Surgical Treatment for Primary and Secondary Liver Tumors in the Elderly

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Symposium – Liver Cancer in the Elderly
SIOG Annual Conference
Warsaw - Poland
November 10th, 2017

Surgical treatment - resection

- Hepatocellular carcinoma & Intrahepatic cholangiocarcinoma
- Colorectal liver metastasis & other (NET, etc.)

5-year OS HCC


Patterns of Care - CRCLM

- Substandard care – low resection rates
- Increasing age (no based on comorbidity)
- Predictor of “no-treatment/surgery”

Stage 4 CRC

- Colorectum

Orcutt S & Anaya DA. Ann Surg Oncol 2017
Kopetz S et al. JCO 2009

n=14,966
Patterns of Care - HCC

SEER database – n=1675
- 47% received no treatment

**Objectives**
- Evidence supporting the use of treatment – liver resection for the management of malignant liver tumors in the elderly
- Review specific outcomes following hepatectomy
  - Long-term / survival
  - Short-term / postoperative
  - Post-surgical recovery (patient-centered)
- Understand differences in relevant outcomes for the elderly population

**Clinical case**
- 80 y/o male referred with HCC
  - Obesity, steatosis, daily ETOH
- Exam normal - obesity
- Labs within normal limits
- Preserved liver function - Childs A
- AFP 659
- Non-metastatic

**Clinical case**
- Treatment options
  - Best supportive care – hospice
  - Sorafenib
  - Liver directed therapy – TACE / Yttrium90
  - Ablation
  - Transplantation
  - Resection
Clinical case

- Treatment options
  - Sorafenib
  - Liver directed therapy – TACE / Yttrium90
  - Ablation
  - Transplantation
  - Resection

Clinical case

- Comprehensive Geriatric Assessment
  - PACE / Frailty / SAOP3 – no deficits
- Discussed goals of therapy
- Expectations post-surgery
- Multidimensional care
  - Multidisciplinary liver tumor board discussion
  - Conservative yet “aggressive” curative approach
  - Evaluate goals in context of existing options
  - Perioperative multidisciplinary team

Clinical case

- Patient’s perspective
  - Will this prolong my life?
  - What are the risks?
  - Will I survive the surgery?
  - How is the recovery period?
  - Will I have a normal life afterwards?

Clinical case

- Hepatocellular carcinoma
  - N = 919 vs. reference age-adjusted
    - Equivalent 3-year OS
    - Difference in 5-10-year OS
    - Shorter in the older
    - Less years of life lost

Hepatocellular carcinoma

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Overall survival probability</th>
<th>3-year</th>
<th>5-year</th>
<th>10-year</th>
<th>Age (years)</th>
<th>Overall survival probability</th>
<th>3-year</th>
<th>5-year</th>
<th>10-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>0.780 (0.758-0.801)</td>
<td>0.780</td>
<td>0.758</td>
<td>0.801</td>
<td>40-49</td>
<td>0.780 (0.758-0.801)</td>
<td>0.780</td>
<td>0.758</td>
<td>0.801</td>
</tr>
<tr>
<td>50-59</td>
<td>0.601 (0.576-0.627)</td>
<td>0.601</td>
<td>0.576</td>
<td>0.627</td>
<td>50-59</td>
<td>0.601 (0.576-0.627)</td>
<td>0.601</td>
<td>0.576</td>
<td>0.627</td>
</tr>
<tr>
<td>60-69</td>
<td>0.448 (0.424-0.472)</td>
<td>0.448</td>
<td>0.424</td>
<td>0.472</td>
<td>60-69</td>
<td>0.448 (0.424-0.472)</td>
<td>0.448</td>
<td>0.424</td>
<td>0.472</td>
</tr>
<tr>
<td>70-79</td>
<td>0.361 (0.338-0.385)</td>
<td>0.361</td>
<td>0.338</td>
<td>0.385</td>
<td>70-79</td>
<td>0.361 (0.338-0.385)</td>
<td>0.361</td>
<td>0.338</td>
<td>0.385</td>
</tr>
<tr>
<td>80-89</td>
<td>0.300 (0.278-0.323)</td>
<td>0.300</td>
<td>0.278</td>
<td>0.323</td>
<td>80-89</td>
<td>0.300 (0.278-0.323)</td>
<td>0.300</td>
<td>0.278</td>
<td>0.323</td>
</tr>
<tr>
<td>90+</td>
<td>0.252 (0.232-0.273)</td>
<td>0.252</td>
<td>0.232</td>
<td>0.273</td>
<td>90+</td>
<td>0.252 (0.232-0.273)</td>
<td>0.252</td>
<td>0.232</td>
<td>0.273</td>
</tr>
</tbody>
</table>

