

Guidelines for the Use of Minimally Invasive or Open Liver Resection for Isolated Colorectal Liver Metastases

APPENDIX C

Should MIS vs. Open be used for synchronous, resectable and isolated liver metastasis(es) from colorectal cancer, when performed simultaneously with resection of primary?

POPULATION:	synchronous, resectable and isolated liver metastasis(es) from colorectal cancer, when performed simultaneously with resection of primary
INTERVENTION:	MIS
COMPARISON:	Open
MAIN OUTCOMES:	Estimated Blood Loss; Hospital Length of Stay; R0 Resection; Perioperative Transfusion; Disease Free Survival (DFS) - 1yr; Mortality - 5yr; Perioperative complications - Clavien-dindo 3+;
SETTING:	
PERSPECTIVE:	PATIENT-CENTERED
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem		
Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know 		
Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Trivial <input checked="" type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know 	*Outcomes used in decision making by the panel	The panel felt that as there although 5yr Overall Mortality would be most important to patients, the range estimated effects was similar between MIS and Open Hepatectomy. This was also the case for complications, R0 resection, and transfusions. However, the panel felt that there was considerable benefit from decreased blood loss and hospital length of stay with MIS hepatectomy. Ultimately, there was consensus that MIS hepatectomy conferred small benefit.

Outcomes	No of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with Open	Risk difference with MIS
Estimated Blood Loss*	609 (10 observational studies)	⊕○○○ Very low ^{a,b,c}	-	The mean estimated Blood Loss was 0 cc	MD 177.35 cc lower (273.17 lower to 81.53 lower)
Hospital Length of Stay*	827 (11 observational studies)	⊕⊕○○ Low	-	The mean hospital Length of Stay was 0 days	MD 3 days lower (3.82 lower to 2.17 lower)
R0 Resection	706 (7 observational studies)	⊕○○○ Very low ^c	RR 1.02 (0.98 to 1.05)	Study population	
				922 per 1,000	18 more per 1,000 (18 fewer to 46 more)
Perioperative Transfusion	379 (5 observational studies)	⊕○○○ Very low ^d	RR 0.92 (0.58 to 1.45)	Study population	
				178 per 1,000	14 fewer per 1,000 (75 fewer to 80 more)
Mortality - 5yr	81 (3 observational studies)	⊕○○○ Very low ^{d,e}	RR 0.92 (0.80 to 1.07)	Study population	
				816 per 1,000	65 fewer per 1,000 (163 fewer to 57 more)
Perioperative complications - Clavien-dindo 3+	568 (9 observational studies)	⊕○○○ Very low ^d	RR 0.68 (0.42 to 1.12)	Study population	
				154 per 1,000	49 fewer per 1,000 (90 fewer to 19 more)

- a. Several of the studies with the most weight in the meta-analysis had an unclear or high risk of bias.
- b. Although there is quite a bit of heterogeneity, I² 93%, however the studies are all consistent in favoring the intervention.
- c. Small sample size

- d. This outcome had a small sample size and an even smaller event size. In addition, the confidence interval of estimated effects ranged across multiple clinically relevant thresholds.
- e. Several of the included studies were found to have an unclear or high risk of bias, specifically for patient selection. It appears that some of the studies included patients in the MIS cohort that had smaller tumors than the open group.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Large <input type="radio"/> Moderate <input type="radio"/> Small <input type="radio"/> Trivial <input type="radio"/> Varies <input checked="" type="radio"/> Don't know 		<p>Although DFS 1yr was found to have an absolute effect that favored open hepatectomy, the range of anticipated effects ranged from large benefit to large harm. As such the panel felt that the data for this particular outcome was likely under powered to see a difference, thus they voted "Don't Know" for undesirable effects.</p>

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS									
<ul style="list-style-type: none"> <input checked="" type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input type="radio"/> No included studies 	<table border="1" data-bbox="529 1193 1409 1425"> <thead> <tr> <th>Outcomes</th> <th>Importance</th> <th>Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td>Estimated Blood Loss</td> <td>CRITICAL</td> <td>⊕○○○ Very low^{a,b,c}</td> </tr> <tr> <td>Hospital Length of Stay</td> <td>CRITICAL</td> <td>⊕⊕○○ Low</td> </tr> </tbody> </table> <ul style="list-style-type: none"> a. Several of the studies with the most weight in the meta-analysis had an unclear or high risk of bias. 	Outcomes	Importance	Certainty of the evidence (GRADE)	Estimated Blood Loss	CRITICAL	⊕○○○ Very low ^{a,b,c}	Hospital Length of Stay	CRITICAL	⊕⊕○○ Low	
Outcomes	Importance	Certainty of the evidence (GRADE)									
Estimated Blood Loss	CRITICAL	⊕○○○ Very low ^{a,b,c}									
Hospital Length of Stay	CRITICAL	⊕⊕○○ Low									

	<ul style="list-style-type: none"> b. Although there is quite a bit of heterogeneity, 12 93%, however the studies are all consistent in favoring the intervention. c. Small sample size 	
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Values
Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Important uncertainty or variability <input type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability <input checked="" type="radio"/> No important uncertainty or variability 		

Balance of effects
Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input checked="" type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> Don't know 		<p>As the available evidence demonstrated small benefit and unknown undesirable effects, the panel felt that the balance of effects probably favors the intervention. The uncertainty in the decision came from the very low certainty of evidence of the available data.</p>

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know 		

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know		

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention <input type="radio"/>	Conditional recommendation against the intervention <input type="radio"/>	Conditional recommendation for either the intervention or the comparison <input type="radio"/>	Conditional recommendation for the intervention <input checked="" type="radio"/>	Strong recommendation for the intervention <input type="radio"/>
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CONCLUSIONS

Recommendation

The panel suggests that patients with CRLM undergo an MIS rather than open hepatectomy for resectable colorectal liver metastases being resected simultaneously with the resection of the primary cancer when feasible (conditional recommendation, very low certainty evidence)

Justification

The panel judged there are small desirable effects of MIS Hepatectomy over Open which outweighed the unknown undesirable effects. This balance favoring MIS hepatectomy would likely apply to most adult patients with CRLM. However, due to very low certainty evidence, only a conditional recommendation could be made.

Subgroup considerations

Implementation considerations

The data from included studies came from relatively high-volume centers and operations were performed by well-trained surgeons, well past their learning curve. In addition, these trials included mostly patients with only one or two lesions, and very few major hepatectomies. This must be considered in the implementation of these recommendations, which do not necessarily apply to complex liver resections, particularly when surgeons and institutions do not have the training and expertise to safely perform these operations. In general, the recommendation for MIS hepatectomy should be applied only in situations where the surgeons and the facility have the training and experience to perform the resection safely with an appropriate oncologic outcome.

Monitoring and evaluation

Research priorities

- Randomized controlled trials studying the effects of MIS vs open combined resection of CRLM
- Research regarding differences between simultaneous resection of CRLM combined with colon resection vs rectal resection.
- Differences in rates and consequences of incisional hernia after open vs MIS hepatectomy
- Quality of life, short and long-term after open vs MIS hepatectomy
- Return to intended oncologic therapy after open vs MIS hepatectomy
- RCTs better powered to address long term oncologic outcomes