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SPECKLE - TRACKING ECHOCARDIOGRAPHY AS A POWERFUL DIAGNOSTIC TOOL OF EARLY SUBCLINICAL CARDIOTOXICITY IN CANCER PATIENTS DURING AND AFTER CHEMOTHERAPY

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Abstract

Purpose. This article discusses the importance of early diagnosis of cardiotoxicity resulting from chemotherapy treatment of cancer.

Materials and methods. Cardiotoxicity, a side effect of chemotherapy, can manifest at various stages of treatment and significantly reduce patients' quality of life, increasing the risk of developing cardiovascular diseases and mortality. The work emphasizes that speckle-tracking echocardiography is an innovative method for assessing myocardial mechanics, allowing for the detection of subclinical changes in cardiac function at early stages. The authors examine the principles of speckle-tracking echocardiography, its advantages over traditional diagnostic methods, and the importance of integrating this method into clinical practice to optimize treatment strategies for cancer patients.

Conclusions. The article calls for further study of speckle-tracking echocardiography and highlights its potential role in improving prognosis and quality of life for patients undergoing chemotherapy.

Keywords: *speckle-tracking echocardiography, cardiotoxicity, chemotherapy, myocardial mechanics, cardiac function*

Introduction

The prevalence of malignant tumors is a leading cause of death worldwide. However, increasing numbers of cancer patients are surviving to major advances in oncology treatments.

Nevertheless, anti-cancer treatment chemotherapy have extended the lives of patients with malignancies, but for some this benefit is tempered by adverse cardiovascular effects. Chemotherapy is associated with the onset of cardiotoxicity (CTox), which can arise at different intervals: at the time of drug administration to many years after its application. [1]. Chemotherapy-induced CTox is an urgent clinical issue for cancer patients [2]. It is characterized by the negative impact like high blood pressure, abnormal heart rhythms, and heart failure [3]. CTox can manifest even without clinical signs and symptoms complicating early detection and evaluation [2; 4].

The mechanisms of development CTox are diverse and depend on the class and dose of anticancer drugs. Anthracyclines may instigate oxidative stress which damage the structural and functional conditions of the myocardium [5]. Targeted drugs and tyrosine kinase inhibitors can impact the signaling pathways of myocardial cells, leading to disturbances in their function [6]. Such cardiotoxic effects can manifest during and after treatment, leading to a decrease in the quality of life, emergence previously known comorbid diseases and an increase in mortality.

Early diagnosis and monitoring of the cardiovascular system are critically important for minimizing the risk of developing CTox and ensuring adequate treatment of the oncological disease.

Clinical assessment of CTox involves a comprehensive examination of heart function us-

ing diagnostic methods such as echocardiography, cardiac magnetic resonance imaging, and lab monitoring of biochemical markers. CTox management strategies are based on early diagnosis, modification of chemotherapy regimens, and the application of cardioprotective strategies [7]. The advancement of technology in digital processing of ultrasound images has led to the emergence of a new and innovative method for assessing myocardial mechanics, known as speckle-tracking echocardiography (STE). This method has become a vital tool for early diagnosis and assessment of cardiac function, including in patients with cancer post-chemotherapy CTox [8]. It allows for measurement of myocardial deformation and evaluation of contractile capacity in various directions.

Numerous researches demonstrate the capacity STE – to detect subclinical CTox receiving aggressive and combined chemotherapy in oncology patients [9]. STE can detect even minor changes in cardiac function, which may go unnoticed using traditional evaluation methods like ejection fraction [10].

The objective of this review is to provide current information on the role of STE and in early detection of subclinical CTox in in post- chemotherapy cancer patients.

Materials and methods

STE offers a unique opportunity to directly assess changes in the myocardium and cardiac function that may be induced by chemotherapeutic agents. Guidelines have already been published by international organizations such as the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI), which provide protocols and recommendations including information on the use of STE for the quantitative evaluation of heart mechanics. [11; 12]

The new non-invasive method is based on the analysis of the motion of «speckles» – small points on the ultrasound image of the heart, which represent the reflection of ultrasound waves from moving myocardial structures.