Hepatocellular carcinoma

Colorectal liver metastasis

- Multiple retrospective studies
- Retrospective and heterogeneous
- Evolving field
- Limitations to published individual studies / findings

Abstracts reviewed
\[ n = 1020 \]

Abstract titles reviewed
\[ n = 3604 \]

Manuscripts reviewed
\[ n = 71 \]

Quality of Life Studies
\[ n = 2 \]

2584 articles excluded:

- Letters to editors, case reports, review articles

Mortality Studies
\[ n = 38 \]

Survival Studies
\[ n = 21 \]

Overall Survival – Risk difference

1 year OS

- Risk Diff: \[-4.1 \ (95\% CI: -7.6 \text{ to } -0.5); N=1705 pts\]

3 year OS

- Risk Diff: \[-5.8 \ (95\% CI: -10.8 \text{ to } -0.7); N=11054\]

5 year OS

- Risk Diff: \[-6.6 \ (95\% CI: -10.8 \text{ to } -2.4); N=3002\]

Hepatectomy – Overall Survival

1 year OS

- All Elderly: 85.7% (83.3-88.2); N=6; 764 pts
- Young: 89.7% (87.9-91.5); N=1175 pts
- Elderly: 85.5% (81.9-89.1); N=6; 530 pts

3 year OS

- All Elderly: 49.9% (45.4-54.5); N=12; 2565 pts
- Young: 56.6% (52.6-60.7); N=10; 8698 pts
- Elderly: 51.5% (46.9-56.1); N=10; 2356 pts

5 year OS

- All Elderly: 29.8% (19.0-40.7); N=15; 1625 pts
- Young: 39.0% (35.1-42.9); N=11; 2378 pts
- Elderly: 32.3% (28.8-35.7); N=11; 624 pts

Hepatectomy – Disease-free survival

1 year DFS

- All Elderly: 71.0% (63.2-78.8); N=7; 576 pts
- Young: 67.5% (61.5-73.6); N=4; 865 pts
- Elderly: 75.1% (69.4-80.7); N=4; 464 pts

3 year DFS

- All Elderly: 34.1% (27.7-40.5); N=10; 2339 pts
- Young: 33.9% (28.1-39.7); N=7; 7152 pts
- Elderly: 35.6% (27.4-43.7); N=7; 1999 pts

5 year DFS

- All Elderly: 27.5% (17.8-37.2); N=8; 242 pts
- Young: 29.7% (17.2-42.1); N=5; 354 pts
- Elderly: 29.3% (18.1-40.4); N=5; 189 pts
**Impact on Survival**

- Long-term outcomes multi-dependent
  - Efficacy of treatment
  - Risk of treatment – POP death?
  - Competing risks - comorbidities
- Can vary significantly by patient population / histology
  - Varies significantly on an individual basis

**Clinical case**

- Patient’s perspective
  - What are the risks?
  - Will I survive the surgery?

**Postoperative Outcomes**

- Short-term outcomes after surgery (90 d)
  - Mortality < 3% (5.6%)
  - POP complications = 20% (15-40%)
  - Improved dramatically last few decades
    - High-volume centers (perioperative expertise)
    - Less contraindications to surgery
      - Challenges to manage “sicker” patients (older)

**Postoperative Mortality (30-day)**

- Increasing age as a predictor

**Mortality & Morbidity**

- Increasing age as a predictor
Mortality & Morbidity
• Geriatric events and poor outcomes

Mortality & Morbidity
• Current data is limited by mix of population
• Inability to discriminate by relevant markers
  – Cirrhosis
  – CGA – geriatric events
  – Extent of resection
  – Comorbidities
  – Histology
  – Other (surgical approach)

