

Living Donor Liver Transplantation for Colorectal Liver Metastases (CRLM)

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Background

- 50 % of colorectal cancer (CRC) will develop distant disease.
- 30 % of those dying from metastatic CRC have liver alone
- Surgical resection of CRLM potentially curative – 38% 5-yr survival
- Some (25-30%) liver limited CRLM is not resectable
- Chemotherapy for unresectable CRLM -10 % 5 yr survival
- Liver metastases drive disease course
- Unresectable Liver metastases with favorable biology

Rationale for Liver Transplantation in CRLM

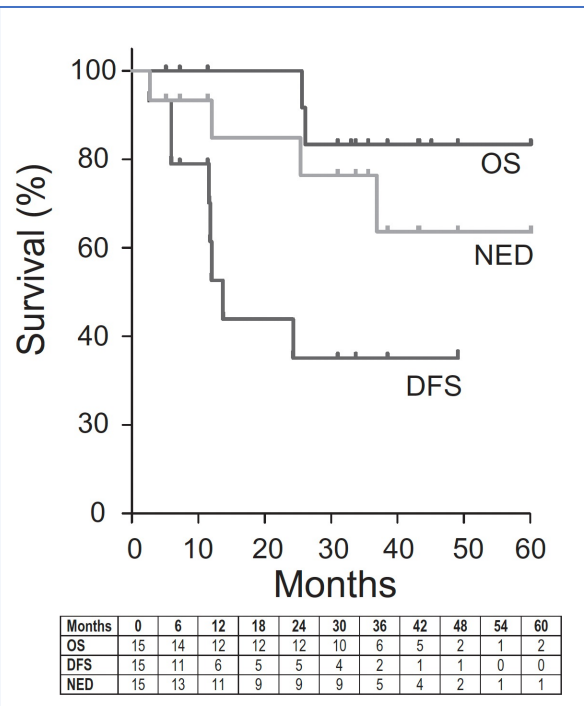
- Disease control in patients with liver alone disease with favorable tumor biology who need a total hepatectomy

Oslo experience SECA II – Renewed Interest

ORIGINAL ARTICLE

Survival Following Liver Transplantation for Patients With Nonresectable Liver-only Colorectal Metastases

Svein Dueland, MD,*✉ Trygve Syversveen, MD,† Jon Magnus Solheim, MD,‡ Steinar Solberg, MD,§ Harald Grut, MD,† Bjørn Atle Bjørneth, MD,*|| Morten Hagness, MD,‡ and Pål-Dag Line, MD‡||



Total 15 patients , median follow up 36 months

Overall Survival – 1,3,5 yr – 100%, 83%, 83%

Disease free survival – 53%, 44%, 35%

Survival after relapse – 100%, 73%, 73% (comp to HCC Liver Transplantation)

6/8 relapse pulmonary – resected

NED status 3-yrs post LT – 76%

SECA II – patient selection

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none">-Histologically verified adenocarcinoma in colon and rectum-No extrahepatic disease on imaging and PET-No local recurrence on colonoscopy-Good performance status ECOG 0 or 1-Standard surgical resection of primary with adequate margins-Received first line treatment-At least 10 % (RECIST) response on chemotherapy-At least one year from CRC diagnosis and listing	<ul style="list-style-type: none">-Weight loss >10 % in last 6 months-Prior extrahepatic disease or local relapse-Right sided-Extensive lymph node disease-Mutations – BRAF v 600, KRAS- Response to chemotherapy- Extrahepatic disease-Undifferentiated or signet ring adenocarcinoma

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SECA II study patients

Characteristics	Patients n=15
Age	59.4 (34.9-71.1)
Primary pT3	11
Location of primary	Left = 13
Kras mutated	1
CEA at LT	2 (1-30)
Number of lesions in liver at LT	5 (1-53)
Synchronous disease	14
Chemotherapy before LT – First line	7
Second line	6
Third line	2
Time from diagnosis to LT	24 months (13.3-112 months)

