Management of Cancer in the Carotid

Grand Rounds
April, 2003
Case Presentation (GBMC 3482822)

- **CC:** 51yo man with painful neck mass and dysphagia
- **HPI:**
  - heavy alcohol and tobacco use
  - R anterior FOM excis Bx 8/2000
    - *in situ SCCa @ outside lab; invasive SCCa @ GBMC*
    - *Lost to follow-up*
  - *Represented October 2001 to outside hospital with dysphagia and large L neck mass*
    - DL/Bx and I&D of neck (presumed branchial cyst)
    - SCCa pyriform sinus & left neck T2N3aM0
  - 70 Gy external beam XRT
    - No Chemotherapy
  - *Returned to GBMC 3/2002 with draining, painful, foul-smelling 10 cm left neck mass*
    - Unable to swallow, PEG, losing wt loss 158 -> 125 lb
• **PMH**
  – No cardiac, pulmonary, neuro, vascular, other PMHx
• **Meds**
  – significant narcotic requirement
• **SocHx**
  – Bus driver
  – 1-2 ppd. 1.5 cases beer/wk.
  – Lives with Mother who accompanies to visits
  – Married. One adult son.
• **FamHx, ROS**
  – Noncontributory
Physical Exam

• **Head & Neck:**
  – Nphx, Ophx, FOL normal except for mucositis and edema
  – B TVF normal mobility
  – 10 cm L neck mass, firm and fixed, with draining tracts
  – radiation skin changes

• **Neuro/Psych:**
  – No neurologic deficits noted on initial exam
  – Depressed affect

• **Cardiopulmonary:**
  – normal exam, no PVD, good exercise tolerance

• **GI/GU/Nutritional:**
  – Weight 125 lb (down >30 lb)
• **Labs**
  – CBC/CMP/LFT  HCT 29.7, Cr 0.5
  – metastatic workup (CXR, Chest CT, LFTs) negative

• **CT Scan**
  – [Dr. Wang to review]
• **MRI/MRA** [Dr. Wang to Review]
  – Tumor abutting/partly encasing carotid
  – Normal MRA

• **Angiogram with Left Balloon Test Occlusion**
  – no intima invasion/occlusion
  – no dominance
  – good collateral flow via normal circle of Willis
  – no clinical neurologic deficits after 25 min BTO
• $^{99m}$Technetium HMPOA SPECT perfusion scan
  – 25 mCi HMPOA injected IV 25 min into BTO
  – Symmetric, normal cortical tracer perfusion
• **Therapeutic options considered**
  – *Do nothing / Hospice*
  – *Chemotherapy*
  – *Additional XRT (e.g., IMRT)*
  – *Radical resection*
    • *Carotid resection vs adventitial peel*
    • *Carotid ligation vs revascularization*
    • +/- *brachytherapy*
• **Procedure**
  
  – Dr. Pinhiero; 5/3/2002
  – Neurovascular Surgeon and Radiation Oncologist on standby

  – Tracheostomy
  – Direct laryngoscopy with Left pyriform sinus, BOT & tonsil biopsies (negative)
  – Extended radical L neck dissection with resection of CN 10,11,12 and 9x10 cm skin
  – Carotid adventitial peel
  – Pectoralis major myocutaneous flap
  – No brachytherapy catheters placed
• **Pathology**
• **Main specimen**
  • 5.5 x 4.5 x 2.5 cm Keratinizing SCCa
  • marked histiocytic response
  • in the sternocleidomastoid muscle, to dermis
  • spanning levels II, III, and IV
    – margins along carotid wall
      • + at level 4, < 1mm at levels 2,3
    – Internal jugular superior margin
      • “Rare degenerated foci of squamous cell carcinoma with associated histiocytes and calcifications”
    – All other margins negative
Postoperative Course

• **Uneventful initial post-operative course**
  – No evidence of stroke
  – depressed affect
  – CN 10,11,12 defects
  – discharge home NPO with PEG/Trach POD5
  – decannulated POD 12
  – swallow study POD 30

• **readmitted POD 30 for poor enteral intake**
  – SLP, nutritional, psychiatric, social evaluation
The Dilemma of Carotid Involvement in Head & Neck Cancer

- Complete tumor removal provides the best chance of cure for advanced SCCa in neck
  - 67% with + margins recur locally despite post-op XRT
    [Zieske/Johnson/Myers Arch OHNS '86]

But...

