Στεφανιαία νόσος-ενδοθηλιακή δυσλειτουργία

ΤΣΑΓΑΛΟΥ ΕΛΕΥΘΕΡΙΑ
ΘΕΡΑΠΕΥΤΙΚΗ ΚΛΙΝΙΚΗ ΠΑΝΕΠΙΣΤΗΜΙΟΥ ΑΘΗΝΩΝ
Risk of coronary heart disease after cancer diagnosis

- 6 months RR=1.70, 95% CI 1.66–1.75
- 6 to 12 months RR=1.1, 95% CI 1.06–1.14
- 1 to 4 years RR=1.08, 95% CI 1.06–1.10
- 4 to 10 years RR=1.07, 95% CI 1.04–1.09
- >10 years RR=1.07, 95% CI 1.04–1.11
Coronary artery disease and cancer interaction

- Shared biologic mechanisms
- Shared risk factors
- Cancer Risk Related to the Treatment of CVD
- CVD Risk Related to the Treatment of Cancer
Inflammation
Oxidative Stress and Reactive Oxygen Species
Hormones, Cytokines, Growth factor
Haemostatic activation
Modifiable cardiac risk factors with their estimated cancer risk

Circulation. 2016;133:1104–1114
Cancer Risk Related to the Treatment of CVD and CVD Risk Factors

- Statins
- Aspirin
- Prasugrel
CVD Risk Related to the Treatment of Cancer

- Dasatinib
- Cisplatin
- Bleomycin, vinca alkaloids, cisplatin, carboplatin, gemcitabine, and interferon-α.
- 5-FU
- Cisplatin
- Bevacizumab
- VEGF inhibitors
- Nilotinib
- Ponatinib
- 5-fluorouracil
taxanes
bevacizumab
sorafenib
Endothelial toxicity

- Impaired endothelial cell viability
  - necrosis/apoptosis
  - swelling of the endothelium
  - increase in endothelial permeability

- Endothelial cell dysfunction
  - alternation in NO signalling
  - activation of the endothelin system

Bcr-Abl inhibitors
nilotinib and panotinib,

5-FU, capecitabine, paclitaxel,
gemcitabine, rituximab, and sorafenib
Capillary rarefunction (disruption of angiogenesis)
Endothelial damage or dysfunction

Capillary rarefunction

Alteration of vascular smooth muscle reactivity

Aggregation and procoagulant activity

VASCULAR EVENTS
Chemotherapy – related vasotoxicity

**type I**
long-term and structural risk

- cumulative, dose related
- underlying damage appears to be permanent and irreversible
  (dasatinib, ponatinid etc)

**type II**
transient and mainly functional risk

- not dose-related
- does not appear to occur in all patients
- is expressed in a broad range of severity when it does occur
- is not associated with identifiable ultrastructural abnormalities
  (5FU, taxanes, etc)
Pathophysiological mechanisms of coronary artery disease in cancer treatment

<table>
<thead>
<tr>
<th>Agent</th>
<th>Pathophysiological mechanism</th>
<th>Risk of coronary artery disease and acute coronary syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoropyrimidines</td>
<td>• Endothelial injury</td>
<td>• Up to 18% manifest myocardial ischaemia</td>
</tr>
<tr>
<td>(5-FU, capecitabine, gemcitabine)</td>
<td>• Vasospasm</td>
<td>• Up to 7–10% silent myocardial ischaemia</td>
</tr>
<tr>
<td>Platinum compounds (cisplatin)</td>
<td>• Procoagulant status</td>
<td>• 20-year absolute risk of up to 8% after testicular cancer</td>
</tr>
<tr>
<td></td>
<td>• Arterial thrombosis</td>
<td>• 2% risk of arterial thrombosis</td>
</tr>
<tr>
<td>VEGF inhibitors (bevacizumab, sorafenib, sunitinib)</td>
<td>• Procoagulant status</td>
<td>• Risk of arterial thrombosis: bevacizumab 3.8%, sorafenib 1.7%, sunitinib 1.4%</td>
</tr>
<tr>
<td></td>
<td>• Arterial thrombosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Endothelial injury</td>
<td></td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>• Endothelial injury</td>
<td>• 2–7-fold increased relative risk of myocardial infarction</td>
</tr>
<tr>
<td></td>
<td>• Plaque rupture</td>
<td>• Cumulative 30-year coronary events incidence of 10% in Hogdkin lymphoma survivors</td>
</tr>
<tr>
<td></td>
<td>• Thrombosis</td>
<td>• Risk proportional to irradiation dose</td>
</tr>
</tbody>
</table>
Fluoropyrimidines

