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ORIGINAL INVESTIGATION

Echocardiography WILEY

Focused echocardiography in cardio-oncology

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Abstract

Transthoracic echocardiography (TTE) is the cornerstone of imaging in patients with a malignancy in all stages of their treatment—before, during, and after the completion of it—to identify most of the cardiotoxic complications. However, the restricted time and resources of cardio-oncology services and the high volume of oncological patients and survivors on the other hand limit the access of this population to this modality. Focused Echo in Cardio-Oncology (FECO) in proportion to other focused cardiac protocols is proposed as a valuable tool after the initial standard complete TTE to: (a) identify the potential toxicity expected by the specific cancer therapy applied; (b) assess sequentially the pre-existing abnormality, if any, in relation to therapy; (c) assess the effect of any cardio-protective intervention; (d) identify any cardiac origin of patient complaints during or after therapy; (e) assess cardiac function in asymptomatic patients who develop significant changes in cardiac biomarkers during cancer therapy. Four different protocols of FECO are proposed according to the type of cardiotoxicity anticipated: FECOm (in patients on chemotherapeutics that cause myocardial dysfunction), FECOv (in patients at risk of valvular heart disease), FECOpd (in patients at risk of pericardial disease), and FECOph (in patients at risk of pulmonary hypertension). The application of FECO protocols is aimed to ensure accuracy, reliability, and effectiveness in the early identification of cardiovascular complications, improving quality of life, and being at the same time cost-effective.

KEYWORDS

cancer, cardio-oncology, cardiotoxicity focused echo, echocardiography

1 | INTRODUCTION

Echocardiography and more specifically transthoracic echocardiography (TTE) are the backbone of cardiac imaging in patients diagnosed with cancer.[1,2] A complete baseline echocardiographic study adds important information to the clinical assessment of patients, improving risk stratification before treatment, defining the appropriate surveillance intervals according to the initial cardiotoxicity risk and dictating the necessity for initiating protective medications. During cancer therapy, TTE can identify potential cardiotoxic effects of the regime, allowing for treatment modifications. TTE can further identify late cardiotoxic effects, months or even years after the completion of cancer therapy, highlighting the leading role of echocardiography in the long and challenging trip of the oncological patient.

2 | ECHOCARDIOGRAPHY IN THE CARDIO-ONCOLOGY SERVICE

A dedicated cardio-oncology service is the preferred structure to provide the specific care needed to oncological patients to improve their outcome.[3] This includes a specific outpatient facility for noninvasive imaging with TTE, stress echocardiography, cardiac magnetic

resonance, cardiac computed tomography, and other modalities[4,5] for efficient and meticulous assessment and surveillance of oncological patients. Echocardiography has several advantages compared with other imaging modalities that contribute to its pivotal role in cardio-oncology for baseline but also for serial assessment of these patients. Lack of radiation exposure, safety with no complications, ease of use, reasonable cost, wide availability, versatility, and satisfactory reproducibility are some of them. Its noninvasive nature and the provision within a short time of a broad spectrum of diagnostic information covering most of the cardiotoxic complications of cancer treatment (left ventricular (LV) dysfunction, valvular heart disease, pericardial disease, and pulmonary hypertension) are of critical importance.

Cardio-oncology, however, is a relatively recent field and such organized services are slowly developing over the last few years, with yet limited personnel and resources. With an exemption of a couple of countries, like United Kingdom and United States, in which sonographers may participate in the cardio-oncology services, clinical cardiologists are the ones to perform TTEs in the majority of countries, devoting a remarkable amount of their time to scanning and reporting echocardiographic studies. Either way the resources are always limited as the time that the cardio-oncology service should devote to imaging is standard, even if it operates on a full-time service with adequate personnel.

Another important issue is the resulting cost of cardiotoxicity screening methods. A few studies so far have evaluated the cost-effectiveness of serial echocardiographic studies in adults with cancer and in childhood cancer survivors treated with anthracyclines.[6-9] A common finding is that less frequent cardiac monitoring than recommended by the guidelines may be warranted to decrease the cost. Consequently, efficient use of resources in a cost-effective way is imperative.

Furthermore, the high volume of oncological patients who should be screened by TTE before any treatment, but also the crucial need to follow-up closely patients with established cardiovascular (CV) disease, moderate and high cardiotoxicity risk or those who develop a CV complication during therapy, increase significantly the workload related to echocardiography. These raise in turn issues of cost, feasibility, lack of personnel, and resources and in certain cases restrict imaging only to high-risk patients or patients with CV complications as a working solution. Therefore, the vast majority of patients cannot have access to proper cardio-oncology service and in many cases, asymptomatic abnormalities related to cancer therapy, such as LV dysfunction that may lead to overt heart failure (HF), remain undiagnosed until it is too late for intervention.

3 | TIMING OF ECHOCARDIOGRAPHIC ASSESSMENT OF ONCOLOGICAL PATIENTS

Cancer patients need echocardiographic assessment at different stages (Figure 1). A complete baseline TTE study is essential in the majority of patients diagnosed with cancer before any therapy (surgery, chemotherapy, radiotherapy, or interventional radiology treatments) is applied. Subsequently, according to the cardiotoxicity risk estimated for each patient, which depends on patient-related factors (demographics, CV risk factors, established CV disease, etc) and therapy-related factors, there are expert-based recommendations for the respective follow-up intervals.[10,11] For example, after the baseline TTE, patients with breast cancer on trastuzumab should be assessed every 3 months or after a cumulative dose of doxorubicin (or equivalent) of 200mg/m^2 when low risk and more frequently when risk is higher or abnormal results arise at baseline.[11] The pool of the echocardiographic department of the cardio-oncology service is getting bigger and bigger if patients who present with a cardiological symptom during therapy or those who need lifetime surveillance are considered, including survivors from childhood cancers or patients who have received high doses of anthracyclines or thoracic irradiation with expected late cardiotoxic effects.