- Risk of iatrogenic stroke and death are high with common/internal carotid resection
  - 26% CVA, 12% periop death in unselected patients
    [Donald '97]

- Carotid involvement portends poor prognosis regardless of local control
Is Carotid Resection for SCCa Worthwhile?

- **Is it futile?**
  - Is surgery contraindicated by the rate of metastasis?

- **Is it oncologically effective?**
  - Does it improve locoregional control? Palliation?

- **Is it safe?**
  - Is the perioperative M&M rate acceptable compared to alternative therapies for carotid involvement?
  - Is M&M rate different from that for “resectable” N3/ECS?

- **Are there better options?**
  - Adventitial Peel, Brachytherapy, ChemoXRT, Hospice

- **Is your patient a candidate?**
  - How can you select patients to minimize risk?
• **Snyderman & D’Amico ‘92** [UPitt., Am J. Otolar. ‘92]
  – Pooled case-control analyses published 1987-92
  – N=158 carotid resections, 22 papers
  – 180 controls (N3 with ECS but not to carotid)
  – 65% revascularized
    • 82% vein graft
    • 7% allograft
    • 11% EC -> IC
  – 35% no revascularization (or thrombosis)
  – pre-op workup not specified
    • era of transition from BTO to XCT to SPECT CBF
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Is Carotid Artery Resection Futile?

Disease-free survival

Kennedy et al 1977

Followup (months)

% Surviving

N3+ECS N=180

CA Resection N=144/158

p = 0.51

No significant difference in survival between CA resection and “Resectable” N3/ECS

[Snyderman & D'Amico, UPitt., Am J. Otolar. ‘92]
Is Carotid Artery Resection Futile?

- [Snyderman & D’Amico, UPitt., Am J. Otolar. ’92]

Followup (months)

% Surviving CA resection

1980-1992

1939-1979

p = 0.67

No significant difference
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Is Carotid Resection Effective?

- **Locoregional control**
  - Carotid resection bestows prognosis equivalent N3/ECS

- **Distant Metastases**
  - Majority (77%) did not develop distant mets
  - 2/3 recurrences were at the primary or in the neck

- **Palliation**
  - reduced pain
  - reduced blow-out risk
  - cosmesis
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## Is Carotid Resection/Revasc Safe?

Periop M&M: Carotid endarterectomy for vascular disease

<table>
<thead>
<tr>
<th>Study</th>
<th>Pub Date</th>
<th>N</th>
<th>Stroke %</th>
<th>Death %</th>
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<tbody>
<tr>
<td>Sundt Jr</td>
<td>1987</td>
<td>1935</td>
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<tr>
<td>Mackey et al</td>
<td>1990</td>
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<td>1</td>
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<tr>
<td>Archie Jr</td>
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<tr>
<td>Geary et al</td>
<td>1993</td>
<td>1572</td>
<td>1.4</td>
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<td>Peer et al</td>
<td>1994</td>
<td>920</td>
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<tr>
<td>Rockman et al</td>
<td>1996</td>
<td>3975</td>
<td>2.2</td>
<td>1.5</td>
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<tr>
<td>Paty et al</td>
<td>1996</td>
<td>1267</td>
<td>1.1</td>
<td>1.3</td>
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<td>Plestis et al</td>
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<tr>
<td>Lepojarvi et al</td>
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<td>Little &amp; Meyer</td>
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<td>3665</td>
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<td><strong>1990-1997</strong></td>
<td><strong>16257</strong></td>
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<td><strong>1.5%</strong></td>
<td><strong>1.0%</strong></td>
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</table>

[Katsuno et al, Shinsu U, Japan, OHNS 2001]
## Is Carotid Resection/Revasc Safe?

