La terapia nel paziente oncologico con cardiopatia ischemica

Dott.ssa Iris Parrini
Ospedale Mauriziano di Torino
Paziente con cardiopatia ischemica cronica candidato a terapia oncológica

Quale protezione possibile?
2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines

The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC)

Authors/Task Force Members: Jose Luis Zamorano* (Chairperson) (Spain), Patrizio Lancellotti* (Co-Chairperson) (Belgium), Daniel Rodríguez Mañóz (Spain), Victor Aboyans (France), Riccardo Asteegiano (Italy), Maurizio Galderisi (Italy), Gilbert Habib (France), Daniel J. Lenihan* (USA), Gregory Y. H. Lip (UK), Alexander R. Lyon (UK), Teresa Lopez Fernandez (Spain), Dania Mohty (France), Massimo F. Piegoli (Italy), Juan Tamargo (Spain), Adam Torbicki (Poland), and Thomas M. Suter (Switzerland)

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

5-FU = 5-fluorouracil; VEGF = vascular endothelial growth factor.
Rivalutazione clinica e strumentale per stabilire il rischio e la presenza di ischemia

Ottimizzare la terapia cardiologica

Cercare di evitare farmaci che possono indurre ischemia o trombosi

Evitare procedure invasive se la cardiopatia ischemica è stabile in terapia medica ottimale
Optimal Medical Therapy with or without PCI for Stable Coronary Disease

Management of stable CAD should be focused on controlling ischemic symptoms and preventing progression of CAD. If symptoms can be controlled medically, revascularization offers no survival advantage.

PCI did not reduce the risk of death, myocardial infarction, or other major cardiovascular events when added to optimal medical therapy.

Bodeb NgJ2007
Paziente con Sindrome Coronarica Acuta (candidato a CT) con coronaropatia trattabile con intervento

Quale intervento ? Quando ?
Qualora sia necessario intervenire con procedure di rivascolarizzazione (percutanea/chirurgica) si deve tenere in considerazione

✓ l’interferenza con i programmi di chirurgia della neoplasia

✓ la scelta degli stent con il conseguente rischio di trombosi

✓ il tipo e la durata della doppia antiaggregazione
Special considerations

- must be made in respect to either primary or secondary thrombocytopenia
- the propensity of bleeding
- the presence of coagulopathies
- vascular access complications

- hematologic malignancies (acute leukemia, lymphoma and multiple myeloma),
- solid tumor cancers (breast cancer, ovarian, germ cell)
- have thrombocytopenia either as a manifestation of their primary disease or as a consequence of the chemotherapy
patients at high risk for adverse ischemic events based on the clinical presentation, results of their diagnostic workup, coronary anatomy, or in patients with persistent evidence of ischemia despite medical therapy.
May be silent due

• advanced age of the patients
• comorbidities such as diabetes
• or simply because symptoms are masked by the use of analgesics and narcotics
Tako-tsubo syndrome among cancer patients

- a side effect of chemotherapeutic use or antineoplastic agents such as 5-FU, Sunitinib, and Cytarabine
- acute emotional or physical stress

Cancer therapy should be resumed in 2 to 4 weeks, with close monitoring of the patients and administration of β-blockers to reduce the sympathetic myocardial stimulation.

antiplatelet therapy (aspirin, thienopyridine), anticoagulants, β-blockers, ACE inhibitors, statins

is recommended as in the general population, with possible limitations due to a higher rate of thrombocytopenia and bleeding diathesis

Se terapia oncologica in corso ... considerare le interferenze farmacologiche

- **ACE inibitori o sartani**: preferibilmente Ramipril o losartan, valsartan, candesartan, irbesartan e telmisartan

- **Calcio-antagonisti**: Calcio antagonosti non-diidropiridinici (es: diltiazem e verapamil) non dovrebbero essere usati in combinazione con gli antiVEGF per l’interazione con l’isoenzima CYP3A4, conorrendo all’aumento dei livelli ematici del sorafenib, sunitinib, o di altri farmaci.

