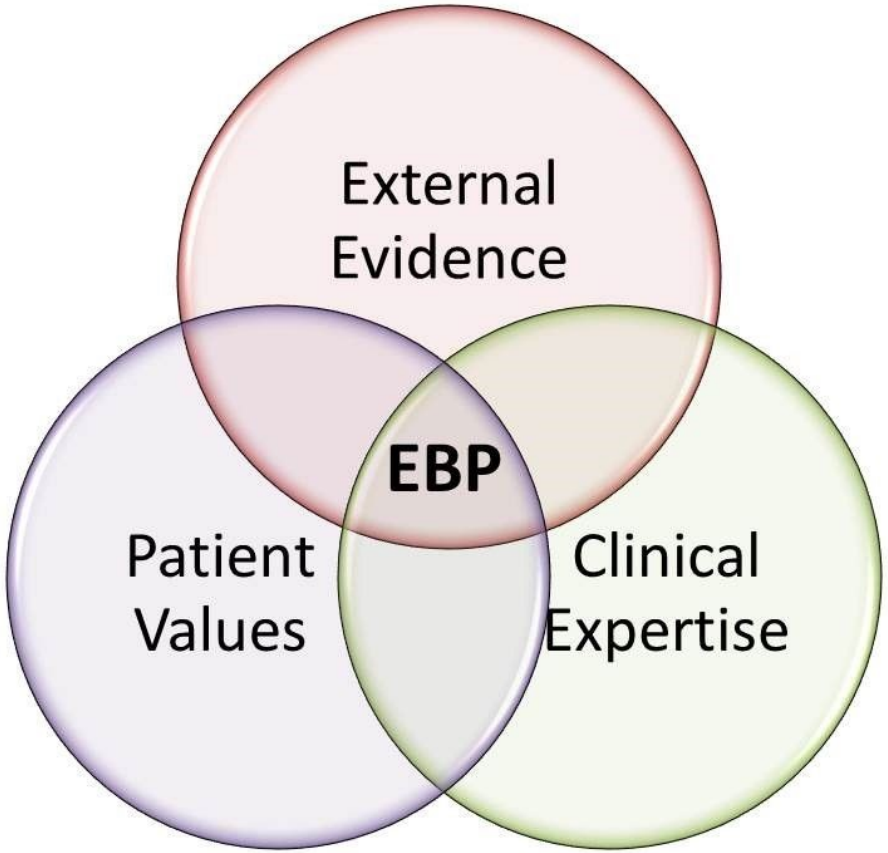
- Strengths
- Limitations
  - 12 cases of addinal ports were still considered as SILC
  - Underpowedered study

- Cant comment of strengths
- Limitations reported have sound effects on the **applicability of the study-**
- **Exclusion criteria affects the generalizability of study**
- **Conclusion is true representative but not much endorsing**

5. Assess the overall structure Research paper

- Overall Structure – Compatible
- Randomized controlled trials – CONSORT- Guidelines were followed and flow diagram was provided

6. Assess the clinical Applicability of the study



- RCT with issues in designing, conducting, analysing and interpreting the results
- Assuming no Type 1/ 2 errors, may have limited applicability
- With the minimal advantage of cosmesis, long term outcomes are inferior, though not statistically significant But may be clinically significant.
- Generalizability may be an issue due to difference in population (Japanese Vs English- Straighter and shorter colons Vs floppy and longer colons)
- Trend is toward robotic surgery than single incision surgery

Outcome

- Not for changing practice
- May have some academic interest
- May need further studies
- Will require training and resources
- Role of business interest can not be ruled out.