Supplement submission

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Cardiovascular imaging in the diagnosis and monitoring of cardiotoxicity: role of echocardiography

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The evaluation by cardiovascular imaging of chemotherapy patients became a central topic in the last several years. The use of drugs for the treatment of cancers increased, and new molecules and protocols were developed to improve outcomes in these patients. Although, these novel approaches also produced a progressive increase in side effects, particularly myocardial dysfunction. Imaging of the heart was highly accurate in the early diagnosis of cancer therapeutics related-cardiac dysfunction.

Echocardiography is the first-line method to assess ventricular function alterations, and it is required to satisfy the need for an early, easy and accurate diagnosis to stratify the risk of heart failure and manage treatments. A careful monitoring of cardiac function during the course of therapy should prevent the onset of severe heart impairment. This review provides an overview of the most important findings of the role of echocardiography in the management of chemotherapy-treated patients to create a clear and complete description of the efficacy of conventional measurements, the importance of comprehensive heart evaluations, the additional role of new echocardiographic techniques, the utility of integrated studies using other imaging tools and the positions of the most important international societies on this topic.

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Introduction

The issue of cardiac function evaluation in patients undergoing chemotherapy is not resolved. Cardiac damage from cancer therapeutics may not become apparent for years or even decades. Therefore, these patients must be followed closely for their entire life. Two-dimensional (2D) echocardiography is the most useful tool to monitor cardiac function because of its safety, wide availability, repeatability and low cost (Fig. 1). The Cardiac Review and Evaluation Committee[1] listed criteria for the diagnosis of cancer therapeutics related-cardiac dysfunction (CTR-CD) in 2002 as a cardiomyopathy that is established by a global or regional decrease of systolic function, symptoms or signs of heart failure, and/or a decline in left ventricle ejection fraction (LVEF) of 5% or more to less than 55% with accompanying signs and symptoms of heart failure, or a decline in LVEF of 10% or more to less than 55% without signs or symptoms of heart failure. A more recent report from the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI)[2] proposed a decrease in the LVEF of more than 10%, to a value less than 53%, for the diagnosis of cardiac toxicity, and this decrease should be confirmed by the repeated performance of cardiac imaging 2–3 weeks after the baseline study.

New parameters, such as strain/strain rate, were developed in the last few years for the earlier detection of myocardial dysfunction, which considerably increased the reliability and sensitivity of echocardiography. These improvements are particularly useful because CTR-CD causes a spectrum of cardiac alterations that ranges from subclinical dysfunction to overt heart failure. Echocardiography is also a precious tool for the evaluation of diastolic function, pericardium, valves and right chambers, which may be damaged by cancer therapy. Other imaging modalities, such as cardiac magnetic resonance (CMR), may improve echocardiographic information when this information is unsatisfactory or when tissue characterization is needed.

Conventional echocardiographic evaluation

LV systolic function: the conundrum of the ejection fraction

LVEF is the most accurate parameter for the routine monitoring of cardiac toxicity in cancer patients. The last recommendations[3] indicate that an LVEF

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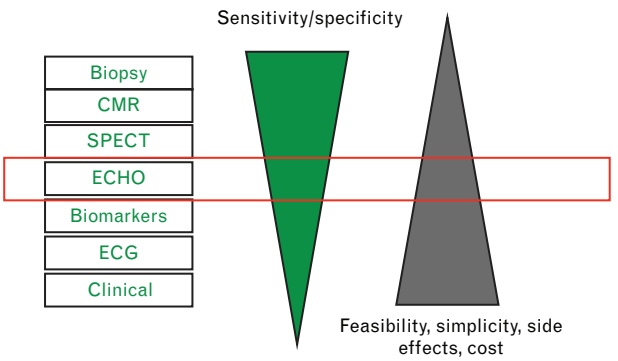
Fig. 1



Echocardiography vs. other modalities for detection of cancer therapeutics related-cardiac dysfunction (CTR-CD).

