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Review Article

CARDIO-ONCOLOGY: A New Specialty, Subspecialty, or "Invention" of Doctors?

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Introduction

Cardio-oncology is a medical subspecialty that combines the knowledge and expertise of cardiology and oncology. It is not an invention of cardiologists, but a response to the need for comprehensive care for patients undergoing cancer treatment and presenting with cardiovascular complications.

Development

Cardio-oncology deals with the prevention, diagnosis, treatment, and monitoring of cardiovascular complications that may arise during cancer treatment. These complications can include drug-induced cardiotoxicity, damage to the vascular system, coronary heart disease, heart failure, arrhythmias, and other related conditions.

Cardio-oncologists work closely with oncologists and other specialists to provide comprehensive care for patients. This involves assessing cardiovascular risk before initiating cancer treatment, closely monitoring cardiovascular health during treatment, taking preventive measures to reduce cardiotoxicity, and providing appropriate treatment and management of cardiovascular complications that may arise.

Cardio-oncology is also engaged in the research and development of strategies to minimize cardiotoxicity and improve cardiovascular outcomes in cancer patients.

Fields of action

The cardio-oncologist intervenes in various oncological medical situations, mainly related to the detection, prevention and management of cardiovascular complications that may arise during cancer treatment. Some of the situations in which the cardio-oncologist should act include:

1. Pre-treatment evaluation: Before starting cancer treatment, the cardio-oncologist evaluates the patient's cardiovascular risk. This involves reviewing medical history, performing heart function tests, and evaluating cardiovascular risk factors. This assessment helps identify patients who might be at higher risk of developing cardiovascular complications during treatment.

2. Prevention of cardiotoxicity: Many drugs used in cancer treatment, such as anthracyclines and tyrosine kinase inhibitors, can cause cardiotoxicity. The cardio-oncologist works with the oncologist to establish strategies to prevent and reduce the risk of heart damage. This may include adjustments to medication doses, the use of heart-protective medications, and regular monitoring of heart function during treatment.

3. Management of cardiovascular complications: If the patient develops cardiovascular complications during treatment, such as heart failure, arrhythmias, or coronary heart disease, the cardio-oncologist is responsible for the diagnosis and management of these conditions. This may involve the use of cardiovascular medications, changes in cancer treatment, and coordination with other specialists, such as interventional cardiologists or cardiovascular surgeons.

4. Long-term follow-up: After cancer treatment ends, the cardio-oncologist performs long-term follow-up to assess heart function and detect any signs of cardiovascular deterioration. This is especially important in patients who received cardiotoxic treatments or those with previous cardiovascular risk factors.

In summary, the cardio-oncologist is involved in the pre-treatment evaluation, prevention of cardiotoxicity, management of cardiovascular complications during treatment, and long-term follow-up of cancer patients. Their primary goal is to ensure patients' cardiovascular health during and after cancer treatment, working closely with the oncologist and other specialists to provide comprehensive, personalized care.

Toxicity from new drugs

One of the most recent challenges is cardiotoxicity induced by immune checkpoint inhibitors (ICIs), a class of drugs used in cancer immunotherapy.

How do Immune checkpoint inhibitors (ICIs) impact the heart?

1. Immune checkpoint inhibitors (ICIs) targeting PD-1 and CTLA-4 are an innovative therapy to effectively treat several types of cancers such as melanoma, non-small cell lung cancer, head and neck squamous cell carcinoma, colorectal cancer, and urothelial carcinoma.
2. However, myocarditis that occurs in cancer patients treated with ICI is rare but fatal, with a reported mortality rate of 40%.
3. Histologically, infiltrating cells in ICI-associated myocarditis are composed of T cells and macrophages, showing the predominance of CD8+ T cells over CD4+ T cells. Since PD-1 and CTLA-4 are primarily expressed in T cells, the researchers speculated that T cells play a crucial role in the development of ICI-associated myocarditis.

4. Cardiac myosin is a cardiac antigen recognized by autoantibodies in patients with myocarditis and dilated cardiomyopathy. Cardiac myosin peptides have the ability to stimulate T cells isolated from myocarditis patients.
5. It is necessary that both the oncologist and the cardiologist have a high suspicion of this ICI-related cardiac toxicity.