4 | FOCUSED ECHOCARDIOGRAPHY IN CARDIO-ONCOLOGY (FECO)

Point of care ultrasound (POCUS) is a general term used to describe the focused use of ultrasound in different clinical settings [in critical care—FICE (Focused Intensive Care Echo),[12,13] in the emergency room,[14,15] during advanced life support—FEEL (Focused echocardiography in emergency life support),[16,17] in trauma/critical

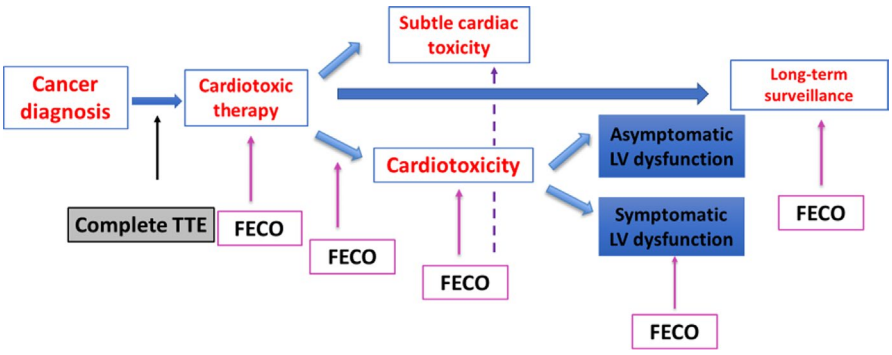

FIGURE 1 Time points at which FECO is indicated in the course of cancer treatment

care—BEAT (Bedside Echocardiographic Assessment in Trauma/Critical Care)[18,19]] by different medical specialties (cardiologists, intensivists, specialists in internal medicine, pediatricians, etc) to perform accurate diagnoses, guide interventions, and assess the result of therapy.[20] FoCUS (Focused Cardiac Ultrasound) is the term proposed by the International Liaison Committee on Focused Cardiac Ultrasound[21] to describe cardiac-specific ultrasound with the scope to answer specific clinical questions in specific clinical contexts.

This paper proposes FECO (Focused Echo in Cardio-Oncology) as a variation of FoCUS tailored to cardio-oncology needs. There are three important differences between FoCUS and FECO. First, FECO is performed by cardiologists and echocardiographers engaged in the cardio-oncology service, and not by other medical specialties, to answer critical clinical questions throughout the cancer process. Second, FECO should not be performed by handheld devices, which do not offer equal options concerning, ECG gating, native data storage, advanced quantification tools, etc Third, FECO may involve advanced imaging techniques, such as speckle tracking and new automatic three-dimensional (3D) transthoracic echo software. These techniques increase the ability to detect smaller changes in myocardial function, with a higher reproducibility than conventional 2D echocardiography, partially attributable to the automated endocardial tracing.[22,23]

FECO, instead of complete TTE, gives the opportunity to trainees in cardiology, fellows or cardiologists with limited or moderate experience in imaging to perform a focused echocardiographic study comprised of some specific views, which can afterwards be analyzed by the expert. Undoubtedly, a basic training in echocardiography and in the appropriate protocols is a prerequisite to ensure acceptable reliability and reproducibility. This will ultimately increase the staff that can scan effectively oncological patients while on the same time, the four suggested protocols will ensure stability, consistency, and continuity in the provided care.

TABLE 1 Characteristics of FECO

- Goal directed
- Problem oriented
- Time saving
- Limited in scope
- Repeatable and reliable
- Quantitative
- Performed either by physicians or by sonographers with interest in cardio-oncology

5 | FECO INDICATIONS

There is no doubt that in the baseline assessment of oncological patients by the cardio-oncology specialist, a complete echocardiographic study is needed to assess the cardiotoxicity risk by identifying pre-existing CV disease. However, in the subsequent visits, FECO could serve as a valuable tool in clinically stable patients to (a) identify the potential toxicity (subclinical or clinical) expected by the specific cancer therapy applied; (b) assess sequentially the pre-existing abnormality, if any, in relation to therapy; (c) assess the effect of any cardio-protective intervention; (d) identify any cardiac origin of patient complaints during or after therapy; (e) assess cardiac function in asymptomatic patients who develop significant changes in cardiac biomarkers during cancer therapy (Figure 1). FECO characteristics are summarized in Table 1.

FECO has the same basic characteristics with FoCUS, but it is more flexible as oncological patients may develop four main types of toxicity identified by echo: LV dysfunction, valvular heart disease, pericardial disease, and pulmonary hypertension. Consequently, the four different protocols proposed according to the type of cardiotoxicity anticipated are the following: FECOm (Focused Echo in Cardio-Oncology in patients on chemotherapeutics that cause myocardial dysfunction), FECOv (Focused Echo in Cardio-Oncology in patients at risk of valvular heart disease), FECOpd (Focused Echo in Cardio-Oncology in patients at risk of pericardial disease), and FECOph (Focused Echo in Cardio-Oncology in patients at risk of pulmonary hypertension). The time points where these four protocols are indicated are presented in Figure 2.

