Kardiologia Polska 2017; 75, 2: 150–156; DOI: 10.5603/KP.a2016.0163

ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Tissue Doppler echocardiography detects subclinical left ventricular dysfunction in patients undergoing chemotherapy for colon cancer: insights from ONCOECHO multicentre study

Edyta Płońska-Gościniak[1], Monika Różewicz[2], Jarosław Kasprzak[3], Andrzej Wojtarowicz[1], Katarzyna Mizia-Stec[4], Tomasz Hryniewiecki[1], Piotr Pysz[4], Andrzej Kułach[4], Artur Bodys[5], Violetta Sulżyc[1], Wojciech Braksator[6], Andrzej Szyszka[7], Beata Zaborska[8], Adrianna Gościńska-Szmagała[9], Maciej Siński[6], Dariusz Kosior[10, 11], Sebastian Szmit[12], Ilona Kowalik[2], Zbigniew Gąsior[4]

[1]Pomeranian Medical University, Szczecin, Poland
[2]Institute of Cardiology, Warsaw, Poland
[3]Medical University of Lodz, Poland
[4]Medical University of Silesia, Katowice, Poland
[5]Voivodship Specialist Hospital, Lublin, Poland
[6]Medical University of Warsaw, Warsaw, Poland
[7]Poznan University of Medical Sciences, Poznan, Poland
[8]Centre of Postgraduate Medical Education, Warsaw, Poland
[9]American Heart of Poland, Tychy, Poland
[10]Central Clinical Hospital of Ministry of the Interior and Administration, Warsaw, Poland
[11]Mossakowski Medical Research Centre, Polish Academy of Sciences, Warsaw, Poland
[12]Department of Pulmonary Circulation and Thromboembolic Disease, Centre of Postgraduate Medical Education, Otwock, Poland

Abstract

Background: Colorectal cancer (CRC) is the second most common cancer in women and the third in men in Poland. The role of chemotherapy (CTX) depends on the stage of CRC: adjuvant CTX is a standard treatment in stage III and should also be considered in stage II with risk factors.

Aim: The aim of the paper was to assess the cardiovascular consequences of CTX in CRC enrolled to the ONCOECHO multicentre study (2012–2014). To identify potential cardiotoxicity, we focused on myocardial function, heart rhythm and conduction disorders, and adverse cardiovascular events.

Methods: Twenty-five CRC patients (12 women, mean age 61.3 [35–76] years), all receiving six-month adjuvant CTX were included. Thirteen patients received 5-fluorouracil (5FU)-based CTX, and 12 patients received a capecitabine-based scheme. Subjects were assessed at baseline and followed-up three, six, and 12 months after the onset of treatment. In this analysis we focused on conduction abnormalities, systolic and diastolic function of the left ventricle (LV), and cardiovascular events.

Results: In 12-month follow-up a decrease of selected tissue Doppler parameters (e.g. S'IVS, S'lat, and E'sept) was observed, and it was significant. LV structural parameters and ejection fraction (EF) remained unaffected. Changes in myocardial performance were not influenced by CTX regimen or treatment with beta-blockers or angiotensin-converting enzyme inhibitors. CTX did not affect LV structural parameters, EF, or conduction system, nor was it associated with cardiovascular events during the 12-month follow-up.

Conclusions: CTX in CRC patients does not affect LV structural parameters and EF. It may, however, trigger subtle changes in myocardial performance detectable by tissue Doppler echocardiography after 12 months. Moreover, it causes a transient increase of QT, which resolves after CTX cessation.

Key words: colon cancer, echocardiography, cardiotoxicity, chemotherapy

Kardiol Pol 2017; 75, 2: 150–156

Address for correspondence:
Andrzej Kułach, MD, PhD, Medical University of Silesia, ul. Ziołowa 47, 40–635 Katowice, Poland, e-mail: andrzejkulach@gmail.com
Received: 08.07.2016 **Accepted:** 04.10.2016 **Available as AoP:** 17.11.2016