(assessed using 2D-modified Simpson's rule) more than 52% for men and less than 54% for women suggests normal systolic function. Although, three-dimensional (3D) measurements of left ventricle volumes were implemented to overcome the need for geometric assumptions. 3D evaluations of LVEF are recommended, if available, because volume calculations are more reliable and the probabilities of chamber foreshortening are lower. The use of myocardial contrast agents may also be useful when endocardial dropout occurs.[2]

Changes in LVEF should be better evaluated in cancer patients by comparing baseline and follow-up studies. The value of LVEF for the diagnosis and monitoring of CTR-CD was been recently confirmed by Cardinale *et al.*[4] who demonstrated that LVEF was useful for the early detection of cardiotoxicity (CTX) and improvement after therapy. Although, several authors questioned the role of LVEF[5–9] because of its low sensitivity for the detection of small changes in left ventricle contractility, particularly if the changes are limited to few segments. Therefore, a careful analysis of regional alterations is strongly recommended beyond the LVEF assessment. Septal and apical patterns of left ventricle dysfunction are more frequently found at an early stage of CTR-CD in the presence of a normal LVEF.

The correct timing of echocardiographic evaluations must be defined to establish the usefulness of LVEF to predict the occurrence of advanced systolic dysfunction. Dodos *et al.*[5] found that LVEF decreased significantly immediately after the completion of anthracycline therapy, and subclinical myocardial alterations were present in more patients than previously noted. Other authors[6–9] demonstrated that LVEF was normal at baseline and in the first months of follow-up in patients treated with anthracyclines, but it decreased subsequently. Ewer *et al.*[10] compared biopsy data with the echocardiographic findings in patients receiving adriamycin and reported no relationship between cumulative drug dose and LVEF or biopsy grades and LVEF, which suggests a poor correlation between changes in biopsy grade and LVEF during follow-up.

Thavendiranathan *et al.*[11] added an important piece in the valuation of the utility of LVEF in this field by demonstrating that this parameter could not estimate a decrease less than 10% within the 95% confidence interval, when performed by different investigators. CTX is defined as a drop of LVEF 10% or more or 5% or more in presence of heart failure symptoms, but this study revealed that the diagnosis provided echocardiography may be significantly inaccurate.

Most of these findings suggest a late alteration of LVEF in chemotherapy-treated patients, but the literature supports its use before[12,13] and after therapy.[14,15] Pretreatment LVEF is generally accepted as a predictor of subsequent CTX. Tan-Chiu *et al.*[16] demonstrated that pretreatment LVEF values were predictive of a later occurrence of heart failure in patients treated with anthracyclines or anthracyclines in addition to trastuzumab. Although, other researchers demonstrated that LVEF assessment was neither sufficiently sensitive nor specific for the early prediction of late CTX after the initiation of cancer therapy.[17] Jensen *et al.*[18] demonstrated no clear association between the percentage decrease in LVEF during treatment and the subsequent development of symptomatic congestive heart failure within the 3-year follow-up period despite the lower absolute values of LVEF before and immediately after treatment.

In conclusion, the prognostic value and the timing of serial measurements of LVEF during treatment to detect and monitor cardiac toxicity remain controversial. Several authors[19–21] found that LVEF was a good tool to predict cardiac damage, but this evidence conflicts with other research. These findings suggest that the effectiveness of LVEF as a valid marker to evaluate CTR-CD should be reconsidered.

Left ventricle diastolic function

The joint ASE/EACVI recommendations on left ventricle diastolic function support the performance of a comprehensive assessment of left ventricle diastolic function in the oncology setting. Patients with systolic dysfunction often exhibit concomitant diastolic dysfunction, but there is little evidence that diastolic dysfunction is an earlier marker for CTR-CD.

Small prospective studies reported that a prolongation of isovolumic relaxation time was predictive of a drop more than 10% in LVEF occurring up to 3 months later, and a significant increase in the myocardial performance index early after anthracycline administration predicted later decreases in LVEF.[22–24] Although, the prognostic value of early changes in left ventricle diastolic function using Doppler analysis after treatment were not replicated in subsequent studies.[25,26]

Several investigators demonstrated an early reduction in the e′ velocity of the mitral annulus using Tissue Doppler Imaging (TDI), which remained reduced during and for several years after treatment,[27,28] although, the use of the E/e′ ratio remains questionable in the oncological setting because E and e′ velocity fluctuations in these patients may be the consequence of changes in loading conditions associated with chemotherapy (e.g. nausea, vomiting, and diarrhoea) more than the result of a real change in left ventricle diastolic performance. In contrast, the heterogeneous reduction in e′ velocity in patients who developed cardiac dysfunction may suggest differences in regional wall stress, apoptosis, or fibrosis.[29]

Briefly, diastolic parameters were not prognostic of CTR-CD, but a conventional assessment of left ventricle diastolic function, including the grading of diastolic function and noninvasive estimation of left ventricle filling pressures, should be added to assessments of left ventricle systolic function.