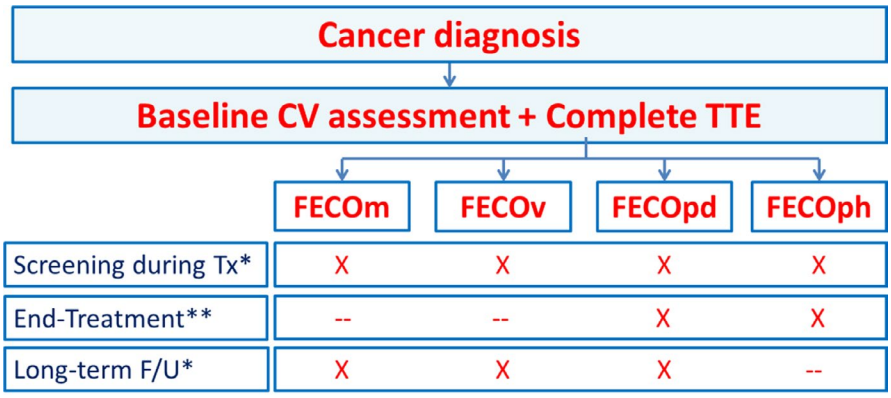

FIGURE 2 Time points at which specific FECO protocols are indicated in cancer patients

TABLE 2 Incidence of myocardial ischemia and myocardial dysfunction of commonly used anti-cancer agents

Myocardial ischemia		Myocardial dysfunction	
Medication	**Incidence**	**Medication**	**Incidence**
Antimetabolites		Antimetabolites	
5-fluorouracil	0.1%-19%	Clofarabine	7%-28%
Capecitabine	0.02%-10%	5-FU	8%-20%
		Capecitabine	2%-7%
		Cytarabine	Unknown
Antitumor antibiotics		Anthracyclines	
Bleomycin	<3%	Doxorubicin	3%-48%
		Idarubicin	5-18%
		Epirubicin	0.9-11.4%
		Mitoxanthone	0.2%-30%
		Liposomal anthracyclines	2%
Alkylating agents		Alkylating agents	
Cisplatin	0.2%-12%	Cyclophosphamide	7-28%
		Ifosfamide	0.5%-17%
		Busulphan	Rare
		Mitomycin	10%
Antimicrotubule agents		Anti-microtubule agents	
Paclitaxel	0.2%-4%	Docetaxel	2.3-13%
Vinblastine	<5%	Paclitaxel	<1%
		Vincristine	25%
Monoclonal antibodies		Monoclonal antibodies	
Bevacizumab	1%-6%	Trastuzumab	2%-28%
Ramucirumab	1.5%-2%	Bevacizumab	1.6-4%
Rituximab	Rare	Pertuzumab	3%-7%
		Ramucirumab	1%-2%
		Alemtuzumab	Rare
		Cetuximab	2%
Small Tyrosine Kinase Inhibitors (TKIs)		Small Tyrosine Kinase Inhibitors (TKIs)	
Nilotinib	2%-25%	Sunitinib	2.7-19%
Sorafenib	1%-2%	Pazopanib	7-11%
Sunitinib	1%-13%	Sorafenib	7%-13%
Pazopanib	2%-10%	Dasatinib	4%-28%
		Imatinib mesylate	2%-4%
		Lapatinib	0.5%-17%
			1.5%-5%
		Nilotinib	1%
		Trametinib	7%-15%
		Ponatinib	1%-3%
		Regorafenib	Frequent
		Cetiranib	Up to 46%
		Vandetanib	9%-32%
Topoisomerase inhibitors		Proteasome inhibitors	
Etoposide	1%-2%	Carfizomib	11%-25%
		Bortezomib	2-5%

(Continues)

TABLE 2 (Continued)

Myocardial ischemia		Myocardial dysfunction	
Medication	**Incidence**	**Medication**	**Incidence**
VEGF inhibitor		VEGF inhibitor	
Aflibercept	3%	Aflibercept	1-6%-8%
Hormone therapy		Miscellaneous	
Aromatase inhibitors	1%-2%	Pentostatin	3%-10%
Anti-androgens	2%-5%		
Estrogen/nitrogen mustard	1%-3%		
Gonadotropin-releasing hormone agonists	1%-5%		
Gonadotropin-releasing hormone antagonists	<1%		
Biologic Response Modifiers		Biologic Response Modifiers	
Interferon	Up to 21%	Interferon	8%-20%
Interleukin-2		Interleukin-2	Unknown

6 | FOCUSED ECHO IN CARDIO-ONCOLOGY IN PATIENTS ON CHEMOTHERAPEUTICS THAT CAUSE MYOCARDIAL DYSFUNCTION (FECOm)

The majority of patients will need to take more than one of different categories of chemotherapeutics or targeted therapies that may impair myocardial function sometimes before, concurrently or after radiotherapy (RT) in the form of myocardial dysfunction or myocardial ischemia. Table 2 includes the chemotherapeutics that can cause myocardial dysfunction or ischemia. [11,24] In this case, FECOm is proposed after the initial complete baseline echo, at time intervals defined by the recent recommendations,[1,10,11] depending on the baseline cardiotoxicity risk, the specific regime administered, and the CV symptoms that may develop. FECOm includes the views and measurements that are presented in Table 3 and Figure 3. The main clinical questions that should be addressed by FECOm are related to the baseline echocardiographic study and include the following:

a. Is there any difference in LV and right ventricular (RV) volumes/dimensions?
b. Is there any difference in the systolic function of LV [left ventricular ejection fraction (LVEF) and left ventricular global longitudinal strain (LVGLS)} and RV (TAPSE, RVFWLS and TV S')[25]?
c. Are there any new regional wall motion abnormalities (RWMAs)?
d. Is there any diastolic dysfunction, [left atrial (LA) volume, tricuspid regurgitation velocity, E/e', e' velocity]?

