Kardiologia Polska 2015; 73, 9: 730–739; DOI: 10.5603/KP.a2015.0071 ISSN 0022–9032

ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

# Assessment of risk factors for mortality in patients with cardiovascular disease and a history of treatment for malignancy

Jarosław Rydzek[1, 2], Zbigniew T. Gąsior[3], Józefa Dąbek[3], Jerzy Wojnar[4], Michał Skrzypek[5]

[1]Świętokrzyskie Centre of Cardiology, Kielce, Poland
[2]Voivodship Polyclinical Hospital, Czestochowa, Poland
[3]Department of Cardiology, SHS, Medical University of Silesia, Katowice, Poland
[4]Department of Internal Medicine and Oncologic Chemotherapy, SMK, Medical University of Silesia, Katowice, Poland
[5]Department of Biostatistics, SPDLM, Medical University of Silesia, Katowice, Poland

## Abstract

**Background:** Patients with advanced cancer after radio- and/or chemotherapy are increasingly commonly hospitalised in cardiology units due to coexisting cardiovascular diseases (CVD). A rational assessment of mortality risk is an important part of patient preparation for invasive cardiac procedures. One disadvantage of cardiac risk scores is the fact that malignancies are not taken into account. At present, accurate estimation of life expectancy is possible in up to 20% of patients with an advanced malignancy.

**Aim:** To evaluate the effect of selected clinical parameters on survival of patients with CVD and coexisting lung or breast cancer after radio- and/or chemotherapy. An additional aim was to identify patients with a high probability of surviving a year in a good general clinical condition.

**Methods:** The study group involved 326 subjects with established CVD and lung cancer (small-cell or non-small-cell) or breast cancer who were selected from the group of 7818 patients receiving palliative care in the Palium hospice in Czestochowa, Poland, in 2008–2012. The obtained data were collected in a database and subjected to a statistical analysis.

**Results:** The strongest factors associated with an increased risk of death among patients with CVD and coexisting advanced lung or breast cancer after chemo- and/or radiotherapy were the type and stage of malignancy, functional status according to the ECOG classification, and the presence of cachexia. Other factors that had a significant effect on survival included higher severity of heart failure symptoms as evaluated by the New York Heart Association class, decreased left ventricular ejection fraction, presence of ischaemic heart disease, chronic obstructive pulmonary disease, fasting hyperglycaemia, and the severity of fatigue, nausea, and pain. When the effects of drug treatment on survival were analysed, significantly increased survival was observed in patients treated with angiotensin-converting enzyme inhibitors while diuretic and glucocorticosteroid use was associated with decreased survival. Among the evaluated groups of patients with CVD and advanced malignancy after radio- and/or chemotherapy, the highest probability of surviving a year in a relatively good general clinical condition was noted in patients with stage 3 breast cancer without cachexia, ischaemic heart disease and persistent somatic symptoms who were treated with tamoxifen, angiotensin-converting enzyme inhibitors and megestrol acetate.

**Conclusions:** This is the first study that evaluated the combined effect of oncological and cardiovascular risk factors on survival of patients with CVD and coexisting cancer after radio- and/or chemotherapy treatment. When the three groups of cancer patients with different prognosis were compared, the study revealed varying effects of each factor depending on the underlying malignancy. The analysis confirmed the significance of the cumulative risk. The present study showed that malignancy-related prognostic factors are important in the context of cardiac evaluation and treatment of cancer patients. It also showed that further research is needed to clarify these issues.

**Key words:** malignancy, cardiovascular diseases, prognosis, therapy

Kardiol Pol 2015; 73, 9: 730–739

**Address for correspondence:**
Prof. Zbigniew T. Gąsior, Department of Cardiology, SHS, Medical University of Silesia, ul. Ziołowa 45, 40–635 Katowice, Poland, e-mail: zgasior@sum.edu.pl
**Received:** 22.10.2014 **Accepted:** 23.02.2015 **Available as AoP:** 25.03.2015

## INTRODUCTION

Patients with an advanced cancer after oncologic treatment are increasingly commonly hospitalised in cardiology units due to coexisting cardiovascular diseases (CVD). Thus, there is an increasing need for various invasive procedures, and patient selection for invasive treatment becomes more complex. A rational assessment of mortality risk is an important part of patient preparation for invasive cardiac procedures. This is particularly important in case of procedures that lead to long-term prognostic benefits.

Life expectancy over 1 year is an important factor when choosing the type of cardiac resynchronisation therapy device and implanting a cardioverter-defibrillator. As indicated by the guidelines, it is also of major importance when selecting patient for surgical myocardial revascularisation or transcutaneous aortic valve implantation. It is also among major factors to be considered when contemplating fibrinolytic therapy for acute proximal deep vein thrombosis, and making decisions regarding angioplasty and stenting.