ICI-induced cardiotoxicity is rare, but it can be fatal if not properly diagnosed and treated. These drugs, which work by stimulating the immune system to attack cancer cells, can also affect heart cells and cause inflammation and heart damage. This can manifest as heart failure, arrhythmias, or even acute cardiovascular events, such as a myocardial infarction.
Given the importance of early identification and treatment of this complication, special surveillance of patients receiving ICI has become a common challenge for both patients and physicians. Cardio Oncology physicians are trained to recognize the early signs and symptoms of cardiotoxicity, perform specific diagnostic tests, and determine the best treatment approach.

Treatment of ICI-induced cardiotoxicity may include a variety of approaches, such as temporary or permanent discontinuation of the drug, use of specific cardiovascular therapies, and collaboration with other specialists, such as cardiologists or oncologists.
In summary, ICI-induced cardiotoxicity is a rare but potentially serious complication in patients receiving cancer immunotherapy. Cardio Oncology has become a necessary specialty to address this challenge, providing specialized surveillance and quality management to ensure the safety and efficacy of cancer treatments in relation to the cardiovascular health of patients.

A bit of history

About 50 years ago, the cardiotoxicity associated with anthracyclines, a class of drugs used in chemotherapy to treat various types of cancer, began to be recognized. These drugs, such as doxorubicin, are very effective in treating cancer, but their use may be limited by the risk of heart damage.
Over the years, significant advances have been made in the understanding and management of cardiotoxicity induced by anthracyclines and other cardiotoxic drugs. Cardiotoxicity has been shown to depend on a variety of factors, including the cumulative dose of the drug, the age of the patient, the presence of prior cardiovascular risk factors, and the presence of other concomitant diseases.

Prevention and therapeutic strategies

To minimize the risk of cardiotoxicity, prevention and management strategies have been developed. Some of these strategies include regular monitoring of heart function during treatment, use of cardioprotective drugs such as iron chelators, and modification of doses or choice of other medications in patients at higher risk.

In addition, different therapeutic approaches have been investigated to treat cardiotoxicity once it has developed. These approaches may include the use of heart-protective medications, such as angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), and in some cases, even the consideration of heart transplantation.

Overall, over the past 50 years, there has been an increase in awareness and knowledge about cardiotoxicity induced by different drugs used in the treatment of cancer. This has led to a better understanding of toxicity mechanisms, as well as the implementation of more effective prevention and management strategies. Although cardiotoxicity remains a challenge, advances in this field have allowed for better patient management, minimizing adverse effects on the heart, and improving cancer treatment outcomes.

Other Cardiotoxic Drugs

In addition to anthracyclines, other drugs used in chemotherapy and targeted therapy have also been identified that can have adverse effects on the heart. Examples include tyrosine kinase inhibitors, such as trastuzumab and sunitinib, and BCR-ABL fusion protein inhibitors, such as imatinib.

Research continues in this field to identify biomarkers that can predict individual susceptibility to cardiotoxicity and enable early intervention. New pharmacological and non-pharmacological strategies to prevent and treat cardiotoxicity are also being explored, including gene therapies and the use of cardiac stem cells.

Over the past 50 years, there has been significant progress in the recognition, prevention, and management of cardiotoxicity induced by different drugs used in cancer treatment. Although it remains a challenge, advances in this field have allowed for better patient care, minimizing adverse effects on the heart and improving cancer treatment outcomes.

Predisposing and aggravating factors for cardiotoxicity

The presence of pre-existing heart disease and radiation therapy to the mediastinum area may increase the risk of cardiotoxicity in patients treated with cardiotoxic medications, such as anthracyclines.

In patients who have a history of myocardial infarction, heart failure, arrhythmias, high blood pressure, or other heart disease, the heart may have a reduced ability to tolerate the additional stress induced by cardiotoxic medications. This can result in an increased risk of heart damage and development of heart dysfunction.
Radiation therapy to the mediastinal area, which includes the heart and nearby blood vessels, may also increase the risk of cardiotoxicity. Radiation can cause direct damage to heart cells, leading to inflammation, fibrosis, and heart dysfunction.
In these patients, it is especially important to perform a thorough evaluation before initiating treatment with cardiotoxic medications. This may include heart function tests, such as echocardiograms or stress tests, to assess the heart's ability to withstand the additional stress. In addition, regular monitoring during treatment is essential to detect any early signs of cardiotoxicity and to take appropriate preventive or therapeutic measures.
In some cases, it may be necessary to adjust medication doses or consider less cardiotoxic alternatives in patients at higher risk. Heart-protective medications, such as angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), may also be used to reduce the risk of cardiotoxicity.