7 | FOCUSED ECHO IN CARDIO-ONCOLOGY IN PATIENTS AT RISK OF VALVULAR DISEASE (FECOv)

Valvular heart disease in patients with cancer can be the result of several causes, including RT, combination of chemotherapy with RT, infective endocarditis due to immune suppression, LV dysfunction and remodeling or tumor location, with the main one being RT. RT-induced valvular heart disease manifests over decades with a

TABLE 3 Focused Echo in Cardio-Oncology in patients on chemotherapeutics that may cause myocardial dysfunction (FECOm)

Suggested views	Suggested measurements
1. Apical 4-chamber view	LVEF, LVGLS, assessment of RWMAs. LA volume, E/e', e' 3D full volume acquisition if available Assessment of MR and TR (color Doppler)
2. Apical 2-chamber view	LVEF, LVGLS, assessment of RWMAs
3. Apical 3-chamber view	LVGLS, assessment of RWMAs
4. Apical 4-chamber view focused on RV	RV dimensions, RVFWLS, RVGLS, TAPSE, S'

Note: LVEF, Left Ventricular Ejection fraction by the biplane Simpson's method; LVGLS, Left ventricular global longitudinal strain from the three apical views; RVFWLS, Longitudinal strain of the free wall of the RV from the apical 4-chamber view focused on RV; RVGLS, Right ventricular global longitudinal strain from the apical 4-chamber view focused on RV; RWMAs, regional wall motion abnormalities; TAPSE tricuspid annular plane systolic excursion

In patients with poor apical echo window, parasternal and subcostal views can be used to assess left and right ventricular dimensions and qualitative function assessment

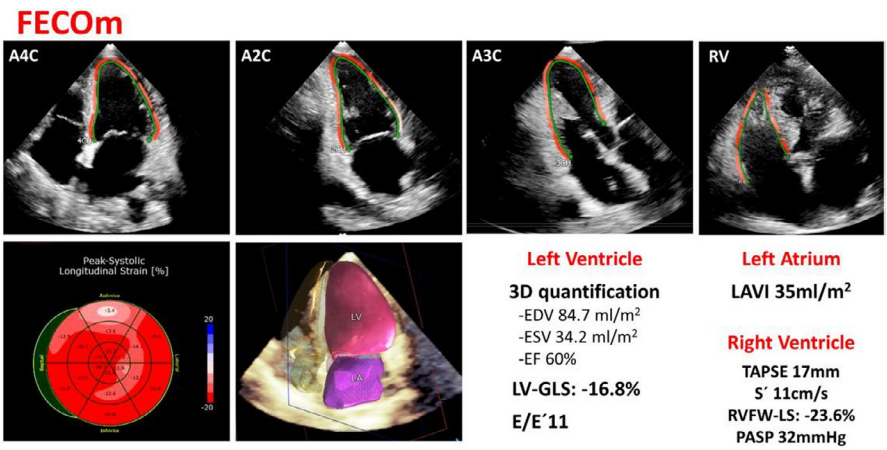

FIGURE 3 Views included in Focused Echo in Cardio-Oncology in patients on chemotherapeutics that cause myocardial dysfunction (FECOm)

reported incidence around 10%.[26,27] The risk factors for RT-induced valvular heart disease include radiation dose, time from radiation exposure, left-sided breast irradiation, combination with anthracyclines, increased age at the time of RT, diabetes mellitus, hyperlipidemia, and the decade of RT administration (1965–1995).[28,29] RT usually affects left-sided valves with regurgitation being more frequent than stenosis followed by ischemic valvular heart disease.[30] In this case, after the baseline complete, standard TTE, FECOv is suggested in the long-term follow-up (Table 4 and Figure 4). It includes views/measurements from FECOm plus specific views for the structural and functional assessment of the specific valve with color Doppler and Doppler measurements needed to estimate valvular heart disease severity. For example, in case of aortic stenosis, additional views and measurements needed are parasternal short axis at the level of the aortic valve, LVOT diameter, VTI at LVOT, and VTI at the aortic valve. If significant changes are identified suggesting moderate or severe disease, a complete echocardiographic study and/or a transoesophageal study should be considered and will be of incremental value.