### Periop M&M: Carotid reconstruction after resection for cancer

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<th>pub date</th>
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<th>Death</th>
<th>%</th>
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<td>East et al</td>
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<td>6</td>
<td>1</td>
<td>17</td>
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<td>Reilly et al</td>
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<td>12</td>
<td>0</td>
<td>0</td>
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<td>Meleca &amp; Marks</td>
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<td>13</td>
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<td>Sessa et al</td>
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<td>Soulier et al</td>
<td>1998</td>
<td>7</td>
<td>0</td>
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<td>Katsuno et al</td>
<td>2001</td>
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<td>1988-2001</td>
<td>150</td>
<td>7</td>
<td>4.7%</td>
<td>10</td>
<td>6.7%</td>
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</tbody>
</table>

[Katsuno et al, Shinsu U, Japan, OHNS 2001]
Is Carotid Artery Resection Getting Safer?

**All cases 1980-1992**

- N=158, **35% without revascularization**
- Major stroke 17%
  - In only 3% of pts who were ligated after normal BTO/CBF
- Periop Death ? (20% in first year)
- 2 year disease-free survival 22%
  - Revascularization did not change outcome

**Revascularized cases 1987-1998**

- N=148, all revascularized
- Major nonfatal stroke 4.7%
- Periop Death 6.8%
- Major Complications 10%

[Snyderman & D'Amico, Am J. Otolar. '92]  
[Katsuno et al, OHNS 2001]
Is Carotid Artery Resection Getting Safer?

• **Better outcomes, but why?**
  – *Publication/selection bias?*
  – *Revascularization* [Meleca & Marks 1994]
    • 58% of 12 pts ligated without revasc stroked
    • 13% of 8 pts revascularized stroked
  – *Better perioperative management*
    • aspiration risk
    • hypotension/anemia risk
    • vascularized flap coverage of carotid
    • Better patient selection


Can CA Resection Be Made Safer?

No Periop M&M
90%

Death
6.8%

Nonfatal Stroke
3.4%

Stroke
1.4%

Infection/Blow
1.4%

Cardiac
2.0%

Hepatic
0.7%

Aspiration
0.7%

Unknown
0.7%

Aspiration prevention
Avoid CA resection with pharyngotomony
Cardiac evaluation/prophylaxis
Patient selection based on cerebral blood flow

[Katsuno et al, OHNS 2001]
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Are There Better Treatment Options?

