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EACVI DOCUMENT

The EACVI survey on cardiac imaging in cardio-oncology

Ivan Stankovic[1]*, Marc R. Dweck[2], Nina Ajmone Marsan[3], Jutta Bergler-Klein[4], Espen Holte[5,6], Robert Manka[7], Jeanette Schulz-Menger[8,9,10], Marta Sitges[11,12,13], and Kristina H. Haugaa[14,15]

[1]Faculty of Medicine, Department of Cardiology, Clinical Hospital Centre Zemun, University of Belgrade, Vukova 9, 11080 Belgrade, Serbia; [2]BHF Centre for Cardiovascular Science, University of Edinburgh, Chancellors Building, Little France Crescent, Edinburgh, EH16 4SB, UK; [3]Department of Cardiology, Leiden University Medical Center, Albinusdreef 2, 2300 RC, Leiden, The Netherlands; [4]Department of Cardiology, University Clinic of Internal Medicine II, Medical University of Vienna, AKH General Hospital Vienna, Waehringer Guertel 18-20, A-1090, Vienna; [5]Clinic of Cardiology, St. Olavs Hospital, Postboks 3250 Torgarden, 7006 Trondheim, Norway; [6]Department of Circulation and Medical Imaging, Norwegian University of Science and Technology NTNU, Trondheim, Postboks 8905, 7491, Trondheim, Norway; [7]Department of Cardiology, University Heart Center, University Hospital Zurich, Rämistrasse 100, 8091, Zurich, Switzerland; [8]Charité Medical Faculty, of the Humboldt University Berlin, ECRC, 13125, Berlin, Germany; [9]DZHK, Partner site, 13125 Berlin, Germany; [10]Helios Clinics Berlin-Buch, Cardiology, 13125, Berlin, Germany; [11]Cardiovascular Institute, Hospital Clínic, Universitat de Barcelona, Villarroel 170, 08036, Barcelona, Spain; [12]Institut d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Villarroel 170, 08036, Barcelona, Spain; [13]CIBERCV, Instituto de Salud Carlos III, Sinesio Delgado, 4, 28029, Madrid, Spain; [14]Department of Cardiology, Oslo University Hospital, Postboks 4950 Nydalen, 0424 Oslo, Norway; and [15]Institute for Clinical Medicine, University of Oslo, Postboks 1171, Blindern, 0318 Oslo, Norway

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Early and late cardiovascular (CV) toxicities related to many cancer treatments may complicate the clinical course of patients, offsetting therapeutic benefits, and altering prognosis. The early detection, monitoring, and treatment of cardiotoxicity 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 the non-uniform availability of advanced imaging techniques and differences in the organization and logistics of cardio-oncology services. The purpose of this EACVI survey 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 the early and late CV toxicities associated with many cancer treatments may complicate a patient's clinical course, offsetting therapeutic benefits, and altering prognosis.[2] Consequently, the 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 CV complications in cancer patients. CV imaging is a cornerstone of every cardio-oncology unit and a standardized approach to the use of echocardiography and other imaging modalities in cancer patients has been proposed by the ESC and EACVI.[3–6] However, the use of imaging in cardio-oncology may vary across Europe because of unequal availability of advanced imaging techniques and differences in the setup of cardio-oncology services.

The purpose of this EACVI survey on 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 then address the current challenges in this rapidly evolving field.

* Corresponding author. Tel: + 38 1113772734; Fax: + 38 1113168878. E-mail: future.ivan@gmail.com

METHODS

The survey was designed by the EACVI Scientific Initiatives Committee according to previously published criteria.[7] Between 6 February and 6 March 2020, the survey consisting of 18 questions was sent to the EACVI survey network (www.escardio.org/eacvi/surveys)[8–11] 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.[3–6] The respondents described the views and current cardiac imaging protocols of their institutions by choosing one or more answers to each survey question. 'None of the above' was also provided as an option to the responders in most questions.

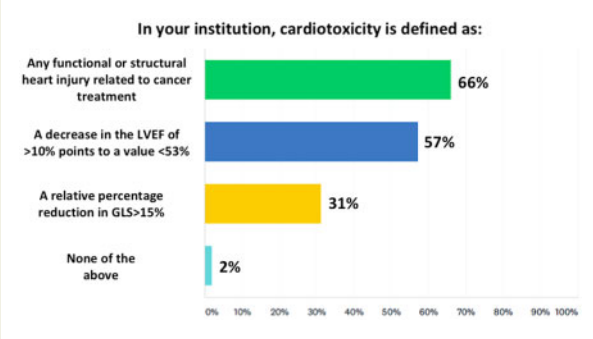

Figure 1 Definitions of cardiotoxicity. GLS, global longitudinal strain; LVEF, left ventricular ejection fraction.