TABLE 4 Focused Echo in Cardio-Oncology in patients at risk of valvular heart disease (FECOv)

Suggested views	Suggested measurements
1. Parasternal long-axis view	LV/RV dimensions
2. Apical 4-chamber view	LVEF, LVGLS, assessment of RWMAs
3. Apical 2-chamber view	LVEF, LVGLS, assessment of RWMAs
4. Apical 3-chamber view	LVGLS, assessment of RWMAs
5. Apical 4-chamber view focused on RV	RV dimensions, RVGLS, RVFWLS, assessment of RWMAs, TAPSE, S'
6. Valve-specific views	Disease-specific measurements Assessment of valve structure

Note: LVEF, Left Ventricular Ejection fraction by the biplane Simpson's method; LVGLS, Left ventricular global longitudinal strain from the three apical views; RVFWLS, Longitudinal strain of the free wall of the RV from the apical 4-chamber view focused on RV; RVGLS, Right ventricular global longitudinal strain from the apical 4-chamber view focused on RV; RWMAs, regional wall motion abnormalities; TAPSE tricuspid annular plane systolic excursion.

8 | FOCUSED ECHO IN CARDIO-ONCOLOGY IN PATIENTS AT RISK OF PERICARDIAL DISEASE (FECOpd)

Pericardial disease may manifest as asymptomatic pericardial effusion (in most cases), pericarditis (constrictive or not), myopericarditis, or tamponade.[31] It can be the result of RT, chemotherapy (Table 5),[32,33] or specific tumors (neoplastic), such as lung, breast or laryngeal cancer, leukemia or lymphomas. RT-induced pericardial disease is more likely if ≥ 30% of the heart receives ≥ 50Gy. [31] Acute pericarditis is the most common acute toxicity of RT, mostly presented in patients with Hodgkin or non-Hodgkin mediastinal lymphoma, lung cancer, esophageal cancer, or thymoma treated with high dose RT. Modern RT techniques have led to significant decrease in its incidence.[34] Delayed pericarditis developed 4 months to years after RT, can have the classical features of pericarditis or in rare cases progress to tamponade.[30] Myopericarditis or pancarditis is the combination of pericarditis with myocardial fibrosis which constitutes the most severe RT-induced toxicity involving the pericardium with ominous prognosis.[35]

Echocardiography is the method of choice to identify pericardial effusion, estimate its size and location and assess the potential hemodynamic compromise in cases of tamponade, constriction, or combination with restriction. Consequently, patients with one of the aforementioned neoplasms or treated with one or more of the anti-cancer drugs mentioned in Table 6 or receiving high dose of RT of the left hemithorax or the mediastinum are suggested to be assessed longitudinally or if they develop a related symptom with FECOpd. The suggested views included in FECOpd are useful for the identification and the semiquantitave assessment of pericardial effusion and are presented in Table 6 and Figure 5. The confirmation of tamponade, constriction, and restriction is much more challenging, requires also

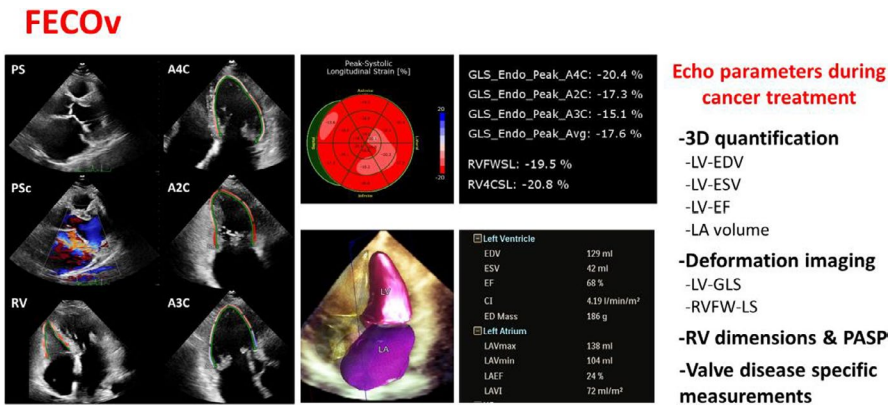

FIGURE 4 Views included in Focused Echo in Cardio-Oncology in patients at risk of valvular disease (FECOv)

TABLE 5 Anti-cancer drugs that can cause pericardial effusion

Category	Specific medication
Tyrosine Kinase Inhibitors (TKIs)	Imatinib, dasatinib, bosutinib
Protein Kinase Inhibitors	Lapatinib, trastuzumab
Alkylating agents	Cyclophosphamide, busulfan,
Antimetabolites	Cytarabine, gemcitabine, 5-fluorouracil, methotrexate
Microtubule inhibitors	Docetaxel
Immunotherapy	IL-2, interferon A,
Miscellaneous	Tretinoin, arsenic trioxide
Anthracyclines	

TABLE 6 Focused Echo in Cardio-Oncology in patients at risk of pericardial disease (FECOpd)

Suggested views	Suggested measurements
1. Parasternal long-axis view	End-diastolic max pericardial effusion
2. Parasternal short-axis view at the level of papillary muscles	End-diastolic max pericardial effusion
3. Apical 4-chamber view	Respiratory variation of MV and TV inflow and PAP (in suspicion of constriction, restriction or tamponade)
4. Any off-axis view according to pericardial effusion location	End-diastolic max pericardial effusion
5. Subcostal 4-chamber view	End-diastolic max pericardial effusion
6. Subcostal vena cava view	Assessment of respiratory variation of IVC

Note: IVC, inferior vena cava; MV, mitral valve; PAP, pulmonary artery pressure; TV, tricuspid valve.