INTRODUCTION

Colorectal cancer (CRC) is one of the most prevalent neoplastic disorders in the world. In Poland it is the second most common cancer in women and the third in men. According to the National Registry of the Oncology Institute in Warsaw, there were 17,450 newly diagnosed cases and 11,296 deaths due to CRC in Poland in 2013 [1]. In comparison to other countries the morbidity rate of CRC in Poland is moderate, but the diagnosis is often established late, with metastatic lesions already present in approximately 25% of patients. Symptoms of CRC depend on its localisation and phase. Different systems of classifications have been developed to stage the disease. Chronologically, they were the Dukes' classification, with later modification by Astler-Coller (MAC, The Modified Astler-Coller Classification) and, currently recommended by the Union for International Cancer Control/American Joint Committee on Cancer (UICC/AJCC), the Tumour-Node-Metastasis (TNM) classification (presently the seventh edition from 2010) [2].

The role of chemotherapy (CTX) depends on the stage of CRC. Adjuvant CTX is a standard treatment in stage III and should also be considered in stage II with risk factors, i.e. T4, number of excised lymph nodes < 12, urgent surgery, and/or infiltration of vessels [3, 4].

The aim of this paper was to assess the cardiovascular consequences of CTX due to CRC among the patients enrolled to the ONCOECHO multicentre study in the years 2012–2014. To identify potential cardiotoxicity, we focused on the cardiac conduction and myocardial function but clinical cardiovascular events were also recorded. To the best of our knowledge this is the first publication to document subclinical systolic myocardial dysfunction using tissue Doppler echocardiography in a CRC population receiving CTX.

Study group

The study population comprised 25 CRC patients (12 women, mean age 61.3 ± 10.5, range 35–76 years) from three centres. Histologically, diagnosis of adenocarcinoma (with mucinous adenocarcinoma in three cases) was established in all cases (in 52% of cases of moderate differentiation — G2). The lesion was located in the caecum (three patients), ascending colon (four patients), hepatic flexure (two patients), transverse colon (three patients), splenic flexure (two patients), sigmoid colon (four patients), rectosigmoid junction (one patient), and rectum (six patients). At the moment of diagnosis 56.2% of tumours were histologically classified as MAC B2.

Exclusion criteria included baseline left ventricular ejection fraction (LVEF) < 55%, regional wall motion abnormalities at rest, myocardial hypertrophy (any LV segment thicker than 13 mm), moderate or severe valvular heart disease, and history of CTX or radiotherapy prior to the CRC diagnosis.

All patients received six-month adjuvant CTX. The most common scheme (applied in 12 patients) was LF1 (six cycles of five-day intravenous administration of 5-fluorouracil [5-FU] and leucovorin over six months). The other nine patients were treated according to the XELOX scheme (infusion of oxaliplatin combined with orally administered capecitabine per 14 days, cycles repeated every 21 days). Three patients underwent 14-day monotherapy with capecitabine repeated every 21 days. Finally, in one patient the FOLFIRI scheme was applied (48-h infusion of 5-FU with irinotecan and calcium folinate or levofolinic acid repeated every 14 days).

METHODS

Medical history, physical examination, and following additional tests were scheduled at baseline (before CTX administration) and again after three, six, and 12 months, including:

Resting electrocardiogram (ECG) — assessment of rhythm origin and frequency, presence of arrhythmia and conduction disorders, QT interval duration, ST segment, and T wave morphology.

Transthoracic echocardiography (TTE) — assessment of LV systolic and diastolic function, size and function of right ventricle (RV), valvular function, presence of pericardial effusion, and additional intracardiac structures. TTE was performed by experienced echocardiographers with a Vivid 9 ultrasound system (GE). The following measurements were made according to American Society of Echocardiography (ASE) [5] and the Section of Echocardiography of Polish Cardiac Society (SE PTK) [6, 7] recommendations:

- left ventricular end-diastolic dimension (LVEDD);
- left ventricular end-systolic dimension (LVESD);
- intraventricular septum dimension in diastole (IVSDd);
- posterior wall dimension in diastole (PWDd);
- left atrial area (LAarea) in apical four-chamber view;
- left atrial volume index (LAVI) calculated in apical four-chamber view according to Simpson's rule;
- LVEF according to simplified Simpson's rule;
- maximum systolic septal and lateral mitral annulus velocities (S'IVS, S'lat);

To assess LV diastolic function evaluation, we measured:

- maximum early-diastolic septal and lateral mitral annulus velocity (E'sept, E'lat);
- maximum early-diastolic filling velocity (E);
- E/E' ratio;
- isovolumetric relaxation time.

