La terapia nel paziente oncologico con cardiopatia ischemica

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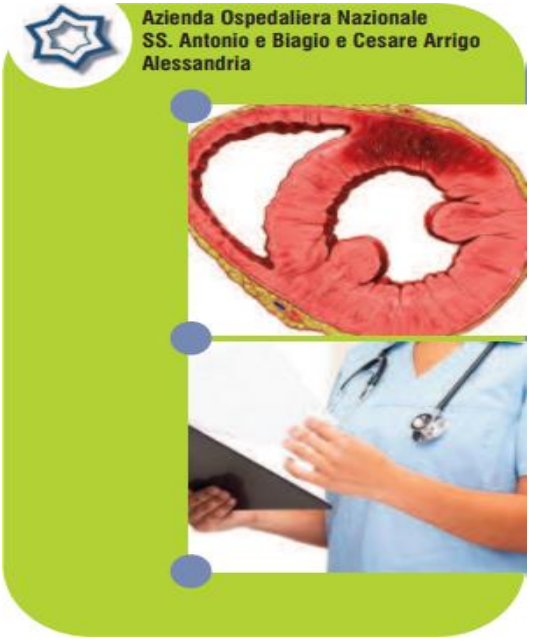

Paziente con cardiopatia ischemica cronica candidato a terapia oncologica

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)

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Table 7 Pathophysiological mechanisms of coronary artery disease in cancer treatment[7,60,81,99,117–123]

Agent	Pathophysiological mechanism	Risk of coronary artery disease and acute coronary syndrome
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 Hogdkin lymphoma survivors • Risk proportional to irradiation dose

5-FU = 5-fluorouracil; VEGF = vascular endothelial growth factor.

Paziente con cardiopatia ischemica cronica candidato a terapia oncologica

- Rivalutazione clinica e strumentale per stabilire il rischio e la presenza di ischemia

- Ottimizzare la terapia cardiologica

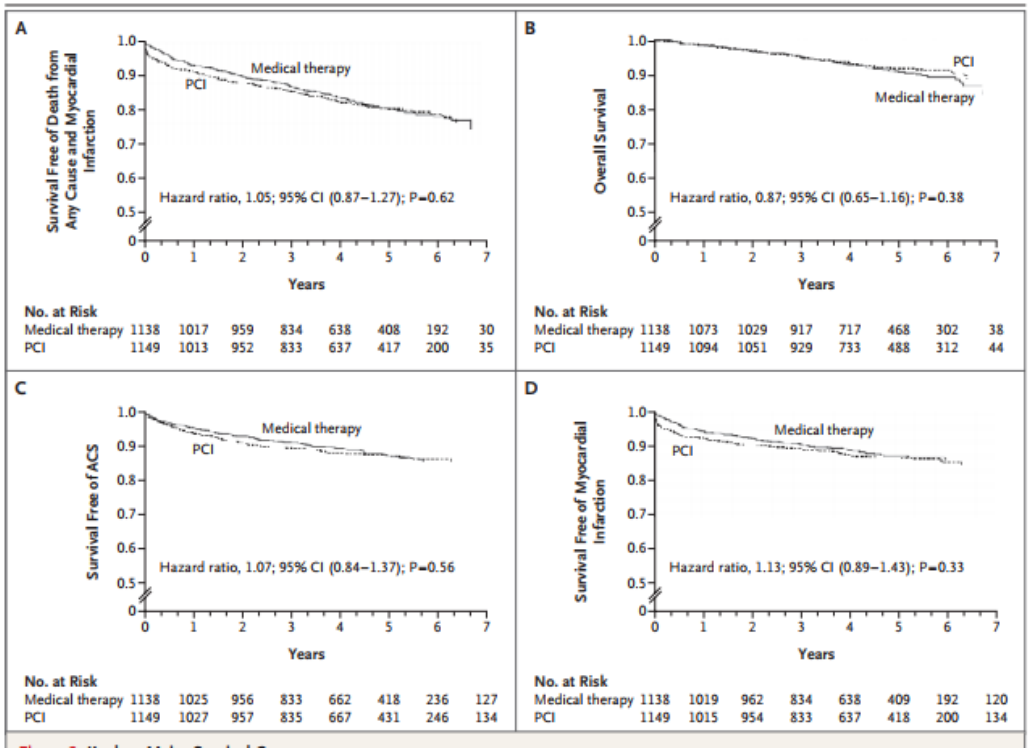
- Cercare di evitare farmaci che possono indurre ischemia o trombosi