Wait time for Liver Transplant in Norway - 29 days

Risk stratification

- **Oslo Score (1 point each)**

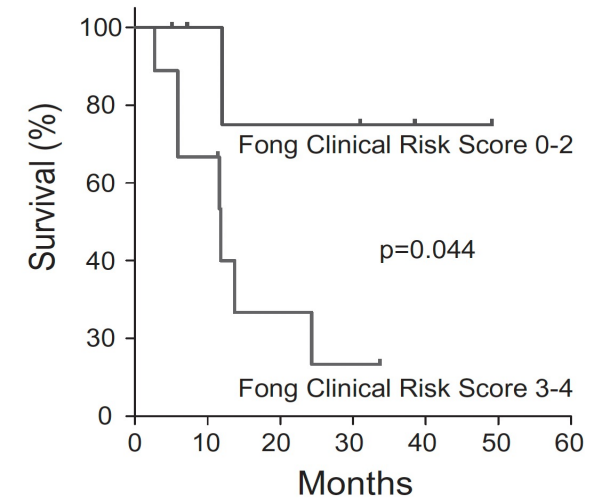
- Largest lesion > 5.5 cm
- CEA > 80 ug/L
- Primary surgery to LT < 2 years
- Progressive disease on chemo

- **Fong Clinical Risk score**

- Synchronous
- Lymph node positive primary
- > 1 lesion
- size > 5 cm
- CEA > 200 ug/l

Indicators of poorer outcomes SECA II

- Node positive primary
- Greater than 8 liver lesions at time of LT
- Fong clinical risk score 3/4



Months	0	6	12	18	24	30	36	42	48	54	60
FCRS 0-2	6	5	3	3	3	3	2	1	1	0	0
FCRS 3-4	9	6	3	2	2	1	0	0	0	0	0