In current cardiology practice, mortality risk scores have become an essential component of patient selection for invasive procedures. The most commonly used cardiac risk scores include GRACE, SEATTLE, EuroSCORE, and STS. However, these commonly used clinical tools do not include malignancy and oncologic treatment in the diagnostic and therapeutic process, leading to an increased debate among experts regarding limitations of the currently used risk scores and the rationale for their improvement and update [1].

Estimation of 1-year survival is most challenging in patients with an advanced malignancy. At about 1 year before dying, a patient with malignancy is usually in a better condition than a patient with diabetes, previous stroke, chronic heart failure, or chronic obstructive pulmonary disease (COPD), while during the terminal month of life, the functional status of a patient with malignancy is usually worse compared to patients with other chronic disease [2]. Patients with an advanced malignancy are at an increased risk of adverse cardiovascular (CV) outcomes, but their short life expectancy often precludes invasive cardiac treatment.

In clinical practice, it is important to answer the question whether specific therapy will bring objective benefits including prolongation of life and improvement of the quality of life. At present, accurate estimation of life expectancy is possible in up to 20% of patients with an advanced malignancy [3–5]. Studies indicate that patients with an advanced malignancy may be, sometimes incorrectly, denied optimal cardiac therapy based on underestimated prognostic factors. On the other hand, use of too invasive diagnostic and therapeutic procedures, often contributing to patient discomfort, may be not justified from the ethical point of view.

Careful evaluation of prognostic factors in patients with an advanced malignancy treated with radio- and/or chemotherapy and concomitant CVD may result in better therapeutic and diagnostic decision.

The main aim of the study was to evaluate the effect of selected clinical parameters on survival of patients with CVD and coexisting lung or breast cancer treated with radio- and/or chemotherapy. An additional aim was to identify patients with a high probability of surviving a year in a good general clinical condition.

## METHODS

### *Study group*

We studied 326 patients with established CVD and breast or lung cancer (small cell or non-small cell) treated with radio- and/or chemotherapy who were selected from the group of 7818 patients receiving palliative care in the Palium hospice in Czestochowa, Poland, in 2008–2012. The patients were divided into three groups depending on the underlying malignancy: breast cancer (BC — 99 patients), non-small cell lung cancer (NSCLC — 196 patients), and small cell lung cancer (SCLC — 31 patients).

### *Study plan*

This prospective case-control study included evaluation of survival in the study group in relation to:

- the type of malignancy and its severity;
- concomitant CVD including ischaemic heart disease (IHD), hypertension, atrial fibrillation, and the severity of heart failure symptoms as evaluated using the New York Heart Association (NYHA) classification;
- other common concomitant diseases: COPD, diabetes, and fasting hyperglycaemia;
- selected prognostic factors of an established value in malignancies: functional status evaluated using the Eastern Cooperative Oncology Group (ECOG) scale, somatic factors such as severity of dyspnoea, pain evaluated using the visual analogue scale, severity of nausea, fatigue evaluated using the Likert scale, and the presence of cachexia;
- selected prognostic factors of an established value in CVD: resting heart rate and left ventricular ejection fraction (LVEF);
- drug treatment used, including angiotensin-converting enzyme inhibitors (ACEI), beta-blockers, megestrol acetate, diuretics, and dexamethasone in all three patient groups, and tamoxifen in patients with BC.

The study protocol included:

- detailed history;
- physical examination;
- blood pressure and heart rate measurements according to the European Society of Hypertension guidelines;
- fasting capillary blood glucose level measurements using the Accu-Chek Active glucose meter (device precision in accordance with the DIN EN ISO 15197:2003 standard).

Patients were evaluated three times: at baseline, after 3 weeks, and within 7 days before death.

### Statistical analysis

Statistical analyses were performed using the SAS package, version 9.2 (SAS Institute Inc., Gary, NC), with the level of statistical significance at $\alpha = 0.05$. Normal distribution of quantitative variables was verified using the Shapiro-Wilk test. Parameters of quantitative variable distribution were compared using the Student *t* test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables with categorisation to two groups, and analysis of variance for normally distributed variables and the Kruskal-Wallis test for non-normally distributed variables with categorisation to more than two groups. Univariate survival analysis was performed using the Kaplan-Meier approach for qualitative descriptors and the Cox regression model for quantitative descriptors. Multivariate analysis was used to summarise simple univariate analysis using the Cox survival analysis with non-proportional hazard function, as the rule of proportional hazards, a prerequisite for the proportional hazard Cox model, was violated. Calculations were performed using a macro prepared for the SAS program. Multivariate model included variables with $p < 0.02$ in univariate analyses, with their stepwise elimination until only significant ($p < 0.05$) variables remained in the model.

To evaluate the effect of the evaluated factors on the likelihood of surviving at least 1 year, univariate logistic regression analysis was used and receiver operating characteristic curves were plotted.