RESULTS

Responding centres

In total, 104 centres from 35 different countries responded to the survey: Serbia (17), UK (16), Spain (8), Norway (7), Germany (7), USA (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.

Personnel in management of cardio-oncology

The care of patients with adverse CV effects from cancer therapy is provided jointly by both cardiologists and oncologists in 56% of responding centres, within a dedicated cardio-oncology unit in 14% of centres, whilst in 42% of centres 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 centres, respectively.

Definition of cardiotoxicity and modalities

It was possible to choose more than one answer describing how different centres prefer to define cardiotoxicity (*Figure 1*). Two-thirds of centres use a broad definition to encompass any structural or functional heart injury related to cancer therapy. Fifty-seven percent use an imaging definition based upon a drop in EF of more than 10% to below 53%. Of interest, the definition based on global longitudinal strain (GLS, 'A relative percentage reduction in GLS > 15%') is used by 31% of responding centres.

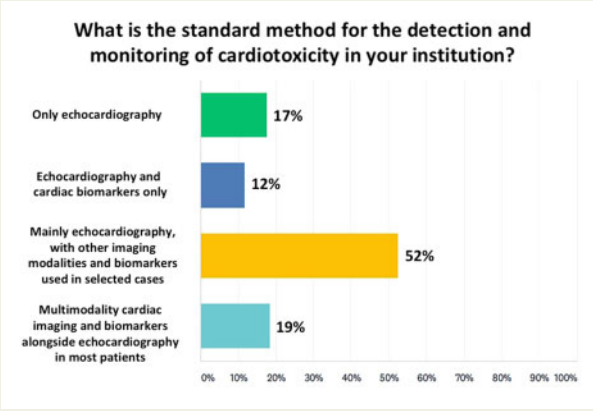

Figure 2 Methods for the detection and monitoring of cardiotoxicity.

In approximately half of the responding centres, the standard method for detecting and monitoring 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 was reported in 19% of centres.

Management of patients undergoing cancer treatment

A baseline echocardiographic examination is performed in all patients prior to commencing chemotherapy regimens with known cardiotoxic potential (74% of the responding centres), in just those 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 centres, routine baseline echocardiography prior to cancer treatment is not performed in any group.

For cardiotoxicity monitoring, left ventricular ejection fraction (LVEF) is more frequently assessed using 2- rather than 3D echocardiography (89% vs. 28%, respectively), while GLS is routinely assessed in 53% of responding centres. 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 centres, while in that circumstance the remaining 55% of centres would use cardiovascular 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, routine echocardiographic follow-up is performed in all patients 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 a value <53%) is observed by echocardiography during cancer treatment, the patient will be diagnosed with cardiotoxicity in approximately half of centres, although confirmation by another echocardiographic study (48% of centres) or CMR (24%) is often performed (*Figure 3*). Furthermore, for a patient with subclinical cardiotoxicity (i.e. asymptomatic GLS reduction of >15% from baseline without a significant LVEF decrease), more frequent cardiac function monitoring is scheduled in the majority of centres (74%), with 68% introducing 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*).

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), only 4% of centres would not perform any further work-up. 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 centres (63%); echocardiography is performed every 5 years in 19% of centres; a periodic non-invasive stress testing, even in asymptomatic patients in being performed in 4% of patients; whilst 14% of centres have an assessment protocol that was not covered by the options in the survey. 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 centres, while a lower threshold for non-invasive tests is generally applied in 31% of centres. In one centre, routine stress tests are performed every 5 years following mediastinal irradiation.

Perception of cardio-oncology practice and management

In total, ~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 level ('the management of cardio-oncology patients in our institution is up to date and sufficient', 20%). Half of respondents (52%) believe 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.