IHPBA Consensus guidelines

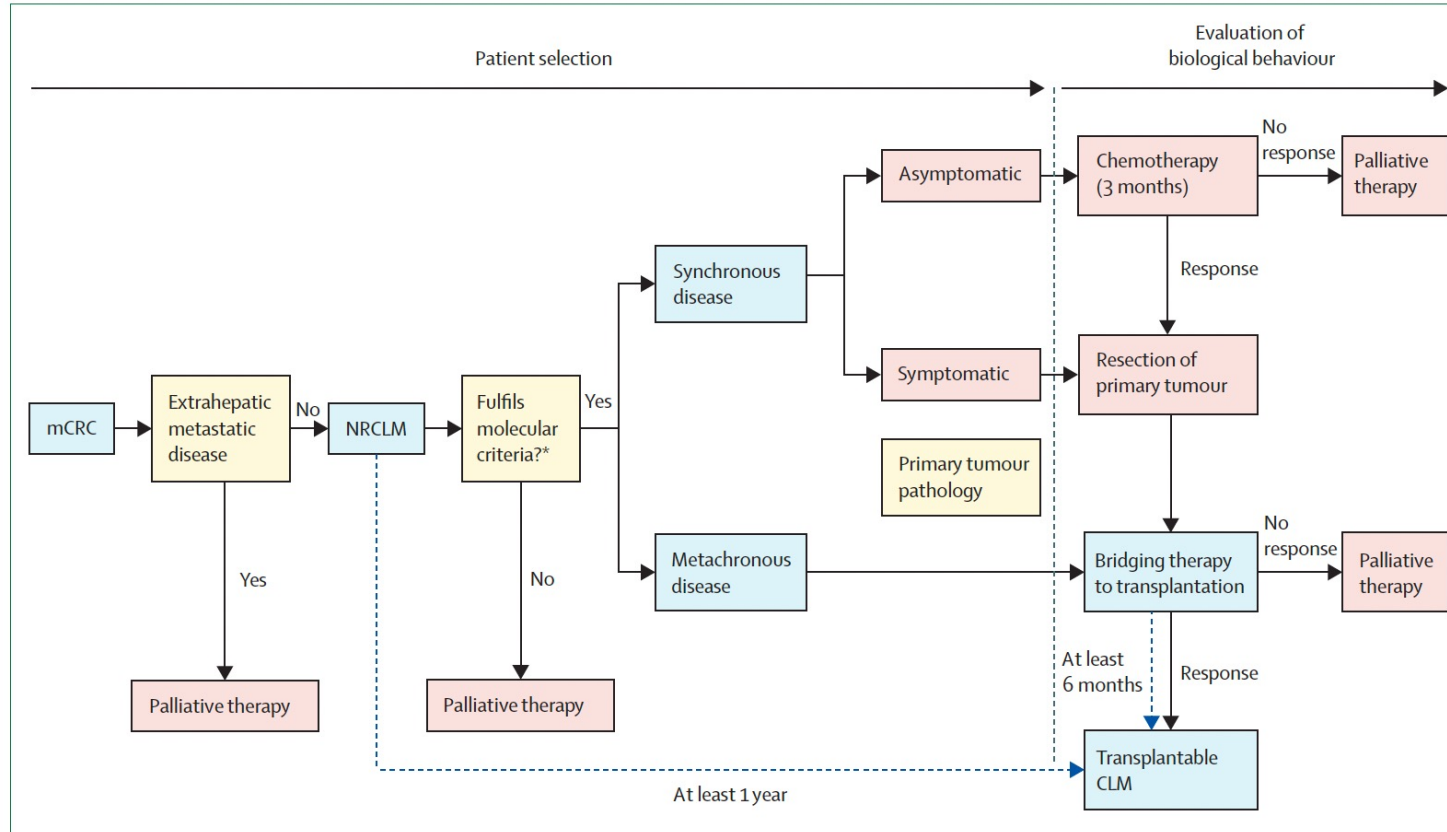


Figure 2: Proposed management algorithm

CLM=colorectal liver metastases. mCRC=metastatic colorectal cancer. NRCLM=non-resectable CLM. *No BRAF V600E mutation, microsatellite stable, and mismatch repair proficient.

Multidisciplinary management

Molecular criteria

1 year b/w diagnosis & LT

Response to bridging treatment for 6 months

5 yr OS pf 50% ethically justifiable to use LT

North American experience

Research

JAMA Surgery | Original Investigation

Recipient and Donor Outcomes After Living-Donor Liver Transplant for Unresectable Colorectal Liver Metastases

Roberto Hernandez-Alejandro, MD; Luis I. Ruffolo, MD; Kazunari Sasaki, MD; Koji Tomiyama, MD, PhD; Mark S. Orloff, MD; Karen Pineda-Solis, MD; Amit Nair, MD; Jennie Errigo, BS; M. Katherine Dokus, MPH; Mark Cattral, MD; Ian D. McGilvray, MD, PhD; Anand Ghanekar, MD, PhD; Steven Gallinger, MD, MSc; Nazia Selzner, MD, PhD; Marco P. A. W. Claasen, MD; Ron Burkes, MD; Koji Hashimoto, MD, PhD; Masato Fujiki, MD; Cristiano Quintini, MD; Bassam N. Estfan, MD; Choon Hyuck David Kwon, MD, PhD; K. V. Narayanan Menon, MD; Federico Aucejo, MD; Gonzalo Sapisochin, MD, PhD, MSc