- 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 sy**mptoms 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 ?

Documento di consenso ANMCO/AICO/AIOM: Snodi clinico-gestionali in ambito cardioncologico

Luigi Tarantini[1] (Coordinatore), Michele Massimo Gulizia[2] (Coordinatore), Andrea Di Lenarda[3] (Coordinatore), Nicola Maurea[4] (Coordinatore), Maurizio Giuseppe Abrignani[5], Irma Bisceglia[6], Daniella Bovelli[7], Luisa De Gennaro[8], Donatella Del Sindaco[9], Francesca Macera[10], Iris Parrini[11], Donatella Radini[3], Giulia Russo[3], Angela Beatrice Scardovi[12], Alessandro Inno[13]

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

Diagnostic catheterization and invasive revascularization procedures

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.

Ischemic Heart Disease: Special Considerations in Cardio-Oncology Giza DE et al Curr Treat Options Cardio Med (2017)

SCA in cancer

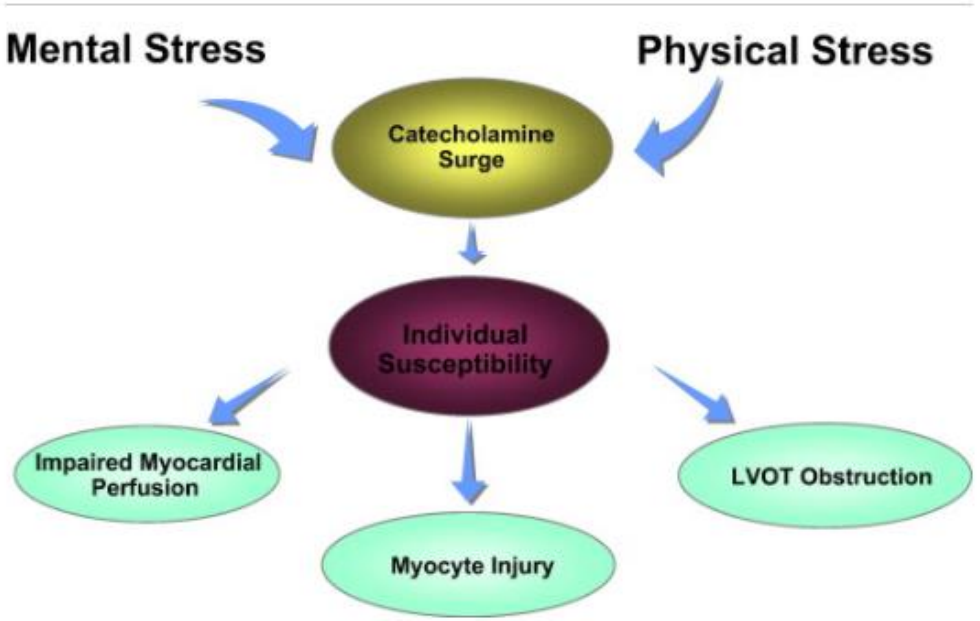
May be silent due

- 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, Sunitinb, 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.



Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. Am Heart J. 2008;155(3):408–17

Acute coronary syndrome

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

Iliescu CA, Grines CL, Herrmann J, Yang EH, Cilingiroglu M, Charitakis K, et al. SCAI expert consensus statement: evaluation, management, and special considerations of cardio-oncology patients in the cardiac catheterization laboratory (endorsed by the cardiological society of India, and sociedad Latino Americana de Cardiologia intervencionista). Catheterization and cardiovascular interventions: official journal of the Society for Cardiac Angiography & Interventions. 2016;87(5):E202–23.

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, concorrendo 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

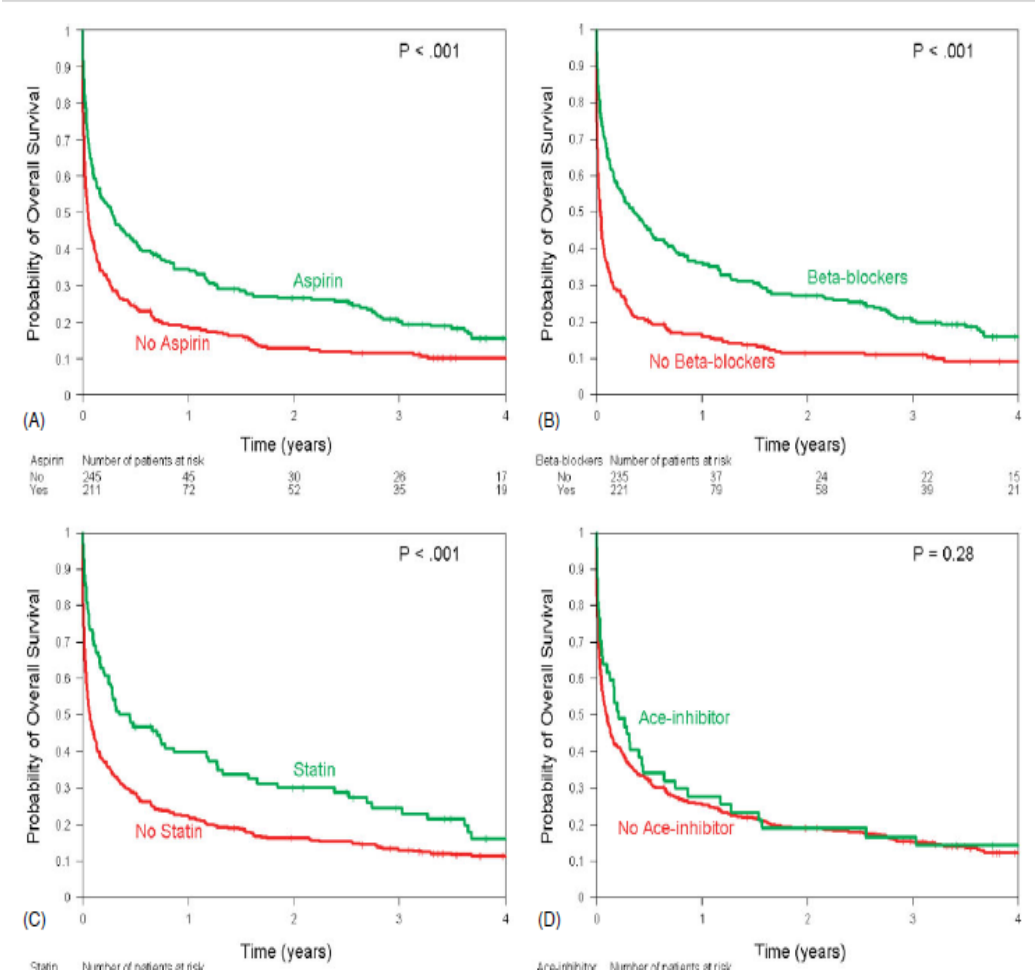
Overcoming multidrug-resistance in cancer: Statins offer a logical candidate Narendra G.Mehta[a]MonicaMehta Medycal hypoyersi 2010

Acute MI

use of aspirin, β-blockers, statins and coronary revascularization improves outcome

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.