Table 1. Characteristics of the study group including demographic data, type of malignancy, concomitant conditions, and drug treatment used

| | |
|---|---|
| Age [years] | 67.8 ± 10 (42–89 years) |
| Gender: | |
| Women | 150 (46%) |
| Men | 176 (54%) |
| Type of malignancy: | |
| Breast cancer | 99 (30.5%) |
| Non-small cell lung cancer | 196 (60%) |
| Small cell lung cancer | 31 (9.5%) |
| Concomitant conditions: | |
| Ischaemic heart disease | 252 (77.3%) |
| Hypertension | 88 (26.9%) |
| Atrial fibrillation | 141 (43.2%) |
| Diabetes | 20 (6.1%) |
| COPD | 153 (47%) |
| Cachexia | 214 (65.6%) |
| Medications: | |
| ACEI | 117 (35.8%) |
| Beta-blocker | 72 (22.0%) |
| Tamoxifene | 33 (10.1%) |
| Megestrol acetate | 156 (47.8%) |
| Diuretic | 167 (51.2%) |
| Dexamethasone | 162 (49.6%) |

ACEI — angiotensin-converting enzyme inhibitor; COPD — chronic obstructive pulmonary disease

## RESULTS

### Study group characteristics

We studied 326 patients aged 42 to 89 years. The mean age of women did not differ significant from that of men (67.1 vs. 68.3 years; $p = 0.36$). No age differences were also noted between patients with various malignancies.

Tables below show basic characteristics of the study group of patients with a malignancy and concomitant CVD, including dichotomous variables (Table 1), ordinal variables (Table 2), and quantitative variables (Table 3).

The median survival from the diagnosis of a malignancy was 96, 12, and 4.8 months in patients with BC, NSCLC and SCLC, respectively ($p < 0.01$). Patient survival in relation to the type of malignancy is shown in Figure 1.

The median survival from admission to the hospice was 2.5, 1.6, and 1.2 in patients with BC, NSCLC and SCLC, respectively ($p < 0.01$). Patient survival from admission to the hospice in relation to the type of malignancy is shown in Figure 2.

Multivariate analysis of parameters associated with survival in patients with BC and concomitant CVD, with corresponding relative hazard values, is shown in Figure 3.

In patients with BC, variables associated with increased survival included treatment with ACEI, megestrol acetate, and tamoxifen ($p < 0.01$), while only a nonsignificant trend was noted for beta-blocker used compared to non-use.

Analysis of survival predictors in patients with NSCLC and CVD is shown in Figure 4.

Reduced survival was associated with more advanced malignancy, higher ECOG class, higher severity of somatic complaints, higher NYHA class, presence of IHD, higher resting heart rate, lower LVEF, fasting hyperglycaemia, concomitant COPD, and use of diuretics and dexamethasone.

Prognostic factors in patients with SCLC are shown in Figure 5.

In patients with SCLC, factors associated with significantly shorter survival included more advanced malignancy, higher ECOG class, higher severity of persisting somatic complaints, higher heart failure severity as evaluated by the NYHA class, presence of IHD, atrial fibrillation, higher resting heart rate, lower LVEF, concomitant COPD, non-use of ACEI, and use of diuretics. In this patient group, treatment with beta-blockers and megestrol acetate was associated with only a trend towards increased survival ($p = 0.58$).

Table 2. Basic descriptive statistics for ordinal variables

| NYHA class | Measurement 1 (n = 326) | | | Measurement 2 (n = 228) | | | Measurement 3 (n = 220) | | |
|---|---|---|---|---|---|---|---|---|---|
| I | 37 (11.3%) | | | 31 (13.6%) | | | – | | |
| II | 62 (19.0%) | | | 43 (18.9%) | | | – | | |
| III | 95 (29.1%) | | | 75 (32.9%) | | | 24 (10.9%) | | |
| IV | 132 (40.5%) | | | 79 (34.6%) | | | 196 (89.1%) | | |
| **Blood pressure [mm Hg]** | **Measurement 1 (n = 326)** | | | **Measurement 2 (n = 232)** | | | **Measurement 3 (n = 224)** | | |
| | **Range** | **Mean** | **Median** | **Range** | **Mean** | **Median** | **Range** | **Mean** | **Median** |
| Systolic | 70–160 | 120 ± 16.8 | 120 | 90–170 | 126.3 ± 15.4 | 130 | 80–170 | 132.9 ± 15.9 | 137.5 |
| Diastolic | 50–100 | 73.2 ± 10.1 | 70 | 60–100 | 79.2 ± 8.2 | 80 | 50–110 | 85.1 ± 9.8 | 80 |
| **ECOG** | **Measurement 1 (n = 326)** | | | **Measurement 2 (n = 261)** | | | **Measurement 3 (n = 251)** | | |
| 0 | – | | | – | | | – | | |
| 1 | 35 (10.7%) | | | 32 (12.3%) | | | | | |
| 2 | 75 (23.0%) | | | 66 (25.3%) | | | | | |
| 3 | 87 (26.7%) | | | 63 (24.1%) | | | 52 (20.7%) | | |
| 4 | 129 (39.6%) | | | 100 (38.3%) | | | 199 (79.3%) | | |
| 5 | -- | | | 65 | | | 10 | | |
| **Severity of fatigue on admission to the hospice [Likert scale] (n = 326)** | | | | | | | | | |
| Not present at all | | | | | | | 31 (9.5%) | | |
| Rather not present | | | | | | | 50 (15.3%) | | |
| Marked fatigue | | | | | | | 93 (28.5%) | | |
| Constant fatigue | | | | | | | 152 (46.7%) | | |
| **Nausea [Likert scale] (n = 326)** | | | | | | | | | |
| 1 | | | | | | | 98 (30.0%) | | |
| 2 | | | | | | | 86 (26.4%) | | |
| 3 | | | | | | | 110 (33.7%) | | |
| 4 | | | | | | | 32 (9.8%) | | |

