**The EACVI survey on cardiac imaging in cardio-oncology**

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**ABSTRACT**

Early and late cardiovascular (CV) toxicities related to many cancer treatments may complicate the patient’s clinical course, offsetting therapeutic benefits and altering prognosis. The early detection, monitoring and treatment of cardio-toxicity have therefore become essential parts of cancer patient care. CV imaging is a cornerstone of every cardio-oncology unit but its use may vary across Europe because of non-uniform availability of advanced imaging techniques and different organisation and logistics of cardio-oncology services.

The purpose of the EACVI survey on cardiac imaging in cardio-oncology is to obtain real world data on the current usage of cardiac imaging in cancer patients. Data from 104 centres and 35 different countries confirmed that cardiac imaging plays a pivotal role in the detection and monitoring of cardiac toxicity in oncology patients in Europe and beyond. However, it also revealed gaps between guidelines recommendations and everyday clinical practice, highlighting some of the challenges that need to be overcome in this rapidly advancing field.

**Keywords**: cardiac imaging, cardio-oncology, cardiotoxicity

**INTRODUCTION**

In developed countries, cardiovascular (CV) disease and cancer are the leading causes of morbidity and mortality (1). The prognosis of patients suffering from several common cancers is improving due to earlier detection and advances in therapy. However, both early and late CV toxicities of many powerful cancer treatments may complicate the patient’s clinical course, offsetting therapeutic benefits and altering prognosis (2). Consequently, early detection, monitoring and treatment of cardiotoxicity have become essential parts of cancer patient care.

In order to address these new challenges, multidisciplinary cardio-oncology programs are being developed to improve the management and outcome of cardiovascular complications in cancer patients. Expectedly, CV imaging is a cornerstone of every cardio-oncology unit and the standardized use of echocardiography and other imaging modalities in cancer patients has been proposed by the ESC and EACVI (3,4,5,6).

On the other hand, the use of imaging in cardio-oncology may vary across Europe because of unequal availability of advanced imaging techniques and different setups of cardio-oncology services.

The purpose of the EACVI survey on cardiac imaging in cardio-oncology is to obtain real world data on the current usage of cardiac imaging in cancer patients. In particular we seek to identify areas of potential discrepancy between the recommendations and everyday clinical practice that might allow us to better understand and address the challenges in this rapidly evolving field.

**METHODS**

The survey was designed by the EACVI Scientific Initiatives Committee according to the previously published criteria (7). Between February 6th and March 6th 2020, the survey consisting of 18 questions was sent to the EACVI survey network ([www.escardio.org/eacvi/surveys](http://www.escardio.org/eacvi/surveys)) as an online questionnaire. The questions were based on previously published ESC and EACVI documents and were related to the definition of cardiotoxicity and to the use of cardiac imaging before, during and after cancer treatment (3,4,5,6). The respondents described the views and current cardiac imaging protocols of their institutions by choosing one or more answers to each survey question.

**RESULTS**

**Responding centres**

In total, 104 centres from 35 different countries responded to the survey: Serbia (17), United Kingdom (16), Spain (8), Norway (7), Germany (7), United States of America (6), Slovenia (5), Italy (3), The Netherlands (3), Bosnia and Herzegovina (3), Poland (3), Japan (2), Mexico (2), France (1), Denmark (1), Portugal (1), Chile (1), Colombia (1), Croatia (1), India (1), Ireland (1), Finland (1), Kosovo (1), Egypt (1), Lebanon (1), North Macedonia (1), Moldova (1), Belgium (1), Georgia (1), Malta (1), Myanmar (1), Greece (1), Brazil (1), Panama (1), and New Zeeland (1).

Most centres were tertiary care/University hospitals (67%), followed by secondary care/district hospitals (19%), private hospitals (10%) and primary care centres (4%). The vast majority of respondents were cardiologists (81%), followed by internal medicine specialists (15%), residents (14%), heads of departments or cardiac imaging labs (20%), while only 2% of respondents were oncologists or haematologists. The care of patients with adverse CV effects of cancer therapies is provided by both cardiologists and oncologists in 56% of responding centers – within a dedicated cardio-oncology unit in 13% of centers, while in 42% of centers both cardiologists and oncologists are involved, but there is no formal cardio-oncology team. CV adverse effects are managed only by cardiologists or oncologists in 41% and 3% of responding centers, respectively.