Heart valves

Tumours do not generally affect valves, but valvular heart disease (VHD) may occur in oncological patients for several reasons, including preexisting valve lesions,[30] concomitant radiation therapy,[31] severe infection, or CTR-CD.

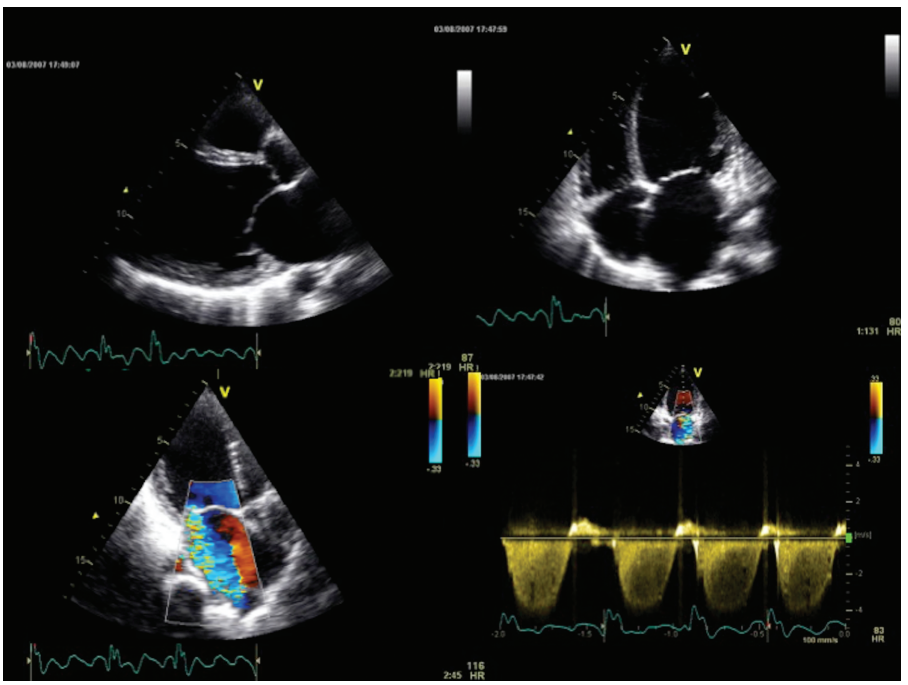
Chemotherapy increases the risk of endocarditis, especially in individuals with predisposing valve lesions (e.g. mitral valve prolapse and bicuspid aortic valve) or indwelling central venous catheters placed for vascular access.[32] The incidence of endocarditis in cancer patients is increased, and it should be suspected in suggestive clinical scenarios.[33] Nonbacterial thrombotic (NBTE) or marantic endocarditis may occur because of malignancy-associated thrombophilia in patients with advanced malignant tumours.[34] Aortic and mitral valve are most commonly involved, but right-sided heart valves may also be damaged.[35,36] NBTE may frequently cause systemic embolism.[37] The most frequent tumours associated with NBTE are lung, pancreas and gastric cancer, and sometimes unknown primary site adenocarcinoma.

Secondary mitral and tricuspid regurgitation may occur late in the course of CTR-CD after significant ventricular dysfunction and geometric remodelling have occurred[2] (Fig. 2).

Transthoracic 2D echocardiography should be the first-line examination in patients with suspicion of valve damage by cancer therapy. This technique is a useful tool to evaluate the presence of valvular vegetations and estimate the severity of valve regurgitations, and transoesophageal echocardiography is the gold standard for a more detailed diagnosis.[38]

Irradiation of the heart can cause the so-called 'radiation-induced heart disease (RIHD)', which commonly affects the valves.[39] The effects of radiation are related to the

Fig. 2



Example of cardiac alterations after anthracyclines for osteosarcoma treatment in a young woman. Atrial fibrillation, left ventricle remodelling and dysfunction leading to a severe functional mitral regurgitation are the most severe therapy complications in this case.