Laboratory tests included peripheral blood morphology, lipidogram, serum fasting glucose level, serum transaminases activity, and serum creatinine concentration/glomerular filtration rate.

Deaths, myocardial infarctions, heart failure, and unplanned cardiovascular hospitalisation during the 12-month follow-up were considered major adverse cardiovascular events (MACE).

Statistical analysis

Numerical variables were presented as arithmetic mean values with standard deviation when normally distributed or as median with interquartile range for non-normal distribu-

tions. Significance of differences was verified with paired Student's t-test (for related variables) or regular Student's t-test (for comparison of two groups). Categorical variables were presented as absolute or relative frequency.

Hypotheses were verified at a significance level of $p < 0.05$ with two-sided testing. Statistical analysis was performed with SAS 9.2 (SAS Institute Inc., Cary NC, USA, 2008) software.

RESULTS

Clinical data, laboratory and ECG findings

Cardiovascular risk factors and concomitant diseases identified in 25 CRC patients are presented in Table 1. Due to these reasons, prior to CTX patients were receiving angiotensin converting enzyme inhibitors (ACEI; n = 7), diuretics (n = 6), beta-blockers (n = 4), and oral anticoagulant (n = 1).

Baseline biochemistry was normal except for mildly lower concentration of haemoglobin (Table 2). No changes in blood pressure (BP), heart rate, and QT interval duration were noted after 12 months of follow-up (Table 3). Interestingly, QT tended to be increased as soon as in the third month of observation and a significant prolongation was registered after six months (up to 392 ± 30 ms, p = 0.016); after CTX cessation QT returned to baseline at the 12th month (Table 4). Neither arrhythmia nor conduction disorders were observed throughout the study.

Echocardiography findings

Transthoracic echocardiography measurements after three months from CTX initiation did not differ from baseline. At six-month follow-up a minor increase in PWDd ($p < 0.03$) and a decrease in S'IVS (7.5 ± 1.2 cm/s vs. 8.7 ± 1.73 cm/s, $p < 0.001$) were observed.

Mean values of TTE parameters at baseline and after 12 months from CTX initiation are presented in Table 5. In 12-month follow-up a decrease of both S'IVS and S'lat was significant. At the same time point a significant decrease of E'sept was noted, which was not observed six months earlier. PWDd after 12 months returned to baseline value after a transient increase was noted, as stated above, after six months. No MACEs occurred during the 12-month follow-up.

We compared the TTE parameters listed in Table 5 between the subgroups of patients who received ACEI and/or beta-blockers due to cardiologic indications before CTX initiation (n = 10) with those who did not (n = 15) — no statistically significant differences were detected.

There were no significant differences in echocardiographic parameter values between patients who received 5-FU/leucovorin-based chemotherapy (n = 13) and patients treated with capecitabine-based CTX (n = 12), neither at the beginning of the study nor after 12 months.

Table 1. Cardiovascular risk factors and concomitant diseases in 25 colorectal cancer patients

Cardiovascular risk factor/ /concomitant disease	N (%)
Arterial hypertension	13 (52.0%)
Diabetes	4 (16.0%)
Hypercholesterolaemia	7 (28.0%)
Tobacco smoking	15 (60.0%)
Family history of cardiovascular disease	8 (32.0%)
Family history of oncologic disorder	17 (68.0%)
Stroke	1 (4.0%)

Table 2. Selected laboratory findings in colorectal cancer patients

Parameter	Mean baseline value
Haemoglobin [mmol/L]	8.7 ± 2.3
Haematocrit [%]	37.8 ± 5.1
MCV [fL]	85.6 ± 6.7
MCHC [mmol/L]	23.6 ± 5.8
Erythrocytes [T/L]	4.42 ± 0.55
Leukocytes [G/L]	7.0 [6.6–9.6]
Platelets [G/L]	299 [262–368]
Glucose [mg%]	111 ± 37
Aspartate transaminase [U/L]	17.5 [15.0–19.0]
Alanine transaminase [U/L]	15.0 [13.0–26.0]
Creatinine [mg%]	0.81 [0.68–0.88]