Yusuf SW, Daraban N, Abbasi N, Lei X, Durand JB, Daher IN. Treatment and outcomes of acute coronary syndrome in the cancer population. Clin Cardiol. 2012;35(7):443–50.

Therapy

- **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

Yusuf SW, Iliescu C, Bathina JD, Daher IN, Durand JB. Antiplatelet therapy and percutaneous coronary intervention in patients with acute coronary syndrome and thrombocytopenia. Tex Heart Inst J. 2010;37(3):336–

SW, Warneke CL, Botz G, Lakkis N, Hirch-Ginsburg C, et al. Impact of aspirin therapy in cancer patients with thrombocytopenia and acute coronary syndromes. Cancer. 2007;109(3):621–7

Duration of DAPT

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

Lagerqvist B, James SK, Stenestrand U, Lindback J, Nilsson T, Wallentin L, et al. Long-termoutcomes with drug-eluting stents versus bare-metal stents in Sweden. N Engl J Med. 2007;356(10):1009–19.

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

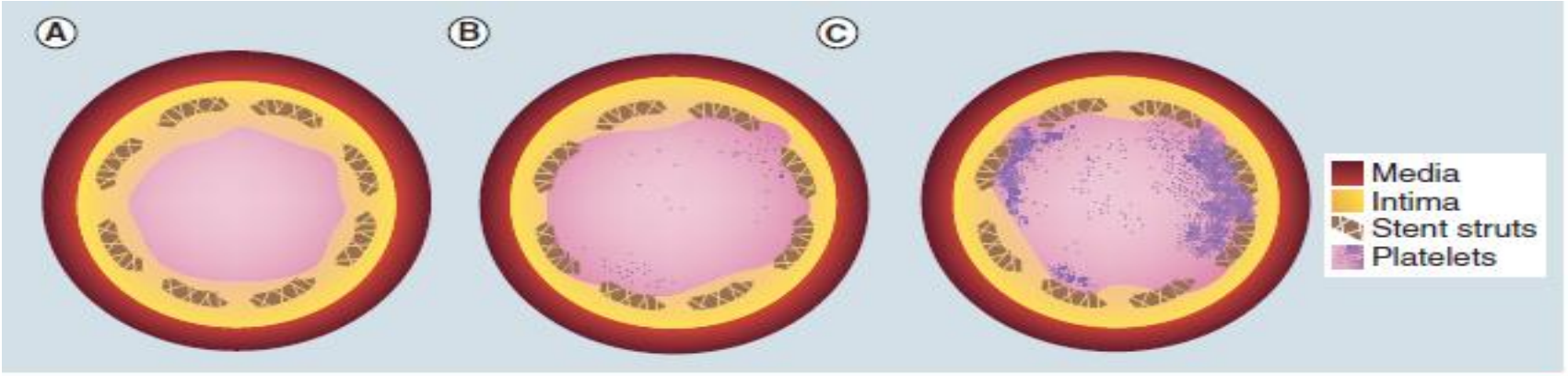
La scelta andrebbe presa collegialmente in base alle caratteristiche del singolo paziente

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.



Management of ischemic coronary disease in patients receiving chemotherapy: an uncharted clinical challenge Bibhu D Mohanty et al Future Cardiology 2017

The need for revascularization must be carefully assessed

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

Ischemic Heart Disease: Special Considerations in Cardio-Oncology Dana Elena Giza, MD et al Curr Treat Options Cardio Med (2017)

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

J Clin Oncol. 2001 Mar 1;19(5):1519-38. **Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology.** Schiffer CA, Anderson KC Bennett CL Bernstein S, Elting LS, Goldsmith M Goldstein M, Hume H, McCullough JJ, McIntyre RE, Powell BL, Rainey JM, Rowley SD Rebulla P, Troner MB, Wagnon AH; American Society of Clinical Oncology.

Vascular access

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