number of treatments and the dose of irradiation, which may be potentiated by adjunctive chemotherapy.[40] RIHD may be acute, but it more frequently onsets several years after irradiation. Recent studies demonstrated a dose–response relationship between radiation and VHD.[41] A recent study in Hodgkin's lymphoma survivors reported that 32% of patients developed asymptomatic VHD after approximately 20 years,[42] but the reason for this association is not known. Luckily, only a minority of patients developed clinically relevant moderate or severe valve dysfunction. The majority (71%) of patients with RIHD had no symptoms, and it is difficult to predict the time of symptom occurrence.[43] Therefore, it would be useful to follow these closely using serial echocardiographic controls. The echocardiographic characteristics of RIHD include fibrosis and calcification of the aortic root, aortic valve annulus, aortic valve leaflets, mitroaortic intervalvular fibrosa, mitral valve annulus, and the base and mid-portions of the mitral valve leaflets.[44–56] 3D echocardiography may be a useful alternative for evaluation in these patients when the visualisation of the mitral commissures is incomplete.[47]

This evidence suggests that cardiac valves should be carefully evaluated in patients undergoing chemotherapy. Patients with baseline or changing valvular findings during chemotherapy should undergo careful reevaluation of serial echocardiographic controls during and after the course of their treatment.[2]

Right ventricular function

Few studies investigated right ventricle function after cancer chemotherapy, although this cardiac chamber may be damaged by primary or metastatic neoplastic involvement or as a consequence of CTR-CD. Clinical evidence of right heart failure is extremely rare, but some drugs, such as anthracycline, cyclophosphamide, and 5-fluorouracil, induce impairment of right ventricle systolic and diastolic function.[48]

Echocardiographic evaluations of the right ventricle in patients receiving cardiotoxic therapeutics should include the following measurements: basal diameter and area, tricuspid annular plane systolic excursion, peak of tricuspid annulus systolic velocity by TDI and fractional area change.[49]

TDI is the most sensitive tool for the early detection of right ventricle damage caused by chemotherapy,[51] and the TEI index is a less sensitive parameter.[52] Changes in right ventricle function as assessed by right ventricle fractional area change and tricuspid annular plane systolic excursion were also reported during chemotherapy.[50]

It is important to measure right ventricle systolic pressure in patients with suspected right ventricle damage. A slight decrease in pulmonary acceleration time and slight increase in pulmonary artery pressure were detected, especially in patients treated with dasatinib.[53] Chemotherapeutic agents rarely cause pulmonary arterial hypertension by increasing pulmonary vascular resistance.[54]

Pericardial involvement

Several chemotherapy agents were related to pericardial disease: anthracyclines,[55] cyclophosphamide,[56] methotrexate,[57] arsenic trioxide,[58] and less frequently, 5-fluorouracil,[59] docetaxel[60] and tyrosine-kinase inhibitors.[61] Pericardial disease induced by chemotherapy generally manifests as pericarditis (usually as pericardial effusion), with or without associated myocarditis.

Although it is very important to remember during the evaluation of a pericardial effusion that pericardial involvement is very common in oncological patients,[62] this involvement may be secondary to malignancy itself or because of an inflammatory reaction because primary cancers of the pericardium are quite rare.[63–65] Pericardium involvement is more frequently found in lung and breast cancers, leukaemia, lymphomas and malignant melanoma.

Transthoracic echocardiography is the method of choice for the evaluation of patients with suspected pericardial disease because of chemotherapy. The echocardiographic findings in these patients may be entirely normal or show clear evidence of a pericardial effusion. Echocardiography allows a diagnosis and guidance for pericardiocentesis. The pericardial effusion should be quantified and graded using recognised methods to allow comparisons in subsequent evaluations. Cardiac tamponade must be excluded by recommended echocardiographic parameters in critical patients.[66]

Up to 70–90% patients with significant mediastinal radiation exposure also exhibit evidence of pericardial disease.[33,67] Pericardial injury may be acute or late onset. The initial injury is because of microvascular damage that induces tortuous and permeable neovascularisation in the irradiated pericardium with subsequent fibrosis that leads to the accumulation of a fibrin-rich exudate. The fibrinous exudate is later replaced by fibroblasts that produce collagen, which leads to fibrosis of the pericardium. These changes increase the thickness of the pericardium and may lead to constrictive pericarditis.[68] Constrictive pericarditis is more often associated with radiation-induced cardiac toxicity, but it may also occur after high-dose chemotherapy administration.[2] Echocardiographic signs of constriction should be explored using published guidelines. Other imaging modalities, such as computed tomography or CMR, may be a useful diagnostic complement. CMR is particularly helpful in determining the presence of late gadolinium enhancement for the identification of pericardial inflammation, which requires aggressive anti-inflammatory therapy to prevent constrictive pericarditis.