MCV — mean corpuscular volume of erythrocyte; MCHC — mean corpuscular haemoglobin concentration in erythrocyte

Table 3. Blood pressure (BP) and heart rate at baseline and after 12 months from chemotherapy initiation in colorectal cancer patients (mean ± standard deviation)

Parameter	Baseline value	After 12 months	P
Systolic BP [mm Hg]	129 ± 9.7	127 ± 13.6	0.47
Diastolic BP [mm Hg]	82 ± 8.6	79 ± 11.6	0.10
Heart rate [bpm]	76 ± 12.9	71.8 ± 10.6	0.09

DISCUSSION

Cancer has grown to become a major epidemic of the 21st century. Gradually, as diagnosis is established earlier and treatment efficacy improves, the life expectancy of patients is increasing. Frequent cardiovascular comorbidity warrants

Table 4. QT interval duration at baseline, three, six, and 12 months after chemotherapy initiation in colorectal cancer patients (mean ± standard deviation)

Parameter	Baseline	After 3 months	After 6 months	After 12 months
QT interval [ms]	372 ± 31.7	384 ± 34	392 ± 30*	364 ± 25.7

*$p < 0.05$ vs. baseline

Table 5. Echocardiography findings at baseline and after 12 months of follow-up (mean ± standard deviation)

Parameter	Baseline value	After 12 months	P
LVEDD [mm]	47.7 ± 5.3	48.4 ± 5.0	0.44
LVESD [mm]	30.0 ± 5.6	30.9 ± 5.5	0.46
LVEDV [mL]	102.8 ± 28.6	92.6 ± 23.9	0.17
LVESV [mL]	35.7 ± 12.7	33.3 ± 10.1	0.34
SV [mL]	67.1 ± 17.6	59.3 ± 16.0	0.14
Ejection fraction 4ch [%]	65.9 ± 6.0	64.5 ± 6.1	0.31
Left atrial area [cm^2]	16.9 ± 5.0	17.0 ± 3.3	0.92
LAVI [mL/m^2]	27.5 ± 10.4	26.3 ± 7.2	0.63
E'sept [cm/s]	**7.29 ± 2.13**	**6.21 ± 2.19**	**0.02**
E'lat [cm/s]	9.75 ± 3.31	9.00 ± 2.22	0.42
E [cm/s]	67.6 ± 18.4	65.5 ± 15.0	0.70
Isovolumetric relaxation time [ms]	98.4 ± 13.9	102.4 ± 17.0	0.47
S'IVS [cm/s]	**8.7 ± 1.73**	**7.0 ± 0.91**	**0.0001**
S'lat [cm/s]	**10.24 ± 2.48**	**9.23 ± 1.12**	**0.03**
PWDd [mm]	9.8 ± 1.3	9.8 ± 1.4	0.86
IVSDd [mm]	11.1 ± 0.9	11.4 ± 2.3	0.56
Ejection fraction [%]	65.9 ± 5.7	64.4 ± 6.4	0.31
E/E'	8.2 ± 3.3	9.1 ± 3.2	0.22

4ch — four chamber; SV — stroke volume; LVEDV — left ventricular end-diastolic volume; LVESV — left ventricular end-systolic volume; other abbreviations — see text

involvement of a cardiologist in the managing team. Optimising oncologic and cardiovascular pharmacotherapy to maximise effectiveness and reduce side effects poses a challenge for both groups of specialists. 5-FU, a standard treatment of CRC, is known potentially to exert adverse influence on cardiovascular system. The presented study was aimed to assess the function of conduction system and myocardial performance in patients undergoing CTX during 12 months of follow-up. Reports on CTX cardiotoxicity in CRC patients are scarce. We believe our paper is the first one to document subtle, subclinical myocardial dysfunction by tissue Doppler in this cohort of patients.