In summary, the presence of pre-existing heart disease and radiation therapy to the mediastinum area may aggravate cardiotoxicity in patients treated with cardiotoxic drugs. Thorough evaluation and regular monitoring of these patients is critical to detect and treat cardiotoxicity early.
Anthracycline-induced heart failure can be difficult to treat, as it can be refractory to the classic treatments used for non-anthracycline-related heart failure. However, there are specific strategies that can help manage this condition.

First, optimization of standard treatments for heart failure, such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), beta-blockers, and diuretics, can be considered. These medicines can help improve heart function and relieve symptoms.
In addition, specific medications can be used to protect the heart from the toxic effects of anthracyclines, such as iron chelators (dexrazoxane) and antioxidants (e.g., vitamin E). These medications can help prevent or reduce the cardiotoxicity of anthracyclines.
In more severe cases, advanced supportive therapy, such as ventricular assist devices or even heart transplantation, may be considered, depending on the severity of the heart failure and response to treatment.

Myocardial Biopsy Value

As for myocardial biopsy, it is mainly used in cases of suspected myocarditis or infiltrative heart disease in cancer patients. Myocardial biopsy can provide important diagnostic information about the cause of heart failure and guide treatment. However, it is an invasive technique and is reserved for selected cases where a specific heart disease is suspected that requires an accurate diagnosis for proper management.

In terms of prognosis and therapeutics, myocardial biopsy can help identify the presence of active myocarditis, inflammation, fibrosis, or other specific alterations that may have prognostic implications and guide treatment. The prognosis and therapeutic value of myocardial biopsy depend on the specific findings found in the cardiac tissue. If a treatable cause of heart failure is identified, such as active myocarditis or infiltrative disease, treatment targeting that specific cause may improve a patient's prognosis.

For example, if active myocarditis is found, treatment with anti-inflammatory or immunosuppressive medications may be started to control inflammation and improve heart function. In cases of infiltrative diseases, such as cardiac amyloidosis, early diagnosis through myocardial biopsy may allow the initiation of targeted therapies, such as amyloid protein reduction therapy, which can slow the progression of the disease and improve prognosis.

However, it is important to note that myocardial biopsy is an invasive technique and carries potential risks, such as bleeding, infection, or damage to the heart. Therefore, the decision to perform a myocardial biopsy should be based on a careful assessment of the potential risks and benefits, as well as guidance from a multidisciplinary team of physicians specializing in cardio-oncology and heart disease.

Usefulness of biomarkers as prognosis and monitoring of heart disease.

There are several biomarkers that are used to predict and monitor heart function during cancer drug treatment. Some of the most common biomarkers include:

1. Troponin: Troponin is a cardiac biomarker that rises in the presence of heart damage. Measuring troponin in the blood can help detect oncology drug-induced heart injury and assess the severity of the damage.

2. B-type natriuretic peptide (BNP): BNP is a hormone released by the heart in response to stress or volume overload. BNP levels may increase in the presence of heart failure. Measuring BNP in blood can help assess heart function and detect early signs of heart deterioration.

3. Left Ventricular Ejection Fraction (LVEF): LVEF is a parameter that evaluates the heart's pumping function. Echocardiography is an imaging technique used to measure LVEF and evaluate possible changes in cardiac function during cancer treatment.

4. Myocardial Strain: Myocardial strain is a measure of heart muscle deformation and can be a sensitive indicator of early cardiac dysfunction. It can be evaluated by echocardiography or cardiac MRI.

These biomarkers are used to monitor heart function before, during, and after cancer drug treatment. They allow early detection of potential cardiotoxic effects and can guide decision-making regarding changes in treatment or the addition of cardioprotective therapies. Importantly, the use of biomarkers should be complemented with clinical evaluations and imaging tests for a global assessment of cardiac function.

Present, future and conclusions

The present of cardio-oncology is characterized by a growing recognition of the importance of cardiovascular health in the management of cancer. Increasingly, cardiac assessment and follow-up are being integrated into cancer treatment protocols to prevent and treat cardiovascular complications. In addition, more effective and targeted cardiotoxicity prevention and management strategies are being developed.

As for the future of cardio-oncology, significant advances are expected. More accurate biomarkers and imaging tests are being investigated to detect early cardiotoxicity and allow for more timely treatment. In addition, more targeted and personalized therapies are being developed to reduce the cardiovascular side effects of cancer treatments.