- **Non-operative**
  - Chemo/XRT
  - Chemo or XRT alone
  - Supportive care / Hospice
- **Operative**
  - Carotid resection
    - with revascularization
    - without revascularization
  - Adventitial peel
  - Brachytherapy
    - Many patients have already had external XRT
<table>
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<tr>
<th>Study</th>
<th>Primary sites O/Hy/L/C (%)</th>
<th>Resectable (%)</th>
<th>No. patients (analyzable)</th>
<th>Concurrent chemotherapy</th>
<th>Fractionation</th>
<th>Differences in RT between arms</th>
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<tr>
<td>Wendt et al. [6]</td>
<td>42/36°/22</td>
<td>0</td>
<td>140</td>
<td>No</td>
<td>H split 70.2 Gy 1.8 Gy bid</td>
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<td>Brizel et al. [7]</td>
<td>45/20/16/5</td>
<td>47</td>
<td>130</td>
<td>CDDP/5-FU/LV</td>
<td>H 1.25 Gy bid</td>
<td>75 Gy</td>
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<td>Calais et al. [8]</td>
<td>100/0/0/0</td>
<td>NR</td>
<td>113</td>
<td>No</td>
<td>Conventional</td>
<td>70 Gy with break same</td>
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<td>Adelstein et al. [9]</td>
<td>45/16/36/4</td>
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<td>Jeremic et al. [10]</td>
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<td>65</td>
<td>No</td>
<td>H 77 Gy 1.1 Gy bid</td>
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<td>Adelstein et al. [11]</td>
<td>59/18/9/13</td>
<td>0</td>
<td>95</td>
<td>A) No</td>
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<td>87</td>
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<td>89</td>
<td>C) CDDP/5-FU</td>
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<td>Dobrowsky and Naude [12]</td>
<td>41/17/12/30</td>
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<td>80</td>
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<td>V-CHART</td>
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<td>Staar et al. [13]</td>
<td>74/26/0/0</td>
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<td>Carbo/5-FU</td>
<td>AH 69.9 Gy</td>
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<td>Budach et al. [14]</td>
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<td>171</td>
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<td>Study</td>
<td>Resectable (%)</td>
<td>Locoregional control (%)</td>
<td>Distant failure (%)</td>
<td>3-year PFS (%)</td>
<td>3-year OS (%)</td>
<td>Grade III/IV mucositis (%)</td>
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<td>Wendt et al. [6]</td>
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<td>35 (P&lt;0.004)</td>
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<td>49 (P&lt;0.0003)</td>
<td>38 (P&lt;0.001)</td>
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<td>100</td>
<td>66 (P=0.03)</td>
<td>11</td>
<td>42 (P=0.04)</td>
<td>51 (P=0.02)</td>
<td>71 (P=0.005)</td>
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<td>77 (P&lt;0.001) 5-year</td>
<td>16</td>
<td>62 (P=0.04) 5-year</td>
<td>50 (P=0.55)</td>
<td>84 (P=0.001)</td>
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<td>Jeremic et al. [10]</td>
<td>NR</td>
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<td>43</td>
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<td>50 (P=0.041) 5-year</td>
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<td>12</td>
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<td>90 with the V-CHART arms</td>
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<td>Staar et al. [13••]</td>
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<td>51 (P=0.14) 2-year</td>
<td>NR</td>
<td>48 (P=0.09)**</td>
<td>68 (P=0.01)</td>
<td>2-year</td>
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<td>Budach et al. [14••]</td>
<td>NR</td>
<td>46</td>
<td>31</td>
<td>NR</td>
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<td>Forastiere et al. [15••]</td>
<td>100</td>
<td>58†</td>
<td>7 (P=0.044 vs. C)</td>
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<td>53 2-year</td>
<td>15 2-year</td>
<td>77 2-year</td>
<td>77</td>
<td>36</td>
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</tbody>
</table>
Is Adventitial Peel Adequate?

• **Huvos et al** [Am J Surg 1973]
  – $N = 64$ resected carotid specimens
  – 70% of patients were post-XRT
  – 58% showed microinvasion of carotid wall
    • correlation between XRT and margins not specified
  – All post-XRT carotids had marked atherosclerosis

• **Conclusions**
  – Adventitial peel usually fails to give a clear margin
  – May increase risk for subsequent blowout
Is Carotid Resection for SCCa Worthwhile?

- **Is it futile?**
  - Is surgery contraindicated by the rate of metastasis?
  - Is outcome different from that for “resectable” N3/ECS?

- **Is it oncologically effective?**
  - Does it improve locoregional control? Palliation?

- **Is it safe?**
  - Is the perioperative M&M rate acceptable compared to alternative therapies for carotid involvement?