We analysed 25 CRC patients in whom a histologic diagnosis of adenocarcinoma was uniformly established. The rectum was the most frequent location of the index lesion. Patients were treated according to CTX schemes containing 5-FU or capecitabine. The number of patients included in this analysis is comparable to that in the scarce, previously published reports [8, 9].

Echocardiography findings at baseline were within currently recommended reference ranges [10] except for a minor increase in septal wall thickness (IVSDd of 11.1 ± 0.9 mm) and a decrease in S'IVS.

Throughout the 12 months of follow-up LVEF remained normal (non-significant change from 65.9 ± 5.7% to 64.4 ± 6.4%). LVEDD and LVESD during CTX were slightly larger and returned to baseline values after 12 months. There was, however, a significant worsening in LV functional parameters by tissue Doppler. After a year from CTX initiation E'sept decreased from 7.29 ± 2.13 cm/s to 6.21 ± 2.19 cm/s, $p = 0.02$. Furthermore, concurrently both S'IVS and S'lat have dropped from 8.7 ± 1.73 cm/s to 7.0 ± 0.91 cm/s, $p < 0.0001$ and from 10.24 ± 2.48 cm/s to 9.23 ± 1.12 cm/s, $p = 0.03$, respectively. No other meaningful changes were identified by TTE after 12 months. The authors believe that this is the first report on subclinical LV dysfunction in CRC patients undergoing CTX.

In the existing literature, Balloni et al. [8] reported classic two-dimensional echocardiographic indices of LV function in

25 CRC patients (nine women) with normal baseline ECG and vital parameters treated with 5-FU. No changes in ECG, BP, or heart rate were noted. Echocardiography findings (LVEDD, LV mass) remained unaffected both after six cycles of 5-FU and six months after completion of CTX.

The most commonly reported in literature ECG changes provoked by 5-FU and capecitabine involve ST segment elevation or depression and/or T wave inversion whereas arrhythmias are not typically observed. In our study in three cases ECG showed T-wave inversion at baseline and during the observation period.

Similarly to Balloni's findings, [8] none of our patients experienced any ECG abnormalities. Grandi et al. [11], on the other hand, did identify adverse effects of 5-FU on the cardiovascular system in 16 CRC patients (age 39–74) with initially normal BP, ECG, and echocardiogram. Transient T wave inversion without concomitant angina or myocardial necrosis markers elevation was registered in one patient during the first cycle of CTX and in another during the fifth cycle. Subsequently performed dipyridamole myocardial perfusion scintigraphy was normal in both of these patients. No other deviations in BP, heart rate, LVEDD, and LV mass index were registered throughout a six-month follow-up. No influence of CTX on mean systolic BP, diastolic BP, and resting heart rate was found during 12-month follow-up of our patients. Similarly, Grandi et al. [11] did not observe any changes of BP in CRC patients during treatment with 5-FU, nor six months after its completion.

Transient QT prolongation was observed regardless of CTX regimen in the third month (trend; not significant) and reached statistical significance in the sixth month (Table 4). Most available papers report QTc prolongation during CTX as soon as in the third month of follow-up. Some authors reported altered QT dispersion and QTc increase even during the first cycle of CTX.

Our findings are consistent with these reports; additionally, our data suggest that after CTX regimen termination QT returns to baseline. Although none of our subjects experienced clinically relevant arrhythmia (mean QT in the sixth month was still < 400 ms; only 5/25 patients [20%] had QT > 400 after six months), it is important to pay attention to patients with prolonged or borderline QT at baseline.

Patients treated with pyrimidine analogues (5-FU or capecitabine) may experience angina pectoris, and acute coronary syndrome may be recognised especially if previously they have been diagnosed with ischaemic heart disease. It should be remembered that additional ECG abnormalities and arrhythmias may be observed [12]. Our study presents new findings that QT prolongation is possible, and changes in E'sept as well as in S'IVS and S'lat may occur. Of note, myocardial velocities in the studied group were slightly decreased at baseline, and deteriorated over the observation period.