Hepatectomy – POP Mortality

In-Hospital

<table>
<thead>
<tr>
<th>Age group</th>
<th>Risk difference</th>
<th>N</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Elderly</td>
<td>3.2% (1.5-4.9)</td>
<td>1555 pts</td>
<td></td>
</tr>
<tr>
<td>Young</td>
<td>1.2% (0.7-1.8)</td>
<td>5258 pts</td>
<td></td>
</tr>
<tr>
<td>Elderly</td>
<td>2.8% (0.9-4.8)</td>
<td>1318 pts</td>
<td></td>
</tr>
</tbody>
</table>

30-day

<table>
<thead>
<tr>
<th>Age group</th>
<th>Risk difference</th>
<th>N</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Elderly</td>
<td>2.8% (0.6-4.8)</td>
<td>1159 pts</td>
<td></td>
</tr>
<tr>
<td>Young</td>
<td>1.7% (0.7-2.6)</td>
<td>812 pts</td>
<td></td>
</tr>
<tr>
<td>Elderly</td>
<td>2.4% (0.03-5.1)</td>
<td>303 pts</td>
<td></td>
</tr>
</tbody>
</table>

60-day

<table>
<thead>
<tr>
<th>Age group</th>
<th>Risk difference</th>
<th>N</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Elderly</td>
<td>4.8% (1.8-6.8)</td>
<td>1491 pts</td>
<td></td>
</tr>
<tr>
<td>Young</td>
<td>1.7% (1.3-2.0)</td>
<td>7670 pts</td>
<td></td>
</tr>
<tr>
<td>Elderly</td>
<td>3.5% (1.5-5.6)</td>
<td>1907 pts</td>
<td></td>
</tr>
</tbody>
</table>

POP Mortality – Risk difference

<table>
<thead>
<tr>
<th>Time</th>
<th>Risk difference</th>
<th>N</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-Hospital</td>
<td>1.3% (-0.5-3.2)</td>
<td>6576 pts</td>
<td></td>
</tr>
<tr>
<td>30-day</td>
<td>0.6% (-2.0-2.3)</td>
<td>1115</td>
<td></td>
</tr>
<tr>
<td>60-day</td>
<td>1.6% (-1.5-4.7)</td>
<td>8577</td>
<td></td>
</tr>
</tbody>
</table>

Mortality & Morbidity
• Overall POP mortality is increased in elderly patients (very old in particular and with associated risk factors)
  – Ranges 3-8%
• Selected patients (good risk profile [LM]) have an near-equivalent risk
• Better selection tools to identify those likely to tolerate resection
Clinical case

- Patient’s perspective
- How is the recovery period?
- Will I have a normal life afterwards?

Recovery and Quality of Life

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age group</th>
<th>60-70 years</th>
<th>&gt; 70 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>Age group</td>
<td>60-70 years</td>
<td>&gt; 70 years</td>
</tr>
<tr>
<td>All outcomes</td>
<td>8.2 (5.7)</td>
<td>7.3 (7.1)</td>
<td>7.7 (6.8)</td>
</tr>
<tr>
<td>Freedom from metastasis</td>
<td>8.2 (5.7)</td>
<td>7.3 (7.1)</td>
<td>7.7 (6.8)</td>
</tr>
<tr>
<td>Survival probability</td>
<td>8.2 (5.7)</td>
<td>7.3 (7.1)</td>
<td>7.7 (6.8)</td>
</tr>
<tr>
<td>All resections</td>
<td>54 (32%)</td>
<td>59 (34%)</td>
<td>56 (31%)</td>
</tr>
<tr>
<td>Freedom from metastasis</td>
<td>54 (32%)</td>
<td>59 (34%)</td>
<td>56 (31%)</td>
</tr>
<tr>
<td>Survival probability</td>
<td>54 (32%)</td>
<td>59 (34%)</td>
<td>56 (31%)</td>
</tr>
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POP Transitional Care Needs (Post-acute care)

- Preoperative Treatment
- Postoperative Treatment

Cancer Care Conceptual Model

- Preoperative
- Demographic Variables
- Clinical Variables
- Cancer-Related Variables
- CGA (Elderly-Relevant Variables)
- Pre-Op HRQOL