ECOG — Eastern Cooperative Oncology Group; NYHA — New York Heart Association

Table 3. Basic descriptive statistics for quantitative data

| Parameter (number of observations) | Range | Mean ± SD | Median |
|---|---|---|---|
| LVEF [%] (n = 189) | 20–70 | 36.7 ± 10.9 | 35 |
| Fasting glucose [mg/dL] (n = 326) | 60–330 | 115.3 ± 43.1 | 100 |
| Resting heart rate [bpm]: | | | |
| Measurement 1 (n = 326) | 60–130 | 82.5 ± 13.8 | 80 |
| Measurement 2 (n = 229) | 64–110 | 82.5 ± 9.4 | 80 |
| Measurement 3 (n = 219) | 68–120 | 96.4 ± 10 | 96 |

Measurements of LVEF and blood glucose were performed at baseline, and heart rate was measured during each visit. LVEF — left ventricular fraction; SD — standard deviation

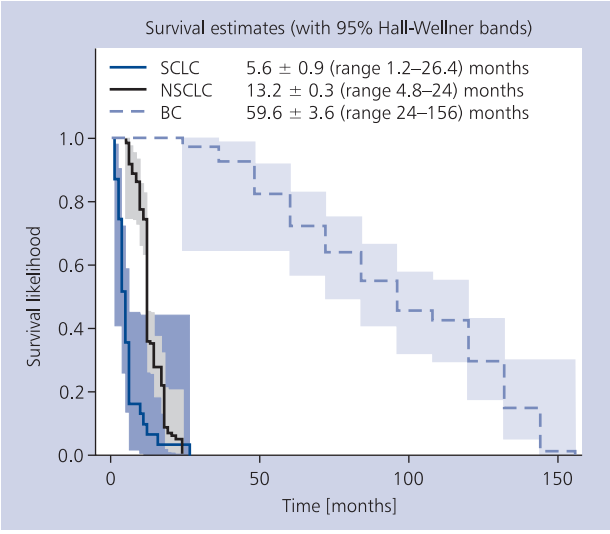


Figure 1. Survival from the diagnosis of malignancy with 95% confidence intervals in relation to the type of malignancy; BC — breast cancer; NSCLC — non-small cell lung cancer; SCLC — small cell lung cancer

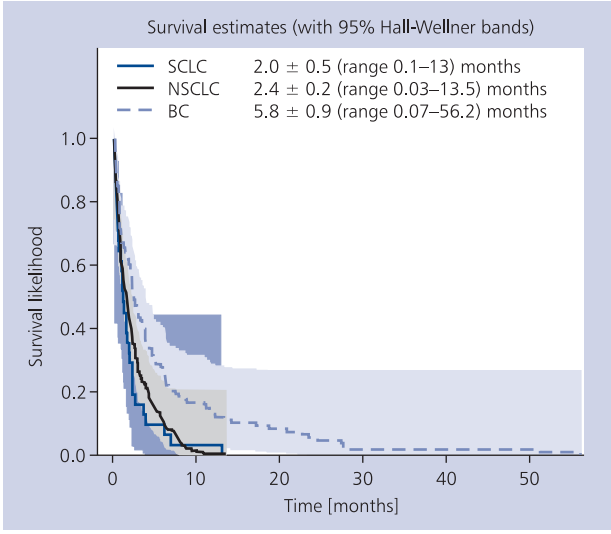


Figure 2. Survival from the admission to the hospice in relation to the type of malignancy; BC — breast cancer; NSCLC — non-small cell lung cancer; SCLC — small cell lung cancer

Our analysis of the study group identified factors associated with the highest likelihood of surviving 1 year. These included the diagnosis of stage III BC, no IHD, grade 1 severity of nausea, treatment with tamoxifen, megestrol acetate, and ACEI, and non-use of dexamethasone.