The available literature has reported cases of takotsubo cardiomyopathy related to 5-FU or capecitabine [13, 14]. There are known published cases on cardiac conduction disturbances induced by 5-FU or capecitabine [15]. The cardiotoxic effects of these drugs seem to be multifactorial [16]. The suggested phenomenon of vasospasm induced by 5-FU or capecitabine cannot explain the possibility of cardiomyopathy, sinoatrial and atrioventricular node dysfunction, takotsubo cardiomyopathy, and QT prolongation with torsade de pointes ventricular tachycardia [17]. Although a recent European Society of Cardiology statement on cardiovascular toxicity of cancer treatment emphasises the ischaemic effect of 5-FU [18], cardiotoxicity of pyrimidines seems to have numerous mechanisms, including apoptosis of myocardium, depletion of high-energy phosphate compounds, increased oxygen consumption, impaired antioxidant defence system, and more [16].

Our findings confirm that further analyses of cardiac effects of pyrimidine analogues are needed with use of modern imaging of the cardiovascular system.

We were unable to identify any other study describing local myocardial function in CRC patients receiving CTX, and therefore our findings of regional alterations of myocardial velocities require further validation in expanded patient populations as well as prolonged follow-up to establish their transient or persistent character.

Limitations of the study

The number of included patients is relatively small but similar to previously published papers related to cardiovascular aspects of 5-FU therapy [8, 9]. Regrettably, novel echocardiography tools such as three-dimensional imaging could be used only in selected patients due to the modest availability of advanced ultrasound systems and were therefore not included in the analysis.

CONCLUSIONS

Chemotherapy with 5-FU or capecitabine in CRC patients does not affect conduction system, LV structural parameters, and systolic function measured by LVEF, nor is it associated with cardiovascular events during the subsequent 12 months.

Chemotherapy with 5-FU or capecitabine in CRC patients may trigger subtle changes in myocardial performance, which are solely detectable by tissue Doppler echocardiography after 12 months.

Transient QT prolongation is observed during CTX and resolves after CTX cessation.

Conflict of interest: *none declared*

References

1. Raporty Krajowej Bazy Danych Nowotworowych Centrum Onkologii Instytutu w Warszawie, http://epid.coi.waw.pl/krn/, dostęp 24.02.2016].
2. Sobin L, Gospodarowicz M, Wittekind C. Klasyfikacja nowotworów złośliwych. Via Medica, Gdańsk 2010.
3. Nowotwory układu pokarmowego. In: Potemski P, Polkowski W. eds. Zalecenia postępowania diagnostyczno-terapeutycznego