Retrospective series of LDLT for unresectable CRLM

3 Prominent North American Centers

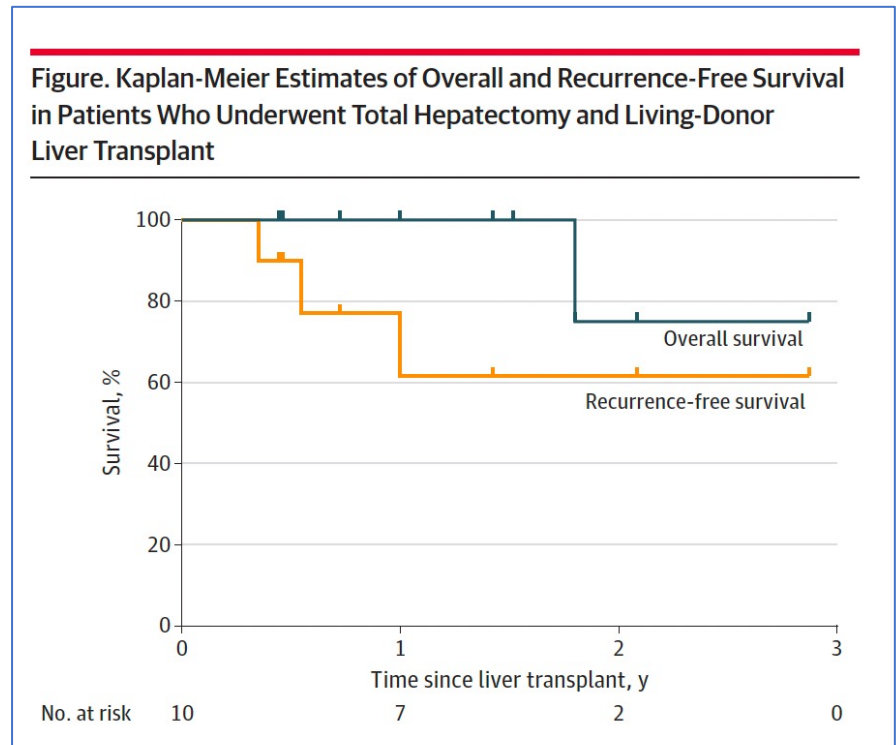
91 candidates considered

10 underwent LDLT (11%)

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Details and outcomes

Characteristic	Patients n=10
Median age (range)	45 (35-58)
Synchronous CRLM	9 (90%)
Time from diagnosis to LT	1.7 yrs (1.1-7.8)
Primary location (right or left colon)	Left 8 (80%)
Na MELD median (range)	6 (6-20)
Olso score median (range)	1.5 (0-2)
Chemotherapy cycles median	22.5
Kras +	3 (30%)
CEA at LT	7.7 (1.6-56.4)
Radiographic or chemical response to treatment	10 (100%)

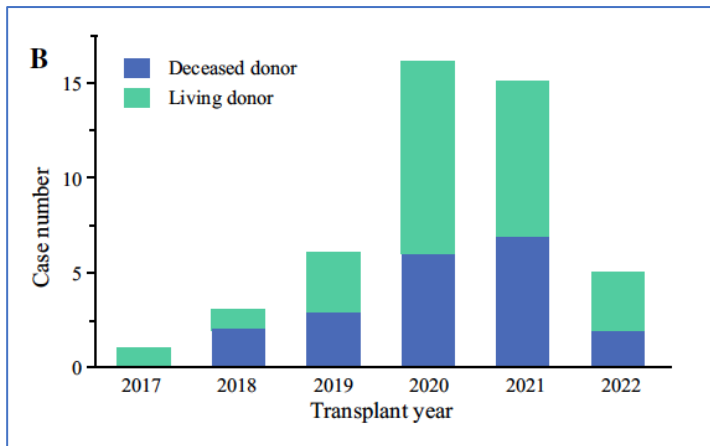




ORIGINAL ARTICLE – HEPATOBILIARY TUMORS

The Current State of Liver Transplantation for Colorectal Liver Metastases in the United States: A Call for Standardized Reporting

Kazunari Sasaki, MD¹, Luis I. Ruffolo, MD², Michelle H. Kim, MD¹, Masato Fujiki, MD, PhD³, Koji Hashimoto, MD, PhD³, Yuki Imaoka, MD, PhD¹, Marc L. Melcher, MD, PhD¹, Federico N. Aucejo, MD³, Koji Tomiyama, MD², and Roberto Hernandez-Alejandro, MD²

