CARDIOVASCULAR CONSIDERATIONS IN THE GERIATRIC PATIENT WITH CANCER

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“JEOPARDY” CATEGORIES

• Age as a risk factor (is it?)
• Drug mix
• Hypertension
• CVD before cancer
• CVD after cancer
AGE AND CARDIAC TOXICITY

Swain et al., Cancer 2003

Above 400mg/m²
HR=3.28 (1.40-7.65)
Wp=0.002
AGE, MS AND CANCER

![Graph showing cancer incidence and metabolic syndrome prevalence across different age groups.]
AGE & COMORBIDITY AND CARDIAC TOX. TRASTUZUMAB

\[ P = 0.013 \]

Jawa et al., Medicine 2016

<table>
<thead>
<tr>
<th>Study name</th>
<th>Std diff in means</th>
<th>Standard error</th>
<th>Variance</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
<th>Z-Value</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardinale 2010</td>
<td>0.200</td>
<td>0.169</td>
<td>0.029</td>
<td>-0.132</td>
<td>0.532</td>
<td>1.181</td>
<td>0.238</td>
</tr>
<tr>
<td>Cochet 2011</td>
<td>-0.269</td>
<td>0.257</td>
<td>0.066</td>
<td>-0.772</td>
<td>0.234</td>
<td>-1.049</td>
<td>0.294</td>
</tr>
<tr>
<td>Guarnieri 2006</td>
<td>-0.083</td>
<td>0.169</td>
<td>0.028</td>
<td>-0.414</td>
<td>0.248</td>
<td>-0.492</td>
<td>0.623</td>
</tr>
<tr>
<td>Morris 2011</td>
<td>0.392</td>
<td>0.221</td>
<td>0.049</td>
<td>-0.040</td>
<td>0.825</td>
<td>1.779</td>
<td>0.075</td>
</tr>
<tr>
<td>Naumann 2013</td>
<td>0.177</td>
<td>0.140</td>
<td>0.019</td>
<td>-0.157</td>
<td>0.390</td>
<td>0.835</td>
<td>0.404</td>
</tr>
<tr>
<td>Negishi 2013</td>
<td>-0.085</td>
<td>0.243</td>
<td>0.059</td>
<td>-0.562</td>
<td>0.392</td>
<td>-0.351</td>
<td>0.726</td>
</tr>
<tr>
<td>Russo 2014</td>
<td>0.455</td>
<td>0.255</td>
<td>0.065</td>
<td>-0.044</td>
<td>0.953</td>
<td>1.786</td>
<td>0.074</td>
</tr>
<tr>
<td>Wadhwa 2008</td>
<td>-0.195</td>
<td>0.191</td>
<td>0.037</td>
<td>-0.570</td>
<td>0.179</td>
<td>-1.022</td>
<td>0.307</td>
</tr>
<tr>
<td>Tarantini 2012</td>
<td>0.182</td>
<td>0.101</td>
<td>0.010</td>
<td>-0.017</td>
<td>0.381</td>
<td>1.793</td>
<td>0.073</td>
</tr>
<tr>
<td>Russo 2012</td>
<td>0.221</td>
<td>0.102</td>
<td>0.010</td>
<td>0.020</td>
<td>0.421</td>
<td>2.159</td>
<td>0.031</td>
</tr>
<tr>
<td>Savelya 2012</td>
<td>-0.100</td>
<td>0.238</td>
<td>0.057</td>
<td>-0.567</td>
<td>0.367</td>
<td>-0.420</td>
<td>0.675</td>
</tr>
<tr>
<td>Std diff in means and 95% CI</td>
<td>0.120</td>
<td>0.048</td>
<td>0.002</td>
<td>0.025</td>
<td>0.215</td>
<td>2.481</td>
<td>0.013</td>
</tr>
</tbody>
</table>
Figure 3. Data analysis of significant variables reporting effect measures for each included study.
OBESITY AND CARDIOTOXICITY

• Network SR/MA for anthracyclines +/- subsequent trastuzumab toxicity
• 15 studies, BC 8745 patients
• OR for BMI >25: 1.38 (1.06-1.80)

• NB: not adjusted for obesity-associated comorbidity

Guenancia et al. JCO 2016
Table 4. Logistic regression models predicting likelihood of experiencing grade 3-4 non-hematological toxicity