- Incidence in the literature ranging widely from 1 to 45%
- Coronary spasm
- The onset of chest pain is often abrupt during infusion
- Can also have a delayed presentation within the first 72 h
- Higher incidence of angina with continuous compared to bolus infusions
- Cessation results in resolution of angina
- Cardiac enzymes are rarely elevated
- Coronary angiography usually does not reveal significant coronary artery disease
- Prophylactic nitrates and calcium channel blockers do not clearly appear to reduce the incidence
- Re-initiation has shown increased incidence of angina with severe complications
Cis platin

- myocardial and cerebrovascular ischaemia in 2% of patients
- endothelial injury (plaque erosion)
- single and even multivessel coronary thrombosis can be evident on angiography without any underlying atherosclerosis
- five-fold increase in cardiovascular mortality in the first year
- 7.1-fold increase in major cardiac events for long term survivors
ACS occurs in 2% of patients treated with bevacizumab

the addition of bevacizumab to 5-FU- more than doubles the incidence

sorafenib has been associated with progression of CAD

nilotinib has a preferential effect on the peripheral arterial circulation

ponatinib cardiovascular events seem to be more common with ponatinib than peripheral artery disease
<table>
<thead>
<tr>
<th>Types</th>
<th>Hodgkin’s disease relative risk</th>
<th>Breast cancer relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>RIHD</td>
<td>&gt;6.3</td>
<td>2–5.9</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>4.2–6.7</td>
<td>1–2.3</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>2.2–12.7</td>
<td>0.9–2</td>
</tr>
</tbody>
</table>
Rate of Major Coronary Events According to Mean Radiation Dose to the Heart

Cumulative risk of first ischemic cardiac event by time for increasing radiation doses

J Clin Oncol, November 16, 2015
How to treat challenges to be addressed

- Patients with cancer are often excluded from clinical trials involving PCI.

- Several comorbid conditions interfere with treatment:
  - Thrombocytopenia
  - Malignant or metastatic gastrointestinal or cerebral disease can increase the risk of bleeding
  - High risk of thrombosis due to hypercoagulable state

- The frequent need for noncardiac surgery in the patient with cancer.
Stable coronary artery disease

Clearance for surgery or cardiotoxic therapy?

- Coronary revascularization before surgery is not necessary before most operations
- Aggressive risk factors management
- Beta blockers, statins, aspirin
- Revascularization might be considered only in patients extremely severe CAD along with poor exercise tolerance
Acute coronary syndrome (STEMI/NSTEMI)

- Treatment according the ESC/AHA/ACC guidelines
- B blocker, statins
- Antiplatelets and anticoagulation
- Radial access for coronary angiography
Recommended revascularization approach used at the MD Anderson Cancer Center
High Bleeding Risk
- Thrombocytopenia
- Dysfunctional Platelets
- Coagulopathy
- Active GI/CNS Lesion
- Treatment with AC for VTE

Cancer
- Tobacco
- Obesity
- Physical Activity
- Poor Nutrition
- Diabetes
- Alcohol
- Hypertension
- Hyperlipidemia

Bidirectional

CAD
- Diabetes
- Tobacco smoking

Renal Failure
- Chronic Inflammatory State
  - IL-1, IL-5 etc.
- LV Systolic Dysfunction
- Stent Thrombosis & In-Stent Restenosis
- DES is better than BMS for ST & ISR
  - Shorter duration DAPT feasible
  - E-ZES (ZEUS trial)
  - PF-DCS (LEADERS FREE trial)
  - COBRA PzF

Increased Risk

Radiation Therapy

+ Need for Cancer related procedure

Shorter duration DAPT preferable

Historically BMS preferred in cancer patients

DES should be considered in cancer patients
ΣΥΜΠΕΡΑΣΜΑΤΑ

- Βιολογικοί παράγοντες, κοινοί παράγοντες κινδύνου, τοξικότητα της χήμειο/ακτινοθεραπείας οδηγούν σε συχνή συνύπαρξη καρκίνου και στεφανιαίας νόσου
- Οι ασθενείς αυτοί παρουσιάζουν ιδιαίτερες προκλήσεις όσον αφορά την αντιμετώπισή τους
- Ο χειρισμός τους απαιτεί λεπτομερή συνεργασία μεταξύ καρδιολόγων και ογκολόγων
- Οι ασθενείς αυτοί δεν πρέπει να στερούνται καρδιολογικής θεραπείας καθώς η προγνωση από τα κακοήθη νοσήματα εχει βελτιωθεί σε σημαντικό βαθμό
- Δεν πρέπει να λαμβάνουν ιδιαίτερα επιθετική θεραπεία καθώς είναι αυτή που μπορεί να βάλει σε κίνδυνο την επιβίωσή τους
Σας ευχαριστώ