- **Are there better options?**
  - Adventitial Peel, Brachytherapy, ChemoXRT, Hospice

- **Is your patient a candidate?**
  - How can you select patients to minimize risk?
Patient selection for planned CA resection

- Unselected Acute Unilateral Carotid Ligation
  - 26% Death
  - 12% Major Stroke

[Nemzek W, in Donald P Surgery of the Skull Base 2001]
Patient selection for planned CA resection

• **Tests of Carotid Ligation Tolerance**
  – Manual Carotid Occlusion [Matas 1911]
    • compress ipsi carotids by hand in office, neuro exam
    • **Advantages**
      – in office test, free
    • **Disadvantages**
      – imprecise due to vasovagal effects
      – difficult to compress carotid amid tumor
      – embolic risk
      – high likelihood of in-office stroke/death
Patient selection for planned CA resection

• Tests of Carotid Ligation Tolerance
  – Doppler Matas
  – Angiography
    • MRA
    • CT angio
    • Intraarterial contrast 4-vessel arteriography
  – Balloon Test Occlusion (BTO)
    • Arteriography
    • Clinical Exam
    • EEG
    • Stump Pressure
Patient selection for planned CA resection

• Tests of Carotid Ligation Tolerance
  – BTO with Cerebral Perfusion Scan
    • Technetium HMPOA SPECT scan during BTO
      – Hexamethylpropyleneamine oxime
      – lipophilic tracer
      – distributes per CBF
  • Xenon CT
    – inhaled Xenon gas diffuses like N20
    – risk of general anesthesia during test
Patient selection for planned CA resection

- **Unselected Acute Unilateral Carotid Ligation**
  - 26% Death
  - 12% Major Stroke

MRA then 4 vessel angio

BTO with clinical exam

BTO with HMPOA SPECT

3-20% Stroke with CA ligation

- **Stroke rate 1.3-2.6%**
  - 5-10% fail exam
  - Complications (0-8%)
    - 1.6% stroke/TIA after test
    - 0.4% permanent
    - 1.2% dissection
    - 0.2% pseudoaneurysm
    - 0.2% embolism

[Nemzek W, in Donald P Surgery of the Skull Base 2001](#)
Preop Evaluation Algorithm

• **Standard preoperative evaluation**
  – surgical
  – medical
  – metastatic w/u
  – neurologic
  – psychosocial
  – **STOP if**
    • metastatic to distant sites
    • frail cardiopulmonary or neurovascular status
      – risk of hypotension, aspiration, stroke
    • preexisting contralateral carotid deficits
Preop Evaluation Algorithm

• MRI/MRA/MRV
  – detail soft tissue around carotid, preop planning
  – CT angio/venogram if pacemaker or other implant
  – STOP if
    • unresectable for other reasons
    • carotid not involved
    • ipsilateral carotid dependence, bad Circle of Willis
Preop Evaluation Algorithm

• 4-vessel Angiogram with Balloon Test Occlusion
  – Clinical assessment
    • STOP if fails clinical exam <20 minutes BTO
  – HMPOA SPECT perfusion scan during BTO
    • Xenon CT alternative
Preop Evaluation Algorithm

• Perioperative Management
  – intraoperative EEG
    • somatosensory, ABR, EMGs
  – keep volume repleted, avoid hypotension
    • may be at odds with free flap
  – Revascularize
    • team approach with vascular/neurosurgeon
  – Wound reconstruction
    • Vascularized flap coverage (PMMF) if carotid spared
      • Meticulous closure to avoid pharyngeal leak
  – Aspiration Precautions
    • trach, PEG, NPO
End Notes

• Need a prospective RCT
  – Publication bias
  – Selection bias
  – Low numbers in most series

• Stroke and Disease-free survival are not the only relevant measures
  – Palliation of pain/wound
  – Mode of death, avoidance of blowout
  – Non-stroke dysfunction (CN9,10,11,12,symp)

• Doesn’t apply to non-SCCa tumors
  – Paragangliomas
Hy and L combined.
Updated 5-year OS 28% versus 42% ($P = 0.05$).
In oropharyngeal cancer patients, OS was improved with chemoradiotherapy.
Induction CDDP/5-FU.
Laryngectomy-free survival.
AH, accelerated hyperfractionated; carbo, carboplatin; CDDP, cisplatin; 5-FU, 5-fluorouracil; overall survival; PFS, progression-free survival; RT, radiotherapy; V-CHART, Vienna (variant) C.