<table>
<thead>
<tr>
<th>Model Description</th>
<th>OR</th>
<th>%95 CI</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total PDI level 1-5</td>
<td>1.07</td>
<td>0.983-1.164</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>Total PDI level 1-3</strong></td>
<td><strong>1.17</strong></td>
<td><strong>1.009-1.346</strong></td>
<td><strong>0.14</strong></td>
</tr>
<tr>
<td>Total level 1 PDI</td>
<td>1.94</td>
<td>1.213-3.098</td>
<td>0.16</td>
</tr>
<tr>
<td>Total level 2 PDI</td>
<td>1.12</td>
<td>0.931-1.352</td>
<td>0.13</td>
</tr>
<tr>
<td>Level 1-5 PDI involving chemotherapeutics</td>
<td>1.27</td>
<td>0.991-1.627</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>Level 1 PDI involving chemotherapeutics</strong></td>
<td><strong>3.01</strong></td>
<td><strong>1.301-6.972</strong></td>
<td><strong>0.15</strong></td>
</tr>
<tr>
<td>Level 2 PDI involving chemotherapeutics</td>
<td>1.02</td>
<td>0.552-1.882</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Note: All models are adjusted for age, gender, body mass index, blood pressure, Eastern Cooperative Oncology Group performance status, aspartate aminotransferase, albumin, bilirubin, creatinine clearance, red blood cell count, bone marrow invasion, stage, and MAX2.
ANTICOAGULATION INTERACTIONS

- 1mg warfarin/d prophylaxis for ports
- 5-FU based regimens cause protein displacement
- Data with new oral anticoagulants?

Masci et al., JCO 2003
TARGETED THERAPIES

• Many targeted therapies interact with C-V drugs, e.g. amiodarone (p450 metabolism, QT prolongation)

• CDK 4/6 inhibitors (ribociclib > palbociclib), QT prolongation

• Ibrutinib, 6-16% risk of atrial fibrillation. In one study, elderly men were more at risk (beside preexisting cardiac conditions) (Reda et al. J Hematol Oncol, 2018). Also risk of bleeding.
VEGF INHIBITORS

• Increased hypertension, bleeding, thromboembolic events

• In lung adenocarcinoma, the toxicity cancels the OS benefit of bevacizumab in patients ≥75yo (Langer et al, Am J Clin Oncol, 2016)

• Due notably to G3 bleeding (≥75: 14% vs 2%; <75: 3% vs 0%)
HYPERTENSION: HIGHLY AFFECTED

**GENERAL**
- Decreased appetite
- Weight loss
- N/V/D

**DRUG SPECIFIC**
- Vincristine etc...autonomous neuropathy
- VEGF inhibitors: HTN
- Steroids

Take home message: Watch and adjust BP meds
FALLS DURING CHEMOTHERAPY

Boler et al., SIOG 2007
TREATING DLBCL IN PATIENTS WITH CHF

• A retrospective cohort of adult DLBCL patients (n=854) uncovered 38 patients with baseline CHF (4.4%) by echo/MUGA

• Median age 71 (21-93), median follow-up 21.2 months (1.4-50.8)

• Patients with diastolic dysfunction were more likely to receive R-CHOP-like regimens, compared to patients with systolic dysfunction

• 56.5% of patients treated by R-CHOP completed treatment (mean cumulative dose of doxorubicin 130 mg/m2) vs 90% of non-R-CHOP (p=0.11)

• Cardiac events 25% in R-CHOP group vs 18% in non-R-CHOP (NS)

Dougoud et al., J Geriatr Med Gerontol, 2017
COLORECTAL CANCER, CVD AND CHF

CRC stage I-III vs without, SEER/Medicare
Median age 78 (66-106), median follow-up 8 years

Fig 2. Cumulative incidence of (A) congestive heart failure (CHF) and (B) cardiovascular disease (CVD). CRC, colorectal cancer.

Kenzik et al., JCO 2018
WHAT IS THE ROLE OF CHEMOTHERAPY?

• 10y cumulative incidence CVD 57.4% vs 22%
• 10y cumulative incidence CHF 54.5% vs 18%
• Interaction between HTN and chemo significant for CVD
• Interaction between diabetes and chemo significant for CHF

Kenzik et al., JCO 2018
CONCLUSIONS

• Beware of drug interactions
• Orthostatic hypotension can be an initial sign of neuropathy
• Be ready to adjust C-V treatments quickly as older patients have less C-V reserve.
• Cancer and its treatments increase the risk of CV morbidity in older survivors
Abstract submission deadline: **JUNE 8, 2018**

Early registration deadline: **JUNE 19, 2018**

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