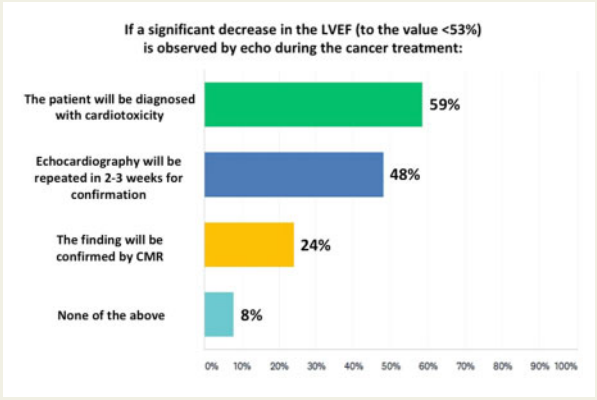

Figure 3 Preferred action in cases of a significant decrease in the left ventricular ejection fraction (LVEF). CMR, cardiac magnetic resonance.

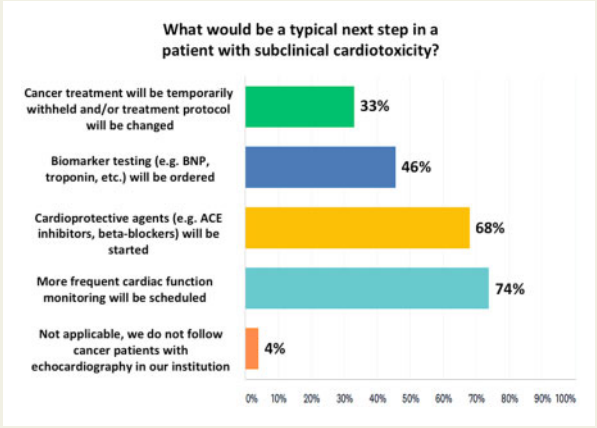

Figure 4 Preferred actions in cases of subclinical cardiotoxicity. ACE, angiotensin-converting enzyme; BNP, brain natriuretic peptide.

DISCUSSION

The most salient finding of this EACVI survey is the heterogeneity in practice observed across almost every aspects of cardiac imaging in cardio-oncology. Such variation is perhaps expected given that cardio-oncology is a relatively new field and one which brings together experts from different backgrounds and areas of expertise. However, 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.

Organization 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 outside of a formal specialist team or unit. According to a 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 within a formal cardio-oncology team, clinic, or unit.[6] Cardiac imaging specialists are indispensable team members within cardio-oncology services and the availability of all imaging modalities (standard and advanced echocardiography, CMR, cardiac CT, and positron emission tomography CT) is considered a pre-requisite 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 organization and logistics, and underline the need for more formal and stronger partnerships between practising cardiologists and oncologists.

Definition, detection and monitoring of cardiotoxicity

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 cardiotoxicity ('any functional or structural heart injury related to cancer treatment') was almost equally popular among the responding centres as the more imaging-focused 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. The EACVI/ASE-recommended protocol for cardio-oncology echocardiography seems to be followed as the majority of centres perform comprehensive echocardiographic examinations in these patients. However, there are a few exceptions to this. The EACVI/ASE protocol mandates 2D strain and 3D imaging acquisition and reporting of both 3D and 2D LVEF and GLS. In the current survey, LV systolic function was assessed using 2D LVEF in the vast majority of centres, while 3D LVEF and GLS were routinely assessed in only 29% and 53% of centres, respectively. The use of advanced echocardiography was therefore lower than expected, and not consistent with the recent results of the EACVI survey on standardization of cardiac chambers quantification. In 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 cardiotoxicity in cases where echocardiographic image quality is suboptimal. In approximately half of responding centres, LVEF is visually estimated in this situation, while CMR or contrast echocardiography is performed in ~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 cardiotoxicity, it could be argued that the ideal would be 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 protocols where echocardiography is only performed in patients with overt cardiac symptoms in others. Follow-up exams are performed using the same imaging techniques in more than 80% of centres; however, other sources of LVEF or GLS variability (different scanners, software, and echocardiographers at follow-up exams) are frequently present and not controlled for.

According to guidelines, once the LVEF decreases more than 10% to a value below 53%, this decrease should be confirmed by repeated cardiac imaging, 2–3 weeks following the baseline study,[4] which is the practice reported by approximately half of centres. However, a third of centres also reported temporarily withholding or changing cancer treatment 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). 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 biomarkers 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 centres, 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 centres apply a lower threshold for non-invasive tests. Therefore, the results of the current survey indicate another discrepancy between clinical practice and guideline recommendation.

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 a history of cancer is not yet clearly perceived as a CV risk factor, warranting further joint action by cardiologists and oncologists.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author and the EACVI.

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