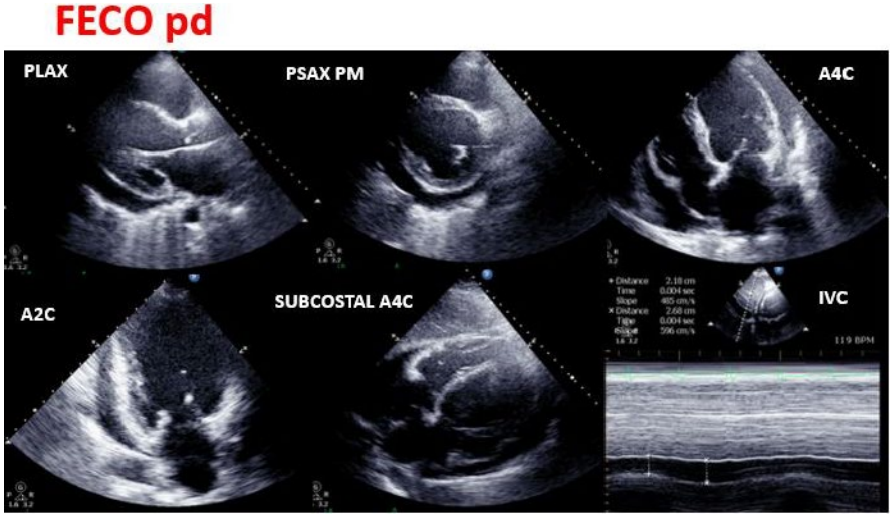

FIGURE 5 Views included in Focused Echo in Cardio-Oncology in patients at risk of pericardial disease (FECOpd)

TABLE 7 Incidence of pulmonary hypertension according to anti-cancer treatment

Anti-cancer therapy	Mechanism	Incidence
Small TKIs	PAH	
Dasatinib		0.6%-11%
Nilotinib, ponatinib, carfilzomib		
Ruxolitinib		3%
Monoclonal antibodies		
Trastuzumab emtansine, rituximab, bevacizumab		
Alkylating and alkylating -like agents		
Mitomycin C	PVOD	3.9/1000/year
Bleomycin	PVOD	
Cyclophosphamide	PVOD	
Paclitaxel		
Tretinoin		
Interferon alpha	PAH	
Thalidomide	PAH	5%
Bone marrow transplantation cyclosporine	PAH, PVOD	1.6%
Radiation therapy	PVOD	

Note: PVOD, pulmonary veno-occlusive disease; PAH, pulmonary arterial hypertension.

clinical and hemodynamic details and undoubtfully requires a standard complete echocardiographic study. However, mitral and tricuspid valve inflow and pulmonary artery pressures support strongly or exclude the clinical suspicion and may lead to further investigation.

9 | FOCUSED ECHO IN CARDIO-ONCOLOGY IN PATIENTS AT RISK OF PULMONARY HYPERTENSION (FECOph)

Pulmonary hypertension (PH) in patients with cancer can develop due to pulmonary arterial hypertension, pulmonary vascular disease, pulmonary embolism, toxicity from chemotherapeutics or RT, infectious or neoplastic pulmonary etiologies or LV disease with dismal prognosis. Patients under therapy with certain chemotherapeutics (Table 7), such as dasatinib,[11] paclitaxel,[36] interferon alpha,[37,38] tretinoin,[39] cyclophosphamide and other alkylating agents,[11] monoclonal antibodies,[38] as well as patients after stem cell bone marrow transplantation or RT, are at increased risk of developing PH.[29] Dasatinib is the most studied medication. The proposed echocardiographic protocol for this population is FECOph, presented in Table 8 and Figure 6. Right ventricular dimensions, overload, and systolic function should be assessed as well as RV systolic pressure. The presence of pericardial effusion as a poor prognostic sign should be highlighted. It is clear, however, that FECOph is useful for assessing echocardiographic probability of PH and not for establishing the diagnosis, but also for the serial assessment of the severity of PH.

10 | PATIENTS UNSUITABLE FOR FECO

FECO may be not appropriate for patients with multiple CV abnormalities in the baseline TTE study, such as heart failure with valvular heart disease or multi-valvular disease. The same probably applies to patients receiving multiple concurrent or sequential therapies with different cardiotoxicity profile, as well as those on newer therapeutic strategies with unknown cardiac toxicities or hemodynamically unstable patients. Finally, patients with nonsatisfactory echocardiographic windows and images are also not suitable for FECO.

This is a consensus document aiming at providing a practical approach to the echocardiographic evaluation of cancer patients, based on experts' opinion and current practices in dedicated centers. There are no evidence-based recommendations in this regard. Clinical trials comparing FECO to traditional TTE in terms of clinical endpoints, cost benefit, and time effectiveness are warranted.

TABLE 8 Focused Echo in Cardio-Oncology in patients at risk of pulmonary hypertension (FECOph)

Suggested views	Suggested measurements
1. Parasternal long-axis view	LV/RV dimensions
2. Parasternal short-axis of the LV (level of papillary muscles)	Estimation of RV overload
3. Parasternal RV inflow view	Max Doppler velocity of TV regurgitation (choice from 3,4 or 5 views)
4. Parasternal short-axis view of pulmonary artery	Max Doppler velocity of PV regurgitation, PVAT
5. Apical 4-chamber view focused on the RV	RV dimensions, RVFWLS, assessment of RWMAs, TAPSE, S'
6. Subcostal view of vena cava	Assessment of respiratory variation of IVC
7. Subcostal 4-chamber view	Assessment of pericardial effusion

Note: IVC, inferior vena cava; PVAT, pulmonary velocity acceleration time; PV, pulmonary valve; RVFWLS, Longitudinal strain of the free wall of the RV from the apical 4-chamber view focused on RV; TV, tricuspid valve.