Advanced echocardiographic evaluation

Myocardial deformation: additional value and practical applications

The uncertain sensibility of LVEF in the evaluation of early impairment of systolic function in patients undergoing anticancer therapy and the development of new techniques to study the myocardial deformation have resulted in a proliferation of studies to determinate the feasibility and accuracy of these new tools in the assessment of CTR-CD. Myocardial deformations can be studied using different ultrasound techniques, including Doppler strain imaging (DSI) and 2D and 3D speckle-tracking echocardiography (STE).[69]

DSI was the first method used, and it was more sensitive than LVEF assessments in recognising left ventricle systolic dysfunction caused by chemo- and radiotherapy in adults and children. DSI identified early cardiac toxicity, even at low drug doses,[70,71] and it also revealed differences in myocardial function at a regional level by identifying segments that were more affected by the cardiotoxic hit (generally, interventricular septum),[72] although, this tool exhibited significant limitations, such as low reproducibility, angle dependency, limited spatial resolution, a high sensitivity to signal noise and high interobserver variability. STE was developed to overcome these limitations. This technique provides a frame-by-frame tracking of natural acoustic markers, and it is angle-independent, not influenced by translational movement because of respiration and tethering from the adjacent myocardium, and it is less sensitive to signal noise. Different deformation parameters may be evaluated. The maximum extent of systolic myocardial deformation (i.e. peak systolic strain) and its peak rate (i.e. peak systolic strain rate) were used regionally and globally.

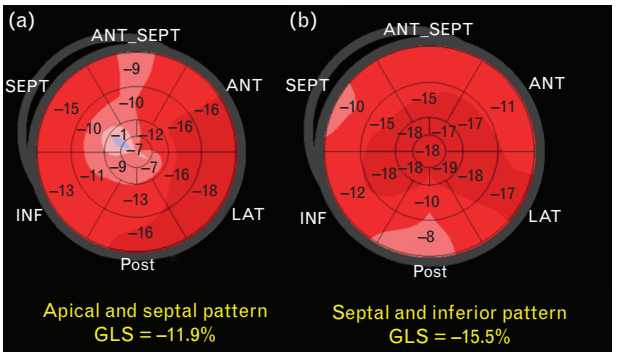
Migrino *et al.*[73] performed one of the first studies using 2D-STE strain in 2008 and demonstrated that this technique recognised early damage caused by anthracyclines. Assessments of longitudinal strain, and specifically global longitudinal strain (GLS), generally provide more consistent results than radial and circumferential myocardial deformation analyses. Systolic GLS is also relatively easy to obtain and reproduce. Therefore, 2D-STE is suitable for application in the clinical setting (Figs 3 and 4).

Many authors subsequently focused their efforts on this topic, and all of these studies may be grouped based on the four main features addressed[72]: identification of CTX in patients previously treated with oncologic therapies; serial evaluations for the prospective early recognition of myocardial damage; prediction of late CTX development; and planning of cardioprotection strategies.

The first group of studies demonstrated that 2D STE was more sensitive than LVEF reduction for the early recognition of asymptomatic left ventricle systolic dysfunction caused by chemotherapy in children and adults. 2D STE detected subclinical systolic myocardial abnormalities in children with acute lymphoblastic leukaemia and adult patients with breast cancer when no significant alterations were detected in conventional echocardiographic parameters.[74–76]