w nowotworach złośliwych 2013. Via Medica, Gdańsk, 2013; 103–210.
4. Korniluk J, Wcisło G, Nurzyński P et al. Leczenie uzupełniające raka jelita grubego. Współczesna Onkologia, 2006; 10: 139–140.
5. Lang RM, Bierig M, Devereux RB, et al. American Society of Echocardiography's Nomenclature and Standards Committee, Task Force on Chamber Quantification, American College of Cardiology Echocardiography Committee, American Heart Association, European Association of Echocardiography, European Society of Cardiology. Recommendations for chamber quantification. Eur J Echocardiogr. 2006; 7(2): 79–108, doi: 10.1016/j.euje.2005.12.014, indexed in Pubmed: 16458610.
6. Kasprzak JD, Hoffman P, Płońska E, et al. Echokardiografia w praktyce klinicznej — Standardy Sekcji Echokardiografii Polskiego Towarzystwa Kardiologicznego 2007. Kardiol Pol, 2007; 65: 1142–1162.
7. Kasprzak JD, Kabłak-Ziembicka A, Mizia-Stec K, et al. Standardy kardiologiczne 2012 okiem echokardiografisty. Medical Tribune Polska, Warszawa, 2012.
8. Balloni L, Porta C, Rossi S, et al. Left ventricular function in colon cancer patients receiving adjuvant fluoro-folate chemotherapy: an echocardiographic study. Oncol Rep. 2000; 7(4): 887–890, doi: 10.3892/or.7.4.887, indexed in Pubmed: 10854564.
9. de Forni M, Malet-Martino MC, Jaillais P, et al. Cardiotoxicity of high-dose continuous infusion fluorouracil: a prospective clinical study. J Clin Oncol. 1992; 10(11): 1795–1801, doi: 10.1200/jco.1992.10.11.1795, indexed in Pubmed: 1403060.
10. Lang RM, Bierig M, Devereux RB 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. J Am Soc Echocardiogr, 2015; 28: 1–39.
11. Grandi AM, Pinotti G, Morandi E, et al. Noninvasive evaluation of cardiotoxicity of 5-fluorouracil and low doses of folinic acid: a one-year follow-up study. Ann Oncol. 1997; 8(7): 705–708, indexed in Pubmed: 9296228.
12. Saif MW, Shah MM, Shah AR. Fluoropyrimidine-associated cardiotoxicity: revisited. Expert Opin Drug Saf. 2009; 8(2): 191–202, doi:10.1517/14740330902733961, indexed in Pubmed: 19309247.
13. Grunwald MR, Howie L, Diaz LA. Takotsubo cardiomyopathy and Fluorouracil: case report and review of the literature. J Clin Oncol. 2012; 30(2): e11–e14, doi: 10.1200/JCO.2011.38.5278, indexed in Pubmed: 22147738.
14. Qasem A, Bin Abdulhak AA, Aly A, et al. Capecitabine-Induced Takotsubo Cardiomyopathy: A Case Report and Literature Review. Am J Ther. 2016; 23(5): e1188–e1192, doi:10.1097/MJT.0000000000000134, indexed in Pubmed: 25549075.
15. Kosmas C, Kallistratos MS, Kopterides P, et al. Cardiotoxicity of fluoropyrimidines in different schedules of administration: a prospective study. J Cancer Res Clin Oncol. 2008; 134(1): 75–82, doi: 10.1007/s00432-007-0250-9, indexed in Pubmed: 17636329.
16. Polk A, Vistisen K, Vaage-Nilsen M, et al. A systematic review of the pathophysiology of 5-fluorouracil-induced cardiotoxicity. BMC Pharmacol Toxicol. 2014; 15: 47, doi: 10.1186/2050-6511-15-47, indexed in Pubmed: 25186061.
17. Stewart T, Pavlakis N, Ward M. Cardiotoxicity with 5-fluorouracil and capecitabine: more than just vasospastic angina. Intern Med J. 2010; 40(4): 303–307, doi: 10.1111/j.1445-5994.2009.02144.x, indexed in Pubmed: 20529041.
18. Zamorano JL, Lancellotti P, Rodriguez Muñoz D, et al. Authors/Task Force Members, ESC Committee for Practice Guidelines (CPG):. 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 Heart J. 2016; 37(36): 2768–2801, doi: 10.1093/eurheartj/ehw211, indexed in Pubmed: 27567406.

Cite this article as: Płońska-Gościniak E, Różewicz M, Kasprzak J, et al. Tissue Doppler echocardiography detects subclinical left ventricular dysfunction in patients undergoing chemotherapy for colon cancer: insights from ONCOECHO multicentre study. Kardiol Pol. 2017; 75(2): 150–156. doi: 10.5603/KP.a2016.0163.

Subkliniczna dysfunkcja lewej komory wykryta metodą doplera tkankowego u pacjentów poddanych chemioterapii stosowanej w raku jelita grubego: wieloośrodkowe badanie ONCOECHO

Edyta Płońska-Gościniak[1], Monika Różewicz[2], Jarosław Kasprzak[3], Andrzej Wojtarowicz[1], Katarzyna Mizia-Stec[4], Tomasz Hryniewiecki[1], Piotr Pysz[4], Andrzej Kułach[4], Artur Bodys[5], Violetta Sulżyc[1], Wojciech Braksator[6], Andrzej Szyszka[7], Beata Zaborska[8], Adrianna Gościńska-Szmagała[9], Maciej Siński[6], Dariusz Kosior[10, 11], Sebastian Szmit[12], Ilona Kowalik[2], Zbigniew Gąsior[4]