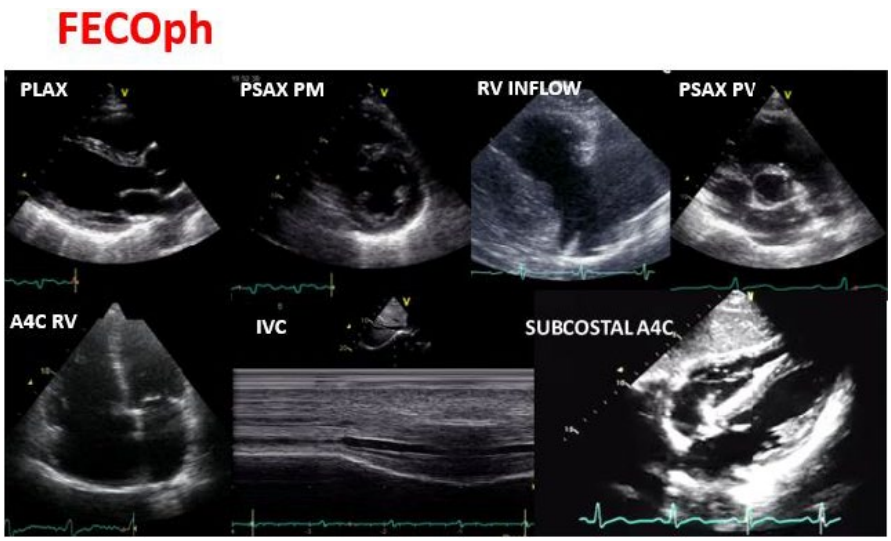

FIGURE 6 Views included in Focused Echo in Cardio-Oncology in patients at risk of pulmonary hypertension (FECOph)

11 | CONCLUSION

FECO can have a central role in the treatment of cancer patients, ensuring their wide access to cardio-oncology services in a cost-effective manner. Oncological patients of any risk can be serially monitored with FECO during and after cancer therapy, including lifelong follow-up in the presence of specific indications. Standard and specialized FECO protocols maximize accuracy, reliability, and effectiveness in early identification of CV complications, thus saving time, limiting costs, and improving quality of care.

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CONFLICT OF INTEREST

There is no conflict of interest related to this manuscript.

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REFERENCES

1. 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. *Euro Heart J Cardiov Imaging*. 2014;15:1063-1093.
2. Virani SA, Dent S, Brezden-Masley C, et al. Canadian Cardiovascular society guidelines for evaluation and management of cardiovascular complications of cancer therapy. *Canad J Cardiol*. 2016;32:831-841.
3. Pareek N, Cevallos J, Moliner P, et al. Activity and outcomes of a cardio-oncology service in the United Kingdom-a five-year experience. *Eur J Heart Fail*. 2018;20:1721-1731.
4. Farmakis D, Keramida K, Filippatos G. How to build a cardio-oncology service? *Eur J Heart Fail*. 2018;20:1732-1734.
5. Lancellotti P, Suter TM, Lopez-Fernandez T, et al. Cardio-Oncology Services: rationale, organization, and implementation: A report from the ESC Cardio-Oncology council. *Eur Heart J*. 2019;40(22):1756-1763.
6. Yeh JM, Nohria A, Diller L. Routine echocardiography screening for asymptomatic left ventricular dysfunction in childhood cancer survivors: a model-based estimation of the clinical and economic effects. *Ann Intern Med*. 2014;160:661-671.
7. Wong FL, Bhatia S, Landier W, et al. Cost-effectiveness of the children's oncology group long-term follow-up screening guidelines for childhood cancer survivors at risk for treatment-related heart failure. *Ann Intern Med*. 2014;160:672-683.
8. Gehling Bertoldi E, Marcolino MS, Rohde LEP, Luiz Ribeiro A, Polanczyk CA. Cost-effectiveness of routine screening for cardiac toxicity in patients treated with imatinib in Brazil. *Value Health Reg Issues*. 2012;1:180-183.
9. Nolan MT, Plana JC, Thavendiranathan P, Shaw L, Si L, Marwick TH. Cost-effectiveness of strain-targeted cardioprotection for prevention of chemotherapy-induced cardiotoxicity. *Int J Cardiol*. 2016;212:336-345.
10. Herrmann J, Lerman A, Sandhu NP, Villarraga HR, Mulvagh SL, Kohli M. Evaluation and management of patients with heart disease and cancer: cardio-oncology. *Mayo Clin Proc*. 2014;89:1287-1306.
11. Zamorano JL, Lancellotti P, Rodriguez Munoz 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 J Heart Fail*. 2017;19:9-42.
12. Walley PE, Walley KR, Goodgame B, Punjabi V, Sirounis D. A practical approach to goal-directed echocardiography in the critical care setting. *Crit Care (London, England)*. 2014;18:681.
13. Nielsen DL, Palshof JA, Larsen FO, Jensen BV, Pfeiffer P. A systematic review of salvage therapy to patients with metastatic colorectal cancer previously treated with fluorouracil, oxaliplatin and irinotecan +/- targeted therapy. *Cancer Treat Rev*. 2014;40:701-715.
14. Sobczyk D, Nycz K, Andruszkiewicz P. Validity of a 5-minute focused echocardiography with A-F mnemonic performed by non-echocardiographers in the management of patients with acute chest pain. *Cardiov Ultrasound*. 2015;13:16.