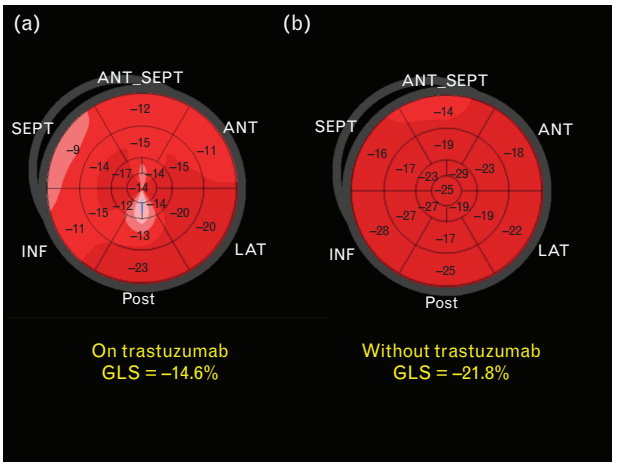
Other investigators[77,78] provided information on serial evaluations of cardiac function before and after oncologic treatments by comparing GLS with LVEF. They found that GLS was the most sensitive and specific measurement for the detection of subclinical myocardial injury early after anthracycline exposure (from 1 day to 3 months after the treatment in the different studies). GLS decreased significantly without any reduction in LVEF.

Fig. 3



Global and regional longitudinal strain by automated function imaging. (a) Apical and septal pattern of myocardial damage after anthracyclines in addition to trastuzumab; and (b) septal and inferior pattern of myocardial damage after trastuzumab.

Fig. 4



Demonstration of left ventricle damage reversibility after trastuzumab in a woman with breast cancer. (a) Decreased regional (anterior segments) and global longitudinal function (GLS = −14.6%) detected during the course of therapy; and (b) improved regional deformation with normalization of global longitudinal function (GLS = −21.8%) 3 months after therapy discontinuation.

Some authors found that longitudinal, radial and circumferential functions were affected, with impairment of all myocardial layers (subendocardial, midmyocardial or subepicardial) by anthracyclines.[78–80]

Sawaya *et al.*[28] demonstrated the capability of early (within 3 months) impairment of myocardial deformation to predict a later (at 6 months) development of CTX in patients with breast cancer treated with anthracyclines and trastuzumab. Good predictive value of regional strain was also reported in smaller studies with shorter follow-up periods.[79,81]

The joint ASE/EACVI consensus[2] recently provided a document containing important information for a practical approach for GLS use in chemo-treated patients based on the large amount of data in favour of GLS for the early detection of subclinical left ventricle dysfunction. The following essential key points were noted. First, measurements of GLS during chemotherapy should ideally be compared with baseline value, and a relative percentage reduction of GLS of less than 8% from baseline is not meaningful, but more than 15% from baseline is very likely abnormal. Second, the same vendor-specific ultrasound machine should be used when using STE for longitudinal follow-up of patients with cancer.[2] This consistency is also important to detect the reversibility of myocardial damage (Fig. 4).

Although few data on evaluations of cardioprotection using 2D STE are available, Negishi *et al.*[82] recently demonstrated that LVEF and GLS improved in patients receiving anthracycline, trastuzumab or both after approximately 1 year of beta-blocker treatment. These results suggest a protective role of this therapy in these patients, but the results should be evaluated in larger populations.

There is only limited experience with the use of rotational and torsional indices in this setting. Mornos *et al.*[83] tried to combine GLS and left ventricle twisting to obtain a new index to evaluate cardiac function before and after 6, 12, 24 and 52 weeks of anthracycline treatment, and they identified an early deterioration of GLS multiplied by left ventricle twisting as the best predictor of later CTX. 3D STE enables the derivation of an index of left ventricle global performance that incorporates left ventricle 3D strain, dyssynchrony and torsion for the sensitive detection of altered left ventricle mechanics in childhood cancer survivors,[84] although rotational indexes are currently used only for research, and further studies are needed to establish their role in the detection of CTR-CD.

In conclusion, the use the same vendor's machine and software version is presently recommended to compare individual patients with cancer when using 2D STE for the serial evaluation of systolic function.[85]