It was possible to choose more than one answer describing the center’s opinion regarding the definition of cardiotoxicity (Figure 1). Of interest, the definition based on global longitudinal strain (GLS, “A relative percentage reduction in GLS>15%”) is used by 31% of responding centers. In approximately half of the responding centers, the standard method for the detection and monitoring of cardiotoxicity is echocardiography, with other imaging modalities and biomarkers used as necessary for selected cases (Figure 2). Seventeen percent of centres reported that echocardiography was the only method used for assessing cardiotoxicity, whilst the routine use of a multimodality cardiac imaging and biomarker strategy alongside echocardiography was reported in 19% of centers.

A baseline echocardiographic examination is performed prior to cancer treatment in patients undergoing chemotherapy with known cardiotoxic potential (74% of the responding centers), patients with existing CV disease or CV risk factors (36%), in all patients, regardless of the type of treatment and CV risk factors (24%) and in patients undergoing radiotherapy in the chest region (20%). In 8% of centers, routine baseline echocardiography prior to cancer treatment is not performed in any group. For monitoring cardiotoxicity, left ventricular ejection fraction (LVEF) is more frequently assessed using two- rather than three-dimensional echocardiography (89 vs. 28%, respectively), while GLS is routinely assessed in 53% of responding centers. Echocardiographic evaluation of a patient undergoing cardiotoxic cancer treatment typically includes the assessment of LV systolic function (98%), LV diastolic function (82%), RV function (79%), valvular function (82%), pulmonary pressures (74%) and the pericardium (85%). Of note, if the quality of the echocardiogram is sub-optimal, the LVEF is visually assessed in 45% of centers, while the remaining 55% of centers in that circumstance would use cardiac magnetic resonance (CMR, 21%), echocardiographic contrast agent (19%), multi-gated blood pool nuclear imaging (8%) and mitral annular plane systolic excursion (MAPSE) or peak systolic velocity of the mitral annulus (6%).

Routine echocardiographic follow up varies according to the type of treatment in 42% of centres. In the remaining centres, echocardiographic follow-up in patients receiving cardiotoxic cancer treatment is performed routinely before each cycle of therapy (20%), every 3-6 months (23%) or only when cardiac symptoms occur or when indicated by the care team (13%). Follow-up examinations are performed using the same imaging techniques (2D echo, 3D echo or strain) in 84% of centres, by the same echocardiography scanner (the same vendor) in 37% of centres and by the same investigator (physician or sonographer) in 17% of centres.

If a significant decrease in the LVEF (to the value <53%) is observed by echocardiography during the cancer treatment, the patient will be diagnosed with cardiotoxicity in approximately half of centres, although different actions may also be taken, including confirmation by another echocardiographic study or CMR (Figure 3). Furthermore, for a patient with subclinical cardiotoxicity (i.e. asymptomatic GLS reduction of >15% from baseline without a significant LVEF decrease or LVEF decrease but above critical values), more frequent cardiac function monitoring is scheduled in the majority of centres (74%), with 68% introducing of cardioprotective agents (e.g. angiotensin-converting enzyme inhibitors, beta-blockers), and 46% biomarker testing. In this clinical scenario, cancer treatment is temporarily withheld and/or the treatment protocol changed in one third of centres (Figure 4).

Only 4% of centres would not perform any further work up in a patient with clinical suspicion of cancer therapy-induced coronary vasospasm

(e.g. chest pain and ST-segment elevation during the treatment with

taxanes or fluoropyrimidines). In the remaining centres, work-up either depends on the probability of obstructive coronary artery disease (54%) or the patient undergoes computed tomography coronary angiography (34%), invasive coronary angiography (33%) or stress echocardiography (18%).