## DISCUSSION

Malignancy and previous oncologic therapy are factors potentially associated with increased 1-year mortality and should be taken into account when selecting patients for invasive CV treatment. Appropriate therapeutic decision must be based on the cumulative risk related not only to the primary CV disorder but also concomitant conditions and symptoms, their treatment, and interactions between these factors.

In our study, we compared three groups of patients with different malignancies with varying prognosis and showed different effects of the evaluated factors depending on specific malignancy (Figs. 3–5).

The presence of coronary artery disease had a significant effect on survival in all three groups of patients with an advanced malignancy. Deaths due to myocardial infarction were documented in 6 patients in the study group. Symptomatic coronary artery disease may be a reason for, sometimes incorrect, denial of appropriate oncologic therapy, while previous oncologic therapy may lead to premature coronary artery disease [6]. On the other hand, myocardial revascularisation may be necessary before appropriate oncologic treatment.

Higher severity of heart failure as evaluated by the NYHA class significantly increased mortality among patients with an advanced malignancy in our study group. In most patients with a history of malignancy who were hospitalised for cardiac reasons, heart failure resulted from the underlying CVD. Drug treatment of heart failure may rapidly reduce its clinical symptoms and have a beneficial prognostic effect.

We found no significant effect of hypertension on survival in the study group. This might have resulted from a relatively short duration of follow-up.

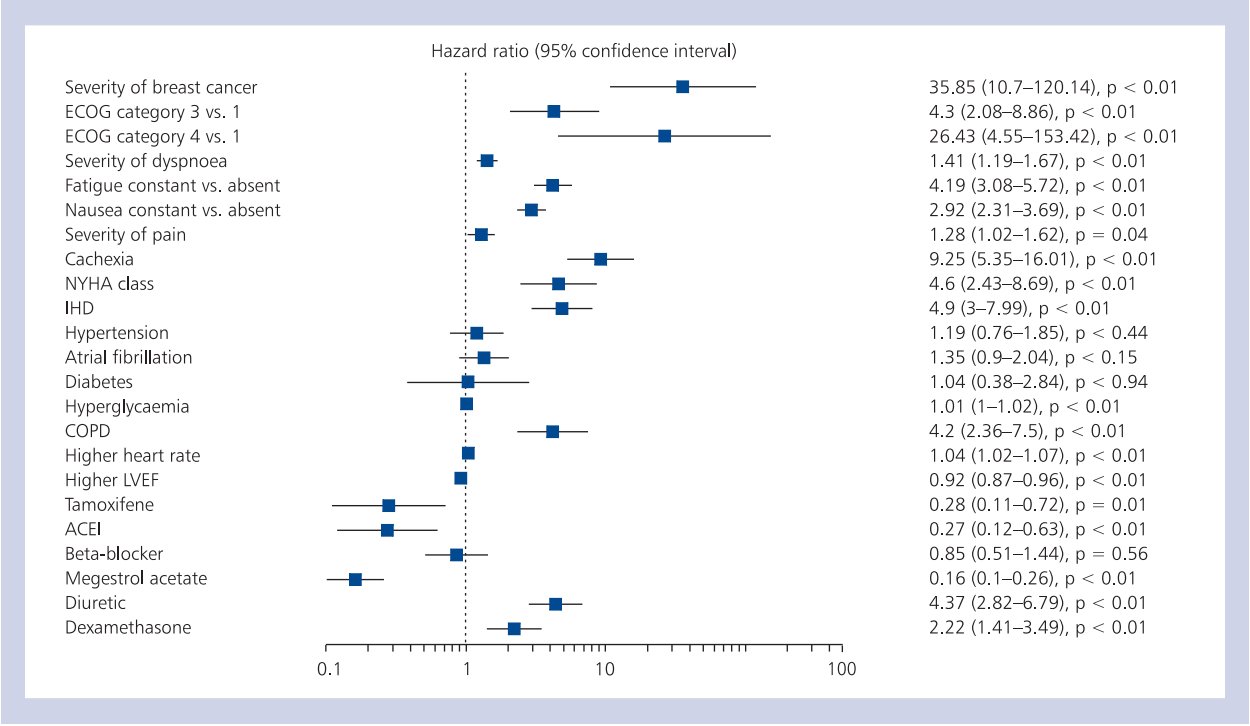


Figure 3. Hazard ratios (HR) for breast cancer (model including all cases, n = 99); ACEI — angiotensin-converting enzyme inhibitor; COPD — chronic obstructive pulmonary disease; ECOG — Eastern Cooperative Oncology Group; NYHA — New York Heart Association; IHD — ischaemic heart disease; LVEF — left ventricular ejection fraction