The left ventricular myocardium (LV) possesses distinctive features in the arrangement of its fibers that enable to contract in three different directions: radial, circumferential, and longitudinal (Figure 1).

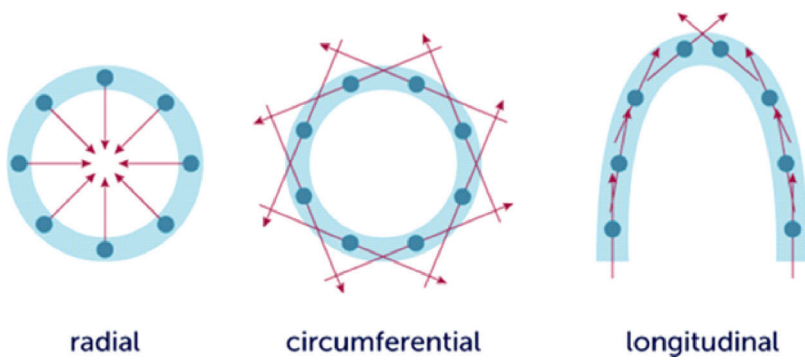

Figure 1. Left ventricular function [13]

Radial motion: The myocardial fibers surrounding the LV cavity contracts during contraction, moving from the periphery towards the center of the heart. This radial motion results in a reduction of the LV cavity diameter and the expulsion of blood into the aorta.

Circumferential motion: The myocardial fibers are aligned parallel to the inner surface of the LV, enabling it to perform circumferential motion around its axis during contraction. This assists in effectively moving blood within the LV and directing its expulsion in the proper direction.

Longitudinal motion: Myocardial fibers also extend along the long axis of the LV. During the heart's contraction, they contract longitudinally, facilitating the reduction of the LV and the ejection of blood into the aorta. A significant aspect of heart function is its ability of rotation, twisting (twist), and untwisting (Figure 2). These movements mirror the mechanics of heart contraction and allow for more efficient blood movement. Such multi-planar motion of the myocardium contributes to effective blood pumping and the maintenance of normal heart function.

Strain (or deformation) refers to the change in length and shape of the myocardium during the cardiac cycle and reflects its contractile function (Figure 3).

Figure 2. Schematic illustration of cardiac twisting, rotation and untwisting function [14]

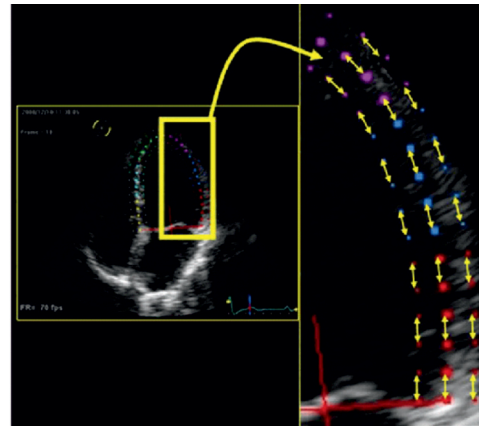

Figure 3. Left ventricle global longitudinal strain by 2D speckle tracking.
(Source: provided by the authors)

Considering the anatomical structure of the myocardium, using speckle-tracking echocardiography (STE), we can identify the following main types of deformation:

Global Longitudinal Strain (GLS): This is a measure of the myocardial longitudinal deformation, reflecting the contraction and stretching of the heart muscle in the longitudinal direction. GLS is a crucial indicator of the overall contractility of the myocardium and can be used to assess the heart's systolic function.

Segmental Longitudinal Strain: Speckle-tracking echocardiography facilitates the quantification of longitudinal deformation across distinct heart segments. This capability is instrumental to identify asynchronous contractions and localized deformations, providing insights for diagnosing and evaluating the impaired function of particular cardiac regions.