[1]Pomorski Uniwersytet Medyczny, Szczecin; [2]Instytut Kardiologii, Warszawa; [3]Uniwersytet Medyczny w Łodzi, Łódź; [4]Śląski Uniwersytet Medyczny, Katowice; [5]Wojewódzki Szpital Specjalistyczny, Lublin; [6]Warszawski Uniwersytet Medyczny, Warszawa; [7]Uniwersytet Medyczny w Poznaniu, Poznań; [8]Centrum Medyczne Kształcenia Podyplomowego, Warszawa; [9]Polsko-Amerykańskie Kliniki Serca, Tychy; [10]Centralny Szpital Kliniczny Ministerstwa Spraw Wewnętrznych i Administracji, Warszawa; [11]Instytut Medycyny Doświadczalnej i Klinicznej im. M. Mossakowskiego, Polska Akademia Nauk, Warszawa; [12]Klinika Krążenia Płucnego i Chorób Zakrzepowo-Zatorowych, Centrum Medyczne Kształcenia Podyplomowego, Otwock

Streszczenie

Wstęp: Rak jelita grubego (CRC) jest jednym z najczęściej występujących nowotworów na świecie. W Polsce znajduje się na trzeciej pozycji wśród mężczyzn oraz na drugiej pozycji wśród kobiet pod względem zachorowań na nowotwory. Rola chemioterapii w leczeniu CRC zależy od stopnia zaawansowania nowotworu. Chemioterapię uzupełniającą stosuje się zawsze w III stopniu zaawansowania, a także w II stadium zaawansowania klinicznego przy obecności czynników ryzyka.

Cel: Celem niniejszej pracy była ocena występowania wczesnych powikłań sercowych u chorych włączonych do badania ONCOECHO w latach 2012–2014, leczonych chemioterapią z powodu CRC. W ramach badania potencjalnej kardiotoksyczności chemioterapii oceniano funkcję skurczową i rozkurczową mięśnia sercowego, zaburzenia rytmu i przewodzenia oraz występowanie niekorzystnych zdarzeń sercowo-naczyniowych.

Metody: Do 12-miesięcznej obserwacji włączono 25 pacjentów z CRC (12 kobiet, średnia wieku 61,3 roku [35–76 lat]), poddanych 6-miesięcznej chemioterapii adjuwantowej. Spośród badanych 13 chorych stosowało chemioterapię opartą na 5-fluorouracylu (5-FU), a pozostałych 12 pacjentów — terapię w schemacie opartym na kapecytabinie. Ocenę przeprowadzono wyjściowo oraz w 3., 6. i 12. miesiącu od rozpoczęcia leczenia. Analiza obejmowała obecność zaburzeń rytmu i przewodzenia, funkcję skurczową i rozkurczową mięśnia sercowego oraz występowanie zdarzeń sercowo-naczyniowych.

Wyniki: Po 12 miesiącach obserwacji niektóre parametry czynności lewej komory (LV) (S'IVS, S'lat i E'sept) uległy pogorszeniu. Frakcja wyrzutowa (EF) i wymiary jam serca pozostały niezmienione. Zmiany parametrów LV uwidocznione metodą doplera tkankowego po 12 miesiącach były niezależne od stosowanego schematu chemioterapii; nie wykazano również zależności między zmianami tych parametrów a stosowaniem inhibitorów konwertazy angiotensyny i beta-adrenolityków.

Wnioski: Stosowanie chemioterapii w CRC nie wpływa na parametry strukturalne ani klasyczne parametry czynności skurczowej LV (LVEF). Może jednak wywoływać subtelne pogorszenie zarówno czynności skurczowej, jak i rozkurczowej mięśnia sercowego wykrywalne przy użyciu doplera tkanowego po 12 miesiącach obserwacji, a także przejściowe wydłużenie odcinka QT ustępujące po zakończeniu chemioterapii.

Słowa kluczowe: echocardiografia, rak jelita grubego, kardiotoksyczność, chemioterapia

Kardiol Pol 2017; 75, 2: 150–156

Adres do korespondencji:
dr n. med. Andrzej Kułach, Śląski Uniwersytet Medyczny, ul. Ziołowa 47, 40–635 Katowice, Poland, e-mail: andrzejkulach@gmail.com
Praca wpłynęła: 08.07.2016 r. **Zaakceptowana do druku:** 04.10.2016 r. **Data publikacji AoP:** 17.11.2016 r.