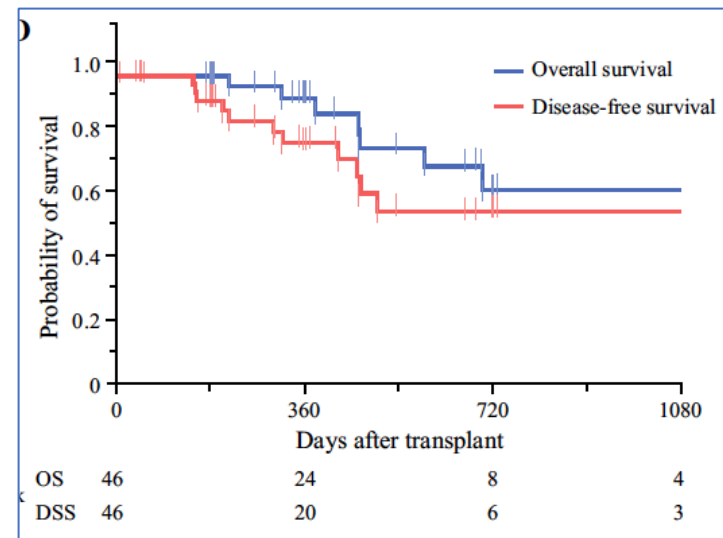


Characteristics	Deceased donor (n=20)	Living Donor (n=26)
Age	51	46
MELD (Median) at transplant	12	8
T bil	2.7	1
Time on waitlist (days)	75	10

Outcomes

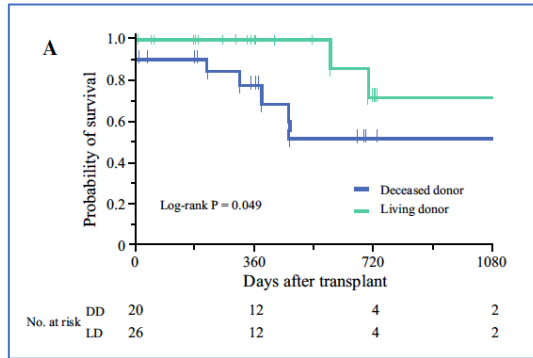


Significant travel for candidates

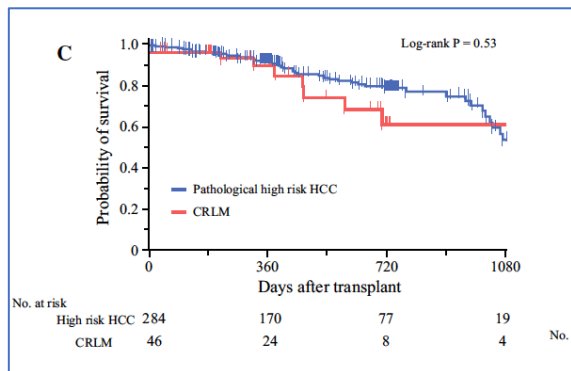


3-yr overall survival - 60%
Patient selection criteria unclear

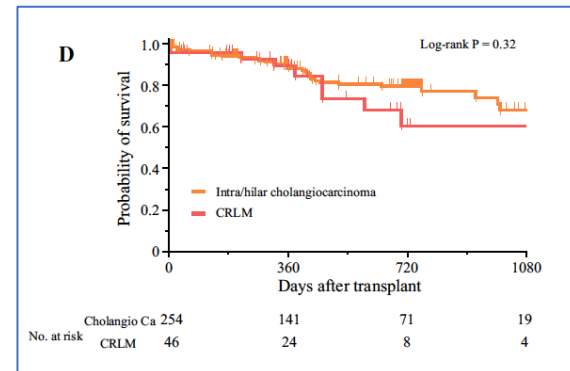
Outcomes



DDLT, LDLT outcomes



CRLM vs high risk HCC



CRLM vs CCA

Summary - LT for CRLM

- Limited experience with encouraging outcomes
- Satisfactory overall survival vs (5 yr OS of unresectable CRLM 10 %)
- High recurrence rate
- Recurrences treatable with excellent outcomes (vs HCC)
- Recurrences are slow growing pulmonary mets that can be resected
- Patient selection is key and needs further refinement
- Living Donation could be key to graft availability (double equipoise)

Protocol at UHTI

- LDLT protocol for non-resectable CRLM is open at University Health Transplant Institute
- LDLT allows access and adjustment of timing
- Extensive LDLT experience at UHTI – advantage
- Potential for impact (numbers) – SECA II 15 patients over a 5-year period, 5 million population

Questions

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