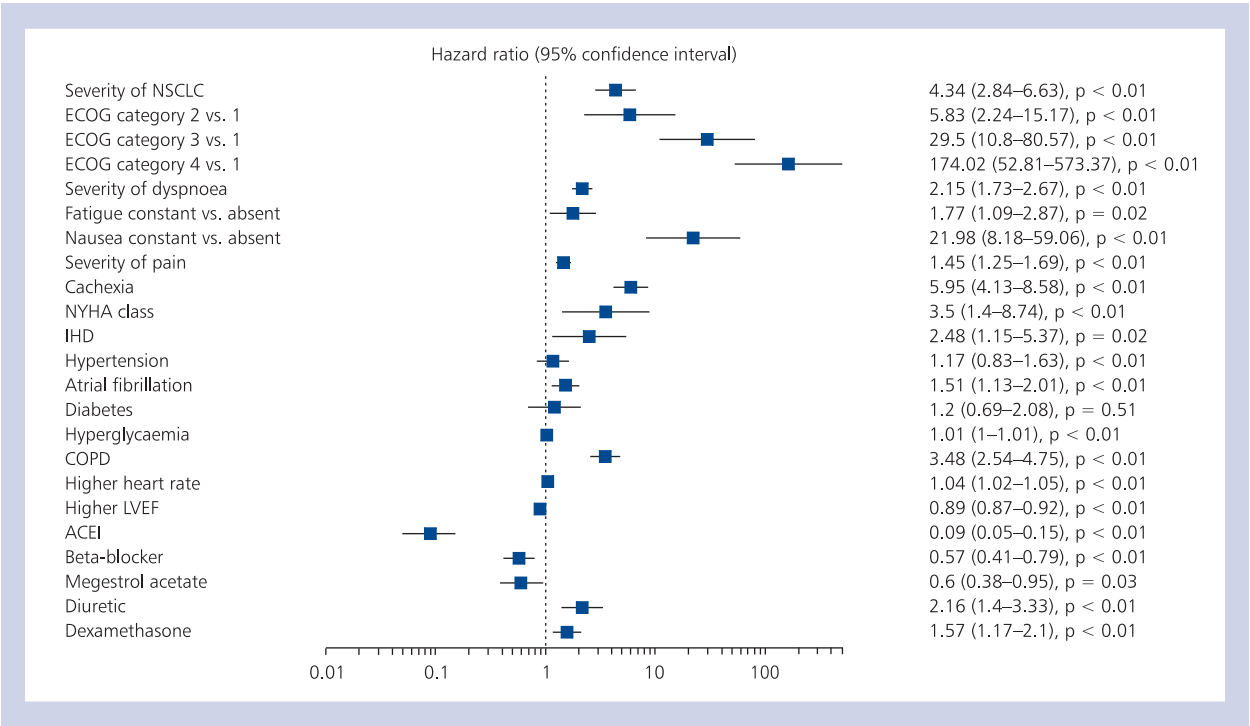


Figure 4. Hazard ratios (HR) for non-small cell lung cancer (NSCLC) (model including all cases, n = 196); ACEI — angiotensin-converting enzyme inhibitor; COPD — chronic obstructive pulmonary disease; ECOG — Eastern Cooperative Oncology Group; NYHA — New York Heart Association; IHD — ischaemic heart disease; LVEF — left ventricular ejection fraction