15. Neskovic AN, Hagendorff A, Lancellotti P, et al. Emergency echocardiography: the European Association of Cardiovascular Imaging recommendations. *Euro Heart J Cardiov Imaging*. 2013;14:1-11.
16. Breitkreutz R, Price S, Steiger HV, et al. Focused echocardiographic evaluation in life support and peri-resuscitation of emergency patients: a prospective trial. *Resuscitation*. 2010;81:1527-1533.
17. Aagaard R, Lofgren B, Grofte T, et al. Timing of focused cardiac ultrasound during advanced life support - A prospective clinical study. *Resuscitation*. 2018;124:126-131.
18. Gunst M, Sperry J, Ghaemmaghami V, O'Keeffe T, Friese R, Frankel H. Bedside echocardiographic assessment for trauma/critical care: the BEAT exam. *J Am Coll Surg*. 2008;207:e1-3.
19. Labovitz AJ, Noble VE, Bierig M, et al. Focused cardiac ultrasound in the emergent setting: a consensus statement of the American Society of Echocardiography and American College of Emergency Physicians. *J Am Soc Echocardiogr*. 2010;23:1225-1230.
20. Ma IWY, Arishenkoff S, Wiseman J, et al. Internal medicine point-of-care ultrasound curriculum: consensus recommendations from the canadian internal medicine ultrasound (CIMUS) group. *J Gen Intern Med*. 2017;32:1052-1057.
21. Via G, Hussain A, Wells M, et al. International evidence-based recommendations for focused cardiac ultrasound. *J Am Soc Echocardiogr*. 2014;27:683.e1-683.e33.
22. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Euro Heart J Cardiov Imaging*. 2015;16:233-270.
23. Lopez-Fernandez T, Thavendiranathan P. Emerging cardiac imaging modalities for the early detection of cardiotoxicity due to anticancer therapies. *Rev Espanola Cardiol (English ed)*. 2017;70:487-495.
24. Amit V. Cardio-oncology: an integrated discipline or just a portmanteau. *J Lancaster General Hospital*. 2017;12:100-111.
25. Keramida K, Farmakis D, Bingcang J, et al. Longitudinal changes of right ventricular deformation mechanics during trastuzumab therapy in breast cancer patients. *Eur J Heart Fail*. 2019;21:529-535.
26. Hull MC, Morris CG, Pepine CJ, Mendenhall NP. Valvular dysfunction and carotid, subclavian, and coronary artery disease in survivors of hodgkin lymphoma treated with radiation therapy. *JAMA*. 2003;290:2831-2837.
27. Malanca M, Cimadevilla C, Brochet E, Iung B, Vahanian A, Messika-Zeitoun D. Radiotherapy-induced mitral stenosis: a three-dimensional perspective. *J Am Soc Echocardiogr*. 2010;23(108):e1-2.
28. Stewart MH, Jahangir E, Polin NM. Valvular heart disease in cancer patients: etiology, diagnosis, and management. *Curr Treat Opt Cardiovasc Med*. 2017;19:53.
29. Russo A, Novo G, Lancellotti P, Giordano A, Pinto FJ. *Cardiovascular Complications in Cancer Therapy*. Springer International Publishing; 2018.
30. Lancellotti P, Zamorano JL, Galderisi M. *Anticancer Treatments and Cardiotoxicity: Mechanisms, Diagnostic and Therapeutic Interventions*. USA: Elsevier Science; 2016.
31. Madan R, Benson R, Sharma DN, Julka PK, Rath GK. Radiation induced heart disease: Pathogenesis, management and review literature. *J Egyptian Nat Cancer Inst*. 2015;27:187-193.
32. Lestuzzi C. Neoplastic pericardial disease: Old and current strategies for diagnosis and management. *World J Cardiol*. 2010;2:270-279.
33. Di Liso E, Menichetti A, Dieci MV, et al. Neoplastic pericardial effusion: a monocentric retrospective study. *J Palliat Med*. 2019;22(6):691-695.
34. Lestuzzi C, Oliva S, Ferraù F. *Manual of Cardio-oncology: Cardiovascular Care in the Cancer Patient*. Cham, Switzerland: Springer International Publishing; 2017.
35. Ling LH, Oh JK, Schaff HV, et al. Constrictive pericarditis in the modern era: evolving clinical spectrum and impact on outcome after pericardiectomy. *Circulation*. 1999;100:1380-1386.
36. Cherifi S, Hermans P, De Wit S, Cantinieaux B, Clumeck N. Acute pulmonary hypertension following paclitaxel in a patient with AIDS-related primary effusion lymphoma. *Clin Microbiol Infect*. 2001;7:277-278.
37. Savale L, Chaumais MC, O'Connell C, Humbert M, Sitbon O. Interferon-induced pulmonary hypertension: an update. *Curr Opinion Pulmon Med*. 2016;22:415-420.
38. McGee M, Whitehead N, Martin J, Collins N. Drug-associated pulmonary arterial hypertension. *Clin Toxicol*. 2018;56:801-809.
39. Lanier GM, Shah N, Garg J. *Cardiotoxicity of Chemotherapeutic Agents*. Nova Science Publishers, Incorporated; 2017.

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