Cancer survivors are not routinely monitored after treatment in the majority of responding centers (63%); echocardiography is performed every 5 years in 19% of centers, a periodic non-invasive stress testing, even in asymptomatic patients in being performed in 4% of patients, while 14% of centers have an assessment protocol that was not covered by the options in the survey. In particular, the diagnostic algorithm to identify coronary artery

disease in long-term cancer survivors is the same as in patients without a history of cancer in 60% of centers, while a lower threshold for non-invasive tests is generally applied in 31% of centers. In one center, routine stress tests are performed every 5 years following mediastinal irradiation.

In total, approximately 40% of respondents are satisfied with their knowledge and practice in this field, either at the individual (“I have the sufficient knowledge”, 21%) or institutional levels (“The management of cardio-oncology patients in our institution is up to date and sufficient”, 20%). A half of respondents (52%) believes the management of cardio-oncology patients in their institution could be improved, while 34% identified as requiring more education and experience in the management of cardio-oncology patients.

**DISCUSSION**

The most salient finding of this EACVI survey is the heterogeneity in practice observed across almost all aspects of cardiac imaging in cardio-onocology. Such variations could be expected given the fact that cardio-oncology is a relatively new field that brings together experts from different backgrounds and areas of expertise. Notwithstanding the lack of universally accepted definitions and protocols, the results of our survey indicate that cardiac imaging plays an important role in the management of oncology patients in Europe and beyond.

**Organisation and logistics of cardio-oncology services**

The majority of respondents were cardiologists from tertiary care centres. However, in less than 15% of responding centres, there was a dedicated cardio-oncology unit. Therefore in the vast majority of centres the care of patients with adverse CV effects of cancer therapies is being provided without a formal specialist team or unit. According to the recent report from the ESC Cardio-Oncology council, specialized CV evaluation and care in all stages of the cancer process should be performed by a multidisciplinary team organized as cardio-oncology team, clinic or unit (6). Cardiac imaging specialists are indispensable team members within cardio-oncology services and availability of all imaging modalities (standard and advanced echocardiography, CMR, cardiac CT and positron emission tomography -CT) is a prerequisite for cardio-oncology services in tertiary hospitals (6). The results of our survey therefore reveal a major gap between current clinical practice and proposed standards in terms of organisation and logistics, and underline the need for more formal and stronger partnerships between practising cardiologists and oncologists.

**Definition, detection and monitoring of cardio-toxicity**

Cardiac damage related to cancer therapeutics may present with a wide spectrum of manifestations. It is therefore not surprising that there is no universal definition of cardiotoxicity, and a wide array of answers were provided by this survey. It is interesting that a comprehensive, but lenient definition of cardio-toxicity (“Any functional or structural heart injury related to cancer treatment”) was almost equally popular among the responding centres as the more specific definition based on LVEF decrement (“A decrease in the LVEF of > 10% points to a value <53%”). Although both definitions are valid, the latter has important practical implications (interruption of cancer treatment, introduction of cardioprotective therapies, etc.) and should be universally applied, as proposed by the EACVI/ASE expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy (5).

Expectedly, echocardiography was the only method that was invariably available and used across each of responding centres, while cardiac biomarkers and other imaging modalities were used to a considerably lesser extent. In principle, the EACVI/ASE-recommended cardio-oncology echocardiogram protocol seems to be followed as the majority of centres reported to perform a comprehensive echocardiographic examinations. However, there are a few exceptions to this. The EACVI/ASE protocol mandates 2D strain and 3D imaging acquisition and reporting of 3D/2D LVEF and GLS. In the current survey, LV systolic function was assessed as 2D LVEF in the vast majority of centres, while 3D LVEF and GLS were routinely assessed by 29 and 53% of centres, respectively. The use of advanced echocardiography was lower than expected, especially if the results of the EACVI survey on standardization of cardiac chambers quantification are put into perspective. It that survey, more than 90% of centres had access to 3D and speckle tracking echocardiography, suggesting the wide availability of these modalities. More frequent use of advanced echocardiography in oncology patients should be further encouraged as 3D LVEF and GLS show a higher accuracy and sensitivity and a lower inter- and intra-observer variability than 2D LVEF (5). It is particularly challenging to detect and monitor cardio-toxicity in cases where echocardiographic image quality is sub-optimal. In approximately half of responding centres, LVEF is visually estimated in this situation, while CMR or contrast echocardiography is performed in approximately 40% of centres. Even though MAPSE or peak systolic velocity of the mitral annulus can be used to assess longitudinal function of the LV instead of GLS (5), these parameters were rarely used in the responding centres (6%).