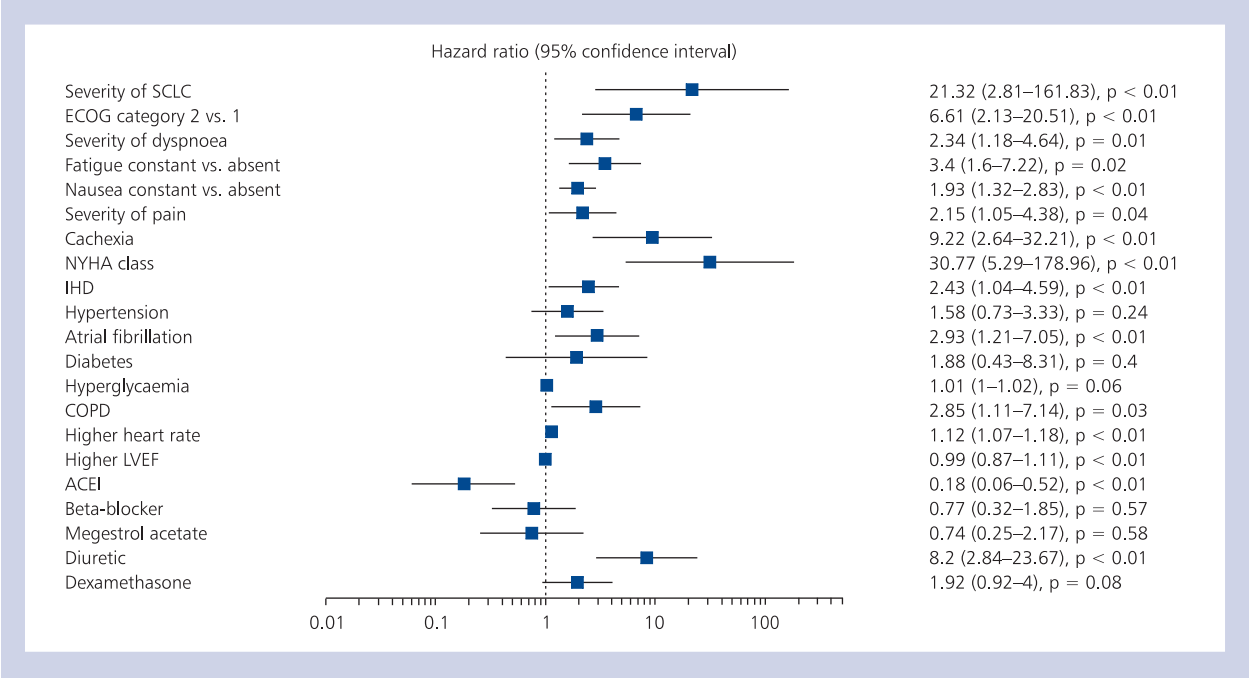


Figure 5. Hazard ratios (HR) for small cell lung cancer (SCLC) (n = 31); ACEI — angiotensin-converting enzyme inhibitor; COPD — chronic obstructive pulmonary disease; ECOG — Eastern Cooperative Oncology Group; NYHA — New York Heart Association; IHD — ischaemic heart disease; LVEF — left ventricular ejection fraction

Atrial fibrillation is associated with twice increased mortality regardless of other established factors contributing to mortality [7, 8]. In our analysis, mortality was increased in patients with atrial fibrillation but the difference in BC patients was not significant.

In a prognostic study of patients with colon cancer and diabetes reported by Feng et al. [9], reduced 5-year survival was shown in diabetic patients. In our study, a nonsignificant trend was noted for an increased mortality among patients with diabetes in all three study groups.

Concomitant COPD had a significant effect on reduced survival in patients with an advanced malignancy. Lung cancer is more common in COPD patients, and COPD is present in about half of patients with lung cancer. In addition, bronchoconstriction is a risk factor for lung cancer in non-smokers. In an 8-year follow-up study of 5648 Canadian patients, Huiart et al. [10] showed then the medical and social burden of CVD associated with COPD is greater than that associated with COPD itself. Morbidity and mortality was also increased compared to the general population.

Most evaluated factors affected the functional status of patients with CVD and an advanced malignancy after oncologic treatment. A high predictive value of the ECOG score in our study reflects the effect of cumulative risk. In the study by Schuit et al. [11], functional status was found to be the strongest factor affecting survival of patients with an advanced malignancy.

Most patients with a malignancy show vexing somatic symptoms that significantly affect the quality of life [12–14]. In our analysis, we found a significant effect of the severity of symptoms associated with malignancy, such as fatigue, nausea, pain, dyspnoea, and cachexia on survival of patients with an advanced malignancy.

Resting heart rate is an established prognostic factor [15, 16]. A relations between resting heart rate and total and CV mortality was found in patients with stable angina, acute coronary syndromes, heart failure, stroke, and hypertension. LVEF is also an established prognostic factor. A previous study suggested that oncologic treatment may lead to impairment of left ventricular function [17]. In our study, a significant effect of both resting heart rate and LVEF on survival was noted in all three patient groups.

Postoperative tamoxifene therapy increases 10-year survival of BC patients by about 11%. In our analysis, we found a significant effect of tamoxifene on survival of BC patients (HR 0.28). The effect of tamoxifene therapy on the CV system in BC patients has also been a subject of a clinical analysis which showed a reduction of CV mortality compared to non-users [18]. Other metaanalyses also showed a reduced risk of myocardial infarction among women receiving tamoxifene [19, 20].

In our study in patients with CVD and an advanced malignancy after oncologic treatment, increased survival was noted among patients receiving ACEI. Two key randomised trials (CONSENSUS, SOLVD) showed that ACEI treatment

reduces mortality among heart failure patients [21, 22]. Early ACEI therapy reduces chemotherapy-induced myocardial damage and protects from anthracycline cardiomyopathy.

Interestingly, beta-blockers may affect migration of cancer cells. Based on laboratory data suggesting an effect of beta-blockers on cancer cell mobility and migration, Powe et al. [23] performed a study in 466 oncologic patients treated with beta-blockers and showed a reduced risk of remote metastases and increased 5-year survival among BC patients treated with beta-blockers. Also in our study, an increased survival among patients treated with beta-blockers was noted in all three study groups but this effect was significant only in the NSCLC group. When interpreting these results, a relatively short duration of follow-up should be taken into account.