Three-dimensional echocardiography: additional value and practical applications

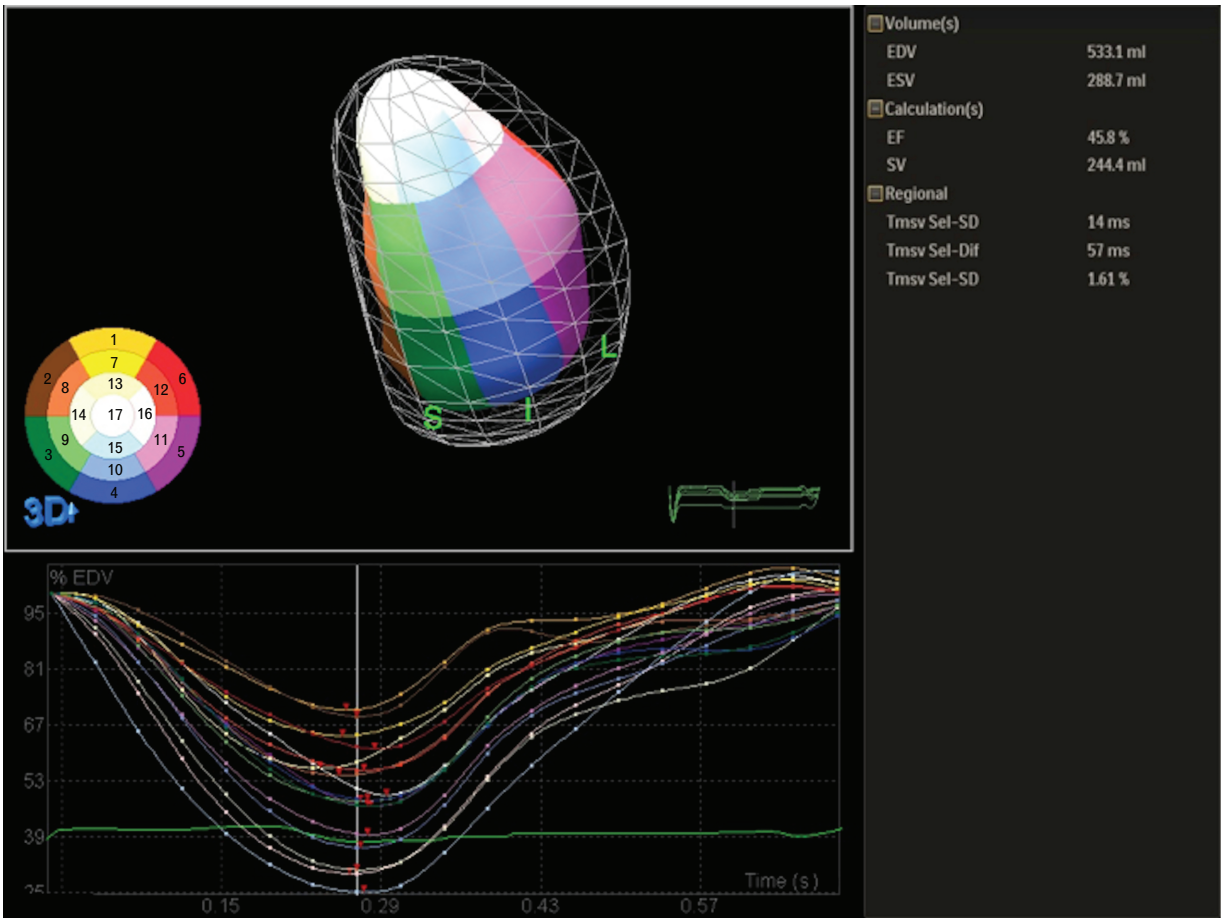
3D echocardiography is more accurate than the 2D modality for left ventricle volume and ejection fraction measurements, and it exhibits a precision that is comparable to CMR (Fig. 5).[86] Advantages include better accuracy in LVEF measurements below the lower normal limits, superior reproducibility and lower temporal variability. The improved accuracy of 3D over 2D echocardiography for the detection of LVEF less than 50% was observed in survivors of childhood cancer.[87] The preeminence of 3D echocardiography may be explained by the fact that it is less affected by acquisition differences from one scan to the next. Moreover, the use of an automated or semiautomated method for the identification of the left ventricle endocardium, compared with the manual tracing of endocardial contour that is required by the 2D method, provides a more accurate estimation of left ventricle volumes.[88,89] Notably, 3D echocardiography is the technique of choice for the monitoring of the cardiac effects of chemotherapy. Serial 3D echocardiographic calculations of LVEF should be encouraged for the monitoring of cardiac toxicity where available,[2] although it is important to realise that this technology needs high-quality images and training and expertise of operators for clinical application in the oncological setting. These concerns limit the widespread application of 3D echocardiography in the oncological setting.

Echocardiography and other imaging modalities: is integration needed?