Radial Strain: Speckle-tracking can also measure the myocardial radial deformation, which reflects the compression and expansion of the heart muscle directionally from the center of the heart towards its periphery (Figure 4). The radial strain can be useful for assessing myocardial function in the walls of the heart.

Circumferential strain: It refers to the measurement of myocardial deformation as it circles the heart's circumference (Figure 5). Circumferential strain is instrumental to assess the myocardial function surrounding the heart's circumference and identifying any dysfunction in this area.

Among the aforementioned deformations, GLS has high sensitivity for detecting even slight changes in cardiac function [4]. During systole the myocardium contracts, and its length decreases. The more negative the GLS value, the stronger and more efficient the myocardial contraction.

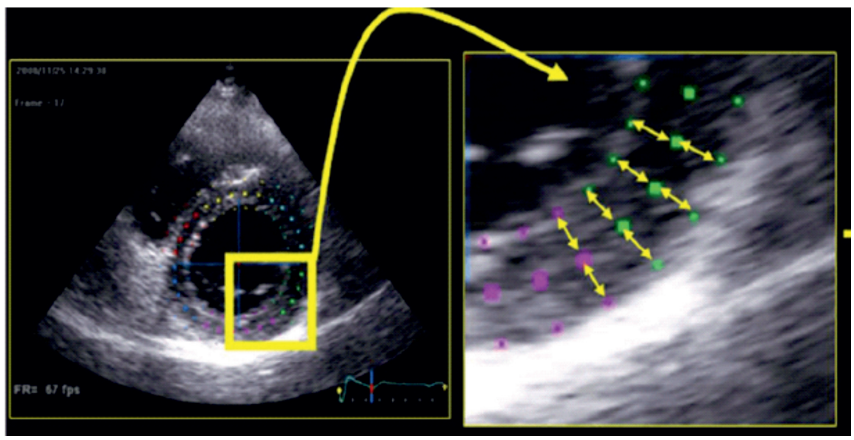

Figure 4. Segmental myocardial deformation by 2D speckle tracking.
(Source: provided by the authors)

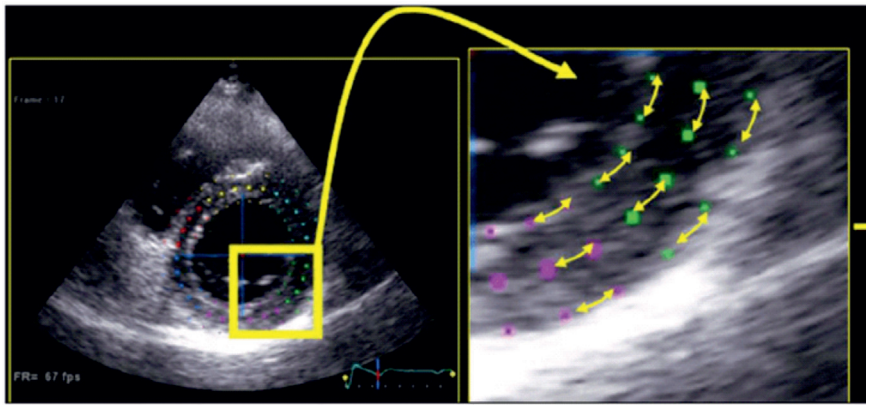

Figure 5. Circumferential strain deformation by 2D speckle tracking
(Source: provided by the authors)

Negative GLS values are typically expressed in percentages and can be, for example, -18 %, -20 %, -22 %, etc. However, generally, it is considered that the normal GLS value ranges from -18 % to -22 % [4; 15].