Most centres perform baseline echocardiography in patients undergoing chemotherapy with known cardiotoxic potential, but also in patients with established CV disease or risk factors or in those undergoing radiotherapy to the chest region. These indications are consistent with existing recommendations (4,5). Given the relative unpredictability of cardio-toxicity it could be argued that the ideal is to perform baseline echocardiography in all patients undergoing cancer therapy, and indeed this is routine practice in 24% of responding centres. During cancer treatment, echocardiographic follow-up protocols varied greatly between centres – from routine exams before each cycle of therapy in some to cardiac symptoms-driven exams in others. Follow-up exams are performed using the same imaging techniques in more than 80% of centres, while the other sources of LVEF or GLS variability (different scanners, software and echocardiographers at follow-up exams) are frequently present.

Once the LVEF decreases more than 10% to a value below 53%, this decrease should be confirmed by repeated cardiac imaging, 2 to 3 weeks following the baseline study (4), which is the practice reported by approximately half of centres. On the other hand, in the presence of subclinical cardiotoxicity (i.e. asymptomatic GLS reduction of >15% from baseline without a significant LVEF decrease or LVEF decrease but above critical values), cancer treatment will be temporarily withheld and/or treatment protocol will be changed in one third of centers. This practice is not in line with the ESC position paper which recommends that cancer treatment should not be stopped, interrupted or reduced in dose based on a new GLS reduction alone (4). However, it is reassuring that the majority of centres would schedule more frequent cardiac function monitoring and would also opt for an integrated approach with cardiac bio-markers in this scenario.

In the acute setting (e.g. chest pain and ST-segment elevation during treatment with taxanes or fluoropyrimidines), further work-up depends on the probability of obstructive coronary artery disease in half of responding centres; in the remaining half, the patient would undergo invasive or CT coronary angiography or stress echocardiography.

**Imaging-based surveillance of long-term survivors**

According to the ESC position paper, evaluation for coronary artery disease, ischaemia and vascular disease is recommended even in asymptomatic patients with a history of mediastinal radiation, starting 5 years post-treatment and then at least every 5 years thereafter (4).

Of note, in more than 60% of centres, no routine monitoring of long-term cancer survivors is available and assessments are driven by symptoms. Furthermore in 60% of centers, the diagnostic algorithms to identify coronary artery disease in long-term cancer survivors are the same as in patients without a history of cancer, while one third of centers apply a lower threshold for non-invasive tests. Therefore, the results of the current survey indicate the need for a more structured imaging-based surveillance of long-term survivors, especially in patients with previous mediastinal radiation.

**CONCLUSIONS**

Cardiac imaging plays a pivotal role in the detection and monitoring of cardiac toxicity in oncology patients in Europe and beyond. Standard echocardiography is the most often used method for this purpose, while advanced echocardiography and other imaging modalities should be used more frequently. Significant variability in the follow-up of long-term cancer survivors among the centres suggests that history of cancer has not yet been clearly perceived as a risk factor for CV disease and warrants further joint actions of cardiologists and oncologists.

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Research Network can be found on the EACVI website. To join the network, please sign in escardio.org/eacvi/surveys.

**CONFLICT OF INTEREST**

None declared.

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**FIGURE LEGENDS**

**Figure 1**. Definitions of cardio-toxicity. LVEF – left ventricular ejection fraction; GLS – global longitudinal strain.

**Figure 2**. Methods for the detection and monitoring of cardiotoxicity.

**Figure 3**. Preferred action in cases of a significant decrease in the left ventricular ejection fraction (LVEF). CMR – cardiac magnetic resonance.

**Figure 4**. Preferred actions in cases of subclinical cardiotoxicity. BNP – brain natriuretic peptide; ACE – angiotensin converting enzyme.