- Postoperative
- HRQOL
- CGA
- Postoperative Outcomes

- Outcomes
- Oncological
- Transitional

Post-acute care - predictors

- In-hospital Complications
- Top Decile: Length of stay
- Hospital Cost
- Discharge Other than Home
- In-hospital Mortality

Abstracts reviewed: n=1020
Abstract titles reviewed: n=3604
Manuscripts reviewed: n=71
Quality of Life Studies: n=2
Survival Studies: n=21
Mortality Studies: n=16

Titles identified: n=5169
Duplicates removed: N=3988
Abstract titles reviewed: n=3984
Abstracts reviewed: n=3920
Manuscripts reviewed: n=71
2584 articles excluded: Letters to editors, case reports, review articles
949 studies excluded: Inclusion criteria not met

Inclusion Criteria:
- >25 elderly (>65yo) patients
- Study type: RCTs, case series, cohort studies
- First hepatectomy
- Raw data on CRLM
- OS: > 12 mo follow up
- DFS: > 12 mo follow up
- If >1 study from same dataset: most relevant selected

949 studies excluded:
- Inclusion criteria not met

Mortality Studies: n=16
Survival Studies: n=21
Quality of Life Studies: n=2

Cancer Surgery Transition Outcomes

- HRQOL
- CGA
- Postoperative Outcomes

Surgery Modifiers:
- Age
- Gender
- Preoperative
- Postoperative therapy

Stratification

CGA (Elderly-Relevant Variables)

Pre-Op HRQOL

Post-acute care - predictors

- In-hospital Complications
- Top Decile: Length of stay
- Hospital Cost
- Discharge Other than Home
- In-hospital Mortality

Stratification

CGA (Elderly-Relevant Variables)

Pre-Op HRQOL

Post-acute care - predictors

- In-hospital Complications
- Top Decile: Length of stay
- Hospital Cost
- Discharge Other than Home
- In-hospital Mortality

Stratification

CGA (Elderly-Relevant Variables)

Pre-Op HRQOL
Post-acute care - predictors

ACS-NSQIP N=55,238

Cancer Care Conceptual Model

Preoperative Treatment Postoperative Outcomes

Outcomes

Age
Demographic Variables
Clinical Variables
Cancer-Related Variables
CGA (Elderly-Relevant Variables)
Pre-Op HRQOL

Cancer Surgery

Surgery Modifiers:
- Type/Extent
- Ostomy
- Postoperative complications
- Postoperative therapy

HRQOL Post-Op Score & Score (from Pre-Op)

Preoperative Outcomes

Oncological Outcomes

Post-acute care - Survival


PAC - HRQoL

Mason M & Anaya DA. SSO 2016

SF-36

PCS

MCS

PAC - HRQoL

N= 329

18%
PAC

82%
No PAC
Transitional care needs – PAC

Mason M & Anaya DA. SSO 2016

Improvements in the recovery phase are essential – linked to PCO (PAC needs and HRQoL), short- and long-term outcomes

Patient-centered outcomes

• Recovery following major surgery appears to be delayed in older patients – PAC needs
  – Predictors: complications, geriatric conditions, baseline function, increasing age
• PAC associated with bad outcomes
  – Inherent slow recovery (PCO)
  – Also – worse survival, worse HRQoL

Clinical case

• Medical work-up (Day 0)
• Counseling in anticipation of possible Sx
• HVPV/gradient measurement
• TACE followed by PVE (Day 14)
• Re-evaluation clinic visit, labs/imaging (Day 49)
• Disease control/biology
• Contralateral liver hypertrophy Tolerability to therapy
• Extended right hepatectomy (Day 56)

Summary and Conclusions

• Liver resection is currently the only curative treatment for the majority of patients with liver malignancies
• Elderly patients represent an increasing number of those with liver tumors and are amenable to curative intent - surgery
Summary and Conclusions

• Liver resection provides survival benefit in elderly patients with liver tumors in whom competing causes of early mortality are not present.
• POP mortality and morbidity is increased but can be mitigated and remain within acceptable standards – selection process/modify RF.

Summary and Conclusions

• Recovery following surgery is the key to maintaining good function and quality of life while minimizing adverse events and poor outcomes.
• Systematic initiatives are required (multidimensional) to accomplish this goal.

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