In 2016, the European Society of Cardiology issued a position statement stipulating that for the diagnosis of CTox, a decrease in the ejection fraction (EF) by more than 10 % from the standard value (53 %), or a GLS lower than – 15 %, should be taken into account [4; 11; 16]. Moreover, the patients individual characteristics, including age, gender, existing comorbidities, and other elements, should be considered, as these can influence GLS readings.

One study demonstrated the development of subclinical CTox in 10 (10.5 %) out of 95 women with breast cancer who underwent anthracycline chemotherapy. This indicates the presence of cardiac function impairments that were not clinically noticeable. The left ventricle GLS data significantly decreased 12 months after chemotherapy compared to the baseline value [12]. Meanwhile, other scientists have shown that a significant reduction in GLS occurs after the third cycle of chemotherapy, which persists in subsequent observations. Additionally, authors reported a study of 86 patients with Hodgkin and non-Hodgkin lymphoma receiving anthracyclines. The GLS significantly decreased after reaching the cumulative dose of chemotherapy drugs [17].

After examining the information on this diagnostic method, we can enumerate the benefits of STE:

• *Non-invasiveness:* STE is a non-invasive method, making it safe and comfortable for patients.

• *Sensitivity:* High sensitivity for subclinical myocardial changes, capability to detect early signs of cardiotoxicity.

• *Detailing:* Provides detailed information on myocardial deformation, rotation, and twisting of the heart, complementing classic indicators.

• *Dynamic monitoring:* Allows for dynamic tracking of changes in cardiac function, adapting therapeutic strategies.

• *Comprehensive analysis:* Integrates data on global and regional myocardial function, offering a complete picture of the heart's condition.

However, the disadvantages of STE include:

• Technical complexity: Requires specialized equipment and qualified professionals for interpreting results.

• Variability: Results can vary depending on the image quality and the operator's experience.

• Standardization: A lack of universal standards and protocols for evaluating and interpreting data.

Comparatively, traditional echocardiography remains the standard for evaluating cardiac function, but STE (speckle tracking echocardiography) offers a more detailed analysis of myocardial mechanics. Cardiac magnetic resonance imaging (MRI), especially with intravenous gadolinium contrast, can provide high-quality images of the myocardium, but STE has the advantage in terms of accessibility, speed, and cost.

Biochemical markers of CTox can be useful for early diagnosis, but STE (speckle tracking

echocardiography) provides the functional and structural data required for a comprehensive assessment of the heart's condition.

STE stands out for its ability to detect subclinical cardiotoxicity earlier, providing valuable information for adapting and optimizing treatment strategies for cancer patients. Despite technical and methodological limitations, its integration into multimodal assessment protocols can improve outcomes for patients undergoing chemotherapy.

There is a growing need to integrate STE (speckle tracking echocardiography) into standard protocols for patient assessment in today's medical practice. This is especially true for individuals who are at different stages of chemotherapy. Early and precise diagnosis of CTox can lead to more personalized and effective treatments.

Effective utilization of STE requires a high level of expertise and skill from the staff. Training and development programs aimed at optimizing the use and interpretation of STE data can significantly enhance patient care quality.

Conducting additional clinical studies can help to determine the optimal protocols for applying STE in a variety of oncological treatment and monitoring scenarios.

Conclusions

There is a need for a deeper exploration of the new STE (speckle tracking echocardiography) method. Its role and significance in oncological practice from a cardiologist’s perspective.

Through this review, we hope to increase awareness and expand knowledge on the application of STE echocardiography in the early diagnosis and monitoring of CTox in patients with oncological pathologies. This can be of significant practical importance for oncologists, cardiologists, and other specialists involved in the treatment of cancer patients.

It's crucial to highlight that the application of STE can also be cost-effective. Early detection of cardiac complications allows for preventive measures or timely treatment, which can reduce the expenses associated with treating cardiac complications in the future. The targeted application of STE before, during, and after chemotherapy will identify early disturbances in heart function and enable the earliest possible adjustment of cardiovascular therapy aimed at supporting the patient and minimizing the toxic effect on the heart. As a result, it aids in keeping the patient on course with the chemotherapy treatment.