As for artificial intelligence (AI), it can play an important role in cardio-oncology. AI can help analyze large amounts of clinical and genetic data to identify patterns and risk factors for cardiotoxicity in cancer patients. It can also help predict individual response to treatment and allow for more personalized care. In addition, AI can help doctors make more informed clinical decisions and provide patients with accurate and understandable information about their cardiovascular health.

The present and future of cardio-oncology are focused on a more comprehensive evaluation and management of the cardiovascular health of cancer patients. AI has the potential to play an important role in this field,

helping to improve the early detection, prevention, and treatment of heart disorders related to cancer treatment. In the future, it is expected that there will be significant advances in the field of oncology drug-induced cardiotoxicity. Research is underway to identify new, more sensitive and specific biomarkers that can more accurately predict and monitor cardiac function during cancer treatment.

In addition, more effective prevention and treatment strategies are being developed to reduce cardiotoxicity. This includes the use of cardioprotective therapies, such as antioxidant agents or medications that protect the heart muscle from the toxic effects of cancer drugs.

In conclusion, oncology drug-induced cardiotoxicity is a major clinical problem that can limit the efficacy of cancer treatment and affect patients' quality of life. Myocardial biopsy can play a crucial role in the diagnosis and management of cardiotoxicity by providing information about the underlying cause and guiding specific therapy.

However, the decision to perform a myocardial biopsy should be carefully considered, taking into account the potential risks and benefits, and should be guided by a multidisciplinary team of physicians specializing in cardio-oncology and heart disease.
Ultimately, it is critical that clinicians and researchers work together to improve understanding of cardiotoxicity and develop more effective strategies to prevent, detect, and treat it, with the goal of optimizing clinical outcomes and improving quality of life for cancer patients.

References

1.Cardinale D, Colombo A, Lamantia G, et al. Anthracycline-induced cardiomyopathy: clinical relevance and response to pharmacologic therapy. J Am Coll Cardiol. 2010; 55(3):213-220. doi: 10.1016/j.jacc.2009.03.095

2.Zamorano JL, Lancellotti P, Rodriguez Muñoz D, et al. 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). Eur Heart J. 2016; 37(36):2768-2801. doi:10.1093/eurheartj/ehw211

3.Armenian SH, Lacchetti C, Barac A, et al. Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol. 2017; 35(8):893-911. doi:10.1200/JCO.2016.70.5400

4.Wei S, Liu L, Zhang J, et al. Cardiotoxicity associated with tyrosine kinase inhibitor sunitinib. Lancet. 2011; 378(9805):2011-2012. doi:10.1016/S0140-6736(11)61605-6

5.Plana JC, Galderisi M, Barac A, et al. Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2014; 15(10):1063-1093. doi:10.1093/ehjci/jeu192

6.Sawaya H, Sebag IA, Plana JC, et al. Assessment of echocardiography and biomarkers for the extended prediction of cardiotoxicity in patients treated with anthracyclines, taxanes, and trastuzumab. Cardiovasc Imaging. 2012; 5(5):596-603. doi:10.1161/CIRCIMAGING.112.973321

7.Cardinale D, Sandri MT, Martinoni A, et al. Left ventricular dysfunction predicted by early troponin I release after high-dose chemotherapy. J Am Coll Cardiol. 2000; 36(2):517-522. doi:10.1016/s0735-1097(00)00725-8

8.Ewer MS, Vooletich MT, Durand JB, et al. Reversibility of trastuzumab-related cardiotoxicity: new insights based on clinical course and response to medical treatment. J Clin Oncol. 2005; 23(31):7820-7826. doi:10.1200/JCO.2005.01.8135

9.Yeh ET, Bickford CL. Cardiovascular complications of cancer therapy: incidence, pathogenesis, diagnosis, and management. J Am Coll Cardiol. 2009; 53(24):2231-2247. doi: 10.1016/j.jacc.2009.02.050

10. Won, T., Kalinoski, H. M., Wood, M. K., Hughes, D. M., Jaime, C. M., Delgado, P., Talor, M. V., Lasrado, N., Reddy, J., & Čiháková, D. (2022). Cardiac myosin-specific autoimmune T cells contribute to immune-checkpoint-inhibitor-associated myocarditis. Cell Reports, 41.