- **Beta-bloccanti** preferibilmente il nebivololo, carvedilolo

- **Statine** Rovustatina e pravastatina, che non interferiscono significativamente con il citocromo CPY2C8205

Overcoming multidrug-resistance in cancer: Statins offer a logical candidate Narendra G.Mehta, Monica Mehta Medycal hypoversi 2010
Compared with the general population, the mortality in cancer patients was high, with a 1-year survival rate of only 26%.

Both lack of appropriate medical therapy for MI and cancer with its complications may have contributed to the poor survival in this population.

Aspirin can be administered to all patients with platelets greater than 10,000/mL according to SCAI guidelines without worsening the outcomes Sarkiss MG, Yusuf.

The administration of P2Y12 agents (Clopidogrel, Ticagrelor) was reserved only for patients with more than 30,000/mL.

Prasugrel, IIB–IIIA inhibitors have not been studied with platelet counts <50,000/ml.


Duration of DAPT

- 2 weeks after balloon angioplasty
- 4 weeks after BMS
- 3 to 6 months after third generation DES
- 12 months after DES

La scelta dello stent: BMS vs DES

Vantaggi:
BMS permette un ridotto periodo di DAPT

Svantaggi:
DES meno trombogenici ma è necessaria una DAPT di più lunga durata

La scelta andrebbe presa collegialmente in base alle caratteristiche del singolo paziente

La durata DAPT non dovrebbe ritardare la chemioterapia o la terapia chirurgica oncologica

Alcuni chemioterapici come talidomide, cisplatino e lenalidomide aumentano il rischio di trombosi dello stent

Ischemic Heart Disease: Special Considerations in Cardio-Oncology Dana Elena Giza, MD et al Curr Treat Options Cardio Med (2017)
Differences between various stenting platforms, choice and duration of antiplatelet or procedural antithrombotic therapy, or impact of cancer or cancer treatment on endothelial repair mechanisms all remain largely unstudied with the exception of anecdotal evidence and small retrospective case series.
CANCER TREATMENT (chemotherapy, cancer surgery) can increase the risk of coronary complications. Thrombocytopenia in these patients can result in potential bleeding complications, requiring stopping, which can result in catastrophic thrombotic complication soon after stent implantation.

Complementary invasive procedures, such as fractional flow reserve (FFR), intravascular ultrasound (IVUS), or optical coherence tomography (OCT), can be used to ascertain the need for revascularization.

Deferring revascularization in cancer patients with a FFR > 0.75 has not been associated with increased mortality within 1 year of the procedure.
Catheterization in cancer patients is thrombocytopenia

Prophylactic platelet transfusion in cancer patient

- platelet count <20,000/ml plus high fever, leukocytosis, rapid fall in platelet count or other coagulation abnormalities

- platelet count <20,000/ml in solid tumor patients receiving chemotherapy

Most invasive procedure can be performed with comfort if no coagulation abnormalities are associated and the platelet count is around 40,000 to 50,000/mL

Optimal vascular access, with critical deciding between femoral or radial access site, is required in cancer patients is related to vascular access and potential bleeding complications at the access site.

Femoral approach can lead to a retroperitoneal hemorrhage after sheath removal in a case of a high puncture, radial access site has a lower bleeding risk.
**CABG vs PCI**

**CABG** is recommended when patients have a good outcome and a potentially curable malignancy, has the advantage of not requiring a prolonged antiplatelet therapy.

**PCI** is reserved for more aggressive and metastatic disease (expected survival <1 year).

In CABG the procedure should be considered with a platelet count higher than 50,000/µl,
CONCLUSIONI

- Il cancro e la cardiopatia ischemica sono le due principali cause di morte del mondo e talora coesistono.
- Non vi sono dati sufficienti perché questi pazienti sono stati esclusi dagli studi.
- Se la cardiopatia ischemica è stabile la terapia medica potrebbe essere la scelta migliore.
- Se la cardiopatia ischemica è acuta vi è l’indicazione a procedure invasive ma la scelta dello stent e della durata della doppia antiaggregazione va condivisa con gli altri specialisti in base alle caratteristiche del paziente.
GRAZIE PER L’ATTENZIONE