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ХИМИОТЕРАПИЯДАН КЕЙІНГІ ОНКОЛОГИЯЛЫҚ НАУҚАСТАРДА ЕРТЕ СУБКЛИНИКАЛЫҚ КАРДИОТОКСИКАЛЫҚТЫҢ КҮШТІ ДИАГНОСТИКАЛЫҚ ҚҰРАЛЫ РЕТІНДЕ СПЕКЛ-ТРЕКИНГ ЭХОКАРДИОГРАФИЯСЫ

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Аңдатпа

Мақсаты. Бұл мақалада онкологиялық ауруларды химиотерапиямен емдеу нәтижесінде пайда болатын кардиотоксикалықтың ерте диагностикасының маңыздылығы талқыланады.

Материалдары мен әдістері. Кардиотоксикалық, химиотерапияның жанама әсері, емдеудің әртүрлі кезеңдерінде көрініс табуы мүмкін және науқастардың өмір сүру сапасын едәуір төмендетіп, жүрек-қан тамырлары ауруларының даму қаупі мен өлім-жітімді арттырады. Жұмыста, спекл-трекинг эхокардиографиясы миокард механикасын бағалаудың жаңашыл әдісі ретінде атап өтіледі, бұл әдіс жүрек функциясының субклиникалық өзгерістерін ерте кезеңдерінде анықтауға мүмкіндік береді. Автор-

лар спекл-трекинг эхокардиографиясыны4 жұмыс принциптерін, дәстүрлі диагностикалық әдістермен салыстырғанда оның артықшылықтарын және онкологиялық науқастардың емдеу стратегияларын оптимизациялау үшін осы әдісті клиникалық тәжірибеге интеграциялаудың маңыздылығын қарастырады.

Қорытынды. Мақала спекл-трекинг эхокардиографиясын одан әрі зерттеуге шақырады және химиотерапияға ұшыраған науқастардың болжамы мен өмір сүру сапасын жақсартудағы оның потенциалды рөлін атап өтеді.

Түйін сөздер: *спекл-трекинг эхокардиографиясы, кардиотоксикалық, химиотерапия, миокардтық механика, жүрек функциясы.*

СПЕКЛ-ТРЕКИНГОВАЯ ЭХОКАРДИОГРАФИЯ КАК МОЩНЫЙ ДИАГНОСТИЧЕСКИЙ ИНСТРУМЕНТ РАННЕЙ СУБКЛИНИЧЕСКОЙ КАРДИОТОКСИЧНОСТИ У ОНКОЛОГИЧЕСКИХ ПАЦИЕНТОВ ВО ВРЕМЯ И ПОСЛЕ ХИМИОТЕРАПИИ

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Аннотация

Цель. В данной статье обсуждается важность ранней диагностики кардиотоксичности, возникающей в результате химиотерапевтического лечения онкологических заболеваний.

Материалы и методы. Кардиотоксичность, побочный эффект химиотерапии, может проявляться на разных этапах лечения и значительно снижать качество жизни пациентов, увеличивая риск развития сердечно-сосудистых заболеваний и смертности. В работе подчеркивается, что спекл-трекинговая эхокардиография является новаторским методом оценки механики миокарда, позволяющим выявлять субклинические изменения сердечной функции на ранних стадиях. Авторы рассматривают принципы работы STE, ее преимущества перед традиционными методами диагностики, а также важность интеграции данного метода в клиническую практику для оптимизации лечебных стратегий онкологических пациентов.

Выводы. Статья призывает к дальнейшему изучению STE и подчеркивает ее потенциальную роль в улучшении прогноза и качества жизни пациентов, подвергающихся химиотерапии.

Ключевые слова: *спекл-трекинговая эхокардиография, кардиотоксичность, химиотерапия, миокардиальная механика, сердечная функция*

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