Other imaging modalities, such as radionuclide angiography (MUGA), were referred to as the 'gold standard' to evaluate left ventricle systolic function in patients undergoing chemotherapy for many years.[90] Serial imaging using MUGA effectively monitors anthracyclines-related damage because of its high accuracy and reproducibility of LVEF measurements. The main disadvantage of MUGA is radiation exposure, which reduces its use given the increasing availability of other imaging techniques. MUGA also does not provide comprehensive information on right ventricle function, left and right atrial size, and the presence or absence of valvular or pericardial disease. Therefore, it is frequently used as an adjunct and complementary technique to echocardiography.

CMR is currently considered the reference standard in assessing left ventricle and right ventricle volumes and function, and it was recently used more extensively to detect the acute and chronic complications of cardiotoxic chemotherapeutic agents.[91] CMR is superior to echocardiography for its wide field of view, flexible scanning planes, and lack of ionising radiation.[92] Contrast-enhanced CMR offers a unique capability to assess myocardial tissue characteristics because it possesses an excellent ability to outline myocardial oedema,

Fig. 5



Three-dimensional (3D) reconstruction of left ventricle volumes and ejection fraction measurement showing left ventricle dilation and decreased systolic function (ejection fraction = 45.8%) in a cancer patient treated with anthracyclines.

hyperaemia, iron and necrosis/fibrosis, although this method has several limitations, such as low availability and a higher operational cost, compared with echocardiography. Issues with claustrophobia and hazards associated with ferromagnetic devices in some patients with cancer (e.g. breast tissue expanders used for breast reconstruction after mastectomy) must be considered.

The use of different imaging techniques, such as echocardiography, MUGA and CMR, to evaluate left ventricle volumes and LVEF values in the same patient is not suggested because of the significant difference in results across the techniques. Therefore, the choice of a single tool for the serial monitoring of LVEF during chemotherapy is preferred. Much evidence suggests that CMR should be considered in situations in which the discontinuation of chemotherapeutic regimens secondary to CTX is entertained or when the estimation of the LVEF is controversial or unreliable because of the low quality of echocardiographic images.[2,93]

Position of international scientific societies

International scientific societies finally began to state positions on the issue of echocardiographic monitoring during the course of chemotherapy in response to the growing evidence that the evaluation of the LVEF alone is no longer sufficient to identify chemotherapy-related early myocardial damage.

The two largest scientific societies of echocardiography, the ASE and EACVI, worked together to produce a shared document for the first time and stated positions on the role of various echocardiographic indices in this setting.[2]

Echocardiography was identified as the method of choice to evaluate patients before, during and after cancer therapy, and ejection fraction remained the first and irreplaceable technique. Ejection fraction should be performed using the best available method in the echocardiography laboratory (ideally 3D) in combination with the calculation of the wall motion score index.

LVEF failed to predict the development of CTR-CD. Therefore, a deeper echocardiographic investigation was strongly suggested, when available, to integrate the standard examination with data from different imaging techniques, such as TDI and STE.

The use of diastolic indices was not useful for the early detection of CTX because of their inability to predict subsequent heart failure.

Many studies during chemotherapy demonstrated reductions in all three myocardial layers, but neither radial nor circumferential strains were predictive of subsequent dysfunction. Therefore, the joint ASE/EACVI consensus suggests only the use of GLS by STE for a sensitive diagnosis of CTR-CD, and the same vendor-specific ultrasound machine should be used for serial examinations.

Useful tips for clinicians

Patients who must undergo chemotherapy should first be evaluated by echocardiography and should be followed during and after the treatment with serial echocardiograms performed with a timing decided according to single patient's clinical conditions.

The first examination should be as complete as possible and must include the study of the: systolic function, by LVEF and GLS, diastolic function, heart valves, pericardium and right chambers.

Later checks ought to have to be guided by the results of the baseline examination. In each case, the assessment of systolic function and the pericardium must always be included. 3D echocardiography should be preferred when available for the calculation of volumes and ejection fraction. Is preferable that serial examinations are carried out always with the same echocardiographic system. The evidence of CTR-CD should be discussed with oncologist to decide whether the discontinuation of therapy is needed.

Conclusion

The issue of the diagnosis of CTR-CD is absolutely topical. Recent evidence of the importance of early diagnosis and strict follow-up in these patients have produced in an increasing effort to define a protocol to provide cardiologists and oncologists a prompt diagnosis and better patient management, including eventual cardioprotection therapy.[94,95] Echocardiography plays a first-line role in cases with such a pressing indication.

Conflicts of interest

There are no conflicts of interest.

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