In our study, an increased survival was found among patients receiving megestrol acetate in the BC (HR 0.16) and NSCLC (HR 0.6) group, while only a trend towards increased survival was noted among SCLC patients ($p = 0.58$). Literature review did not show an effect of megestrol acetate on increased survival among patients with malignancy-related cachexia, and the effect of this drug on the quality of life remains debatable [24].

Interesting data were obtained when we analysed the effect of diuretic treatment on survival in patients with CVD and an advanced malignancy. In our study, survival among patients who required diuretics was significantly reduced compared to those patients who were not treated with diuretics. When interpreting these findings, it is likely that patients who required diuretic therapy were in a worse general clinical condition resulting from more severe heart failure.

Worse survival was noted among BC and NSCLC patients who required dexamethasone treatment, while only a trend towards reduced survival was noted in SCLC patients. It has been reported that dexamethasone may increase cancer cell resistance to the cytotoxic effect of oncological drugs [25]. However, worse clinical condition of patients treated with dexamethasone should be also taken into account when interpreting these data.

In summary, we found varying effects of the evaluated factors in the three groups of patients with malignancies characterised by different prognosis.

Our analysis confirmed the significance of the cumulative risk. The present study showed that malignancy-related prognostic factors are important in the context of cardiac evaluation and treatment of cancer patients. Further research is needed to elucidate these issues more clearly.

### *Limitations of the study*

Our study had several major limitations. A relatively short duration of follow-up until death significantly reduced the ability to identify the effect of CVD risk factors on survival in our patients. In addition, confounding variables, e.g. anaemia, and heterogeneity of malignancies might have had a significant effect on survival in our study group. Conventional oncologic therapy and the response to this treatment clearly affected values of the evaluated clinical parameters and prognosis, and limited data presented on this issue reflect our focus more on cardiac than oncologic aspects. We were unable to verify causes of death as autopsies were not performed. Finally, our study was an observational one.

## CONCLUSIONS

1. Independent predictors of survival of patients with CVD and breast or lung cancer after previous oncologic therapy include the type of malignancy and its clinical severity.
2. Negative predictors of survival in the study group were low ECOG functional status, heart failure severity as evaluated by the NYHA classification, significantly reduced LVEF, the presence of IHD, fasting hyperglycaemia, the presence of COPD, significant fatigue, nausea and pain, and the presence of malignancy-related cachexia.
3. Among the evaluated patients with CVD and an advanced malignancy after previous chemo- and/or radiotherapy, the highest likelihood of 1-year survival in a relatively good functional status was noted in patients with breast cancer, without cachexia, IHD and persisting somatic complaints, who were treated with tamoxifene, ACEI and megestrol acetate.

***Conflict of interest:*** *none declared*

### *References*

1. Rosenhek R, Iung B, Tornos P et al. ESC Working Group on Valvular Heart Disease Position Paper: assessing the risk of interventions in patients with valvular heart disease. Eur Heart J, 2012; 33: 822–828. doi: 10.1093/eurheartj/ehr061.
2. Teno JM, Weitzen S, Fennel ML Mor V. Dying trajectory in the last year of life. Does cancer trajectory fit other diseases? J Palliat Med, 2001; 4: 457–464.
3. Christakis N, Lamont E. Extent and determinants of error in doctors prognosis in terminally ill patients: prospective cohort study. BMJ, 2000; 320: 469–472.
4. Maltoni M, Caraceni A, Brunelli C et al. Prognostic Factors in Advanced Cancer Patients: Evidence-Based Clinical Recommendations: a Study by the Steering Committee of the European Association for Palliative Care. J Clin Oncol, 2005; 23: 6240–6248.
5. Glare P, Virik K, Jones M et al. A systematic review of physicians' survival predictions in terminally ill cancer patients. BMJ, 2004; 327: 195–205.
6. Wożakowska-Kapłon B, Szymczyk R, Buda S, Biskup P. Radiotherapy and chemotherapy for oncological diseases — unappreciated risk factors for coronary artery disease? Acute coronary syndrome in 3 women after radiotherapy and chemotherapy: case reports. Kardiol Pol, 2008; 66: 415–419.
7. Heeringa J, van der Kuip DA, Hofman A et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J, 2006; 27: 949–953.
8. Naccarelli GV, Varker H, Lin J, Schulman KL. Increasing prevalence of atrial fibrillation and flutter in the United States. Am J Cardiol, 2009; 104: 1534–1539. doi: 10.1016/j.amjcard.2009.07.022.
9. Feng JI, Zhou XM, Mao WM. Prognostic analysis of colorectal cancer patients with diabetes mellitus in China: the Experience of a Single Institution. Adv Clin Exp Med, 2011; 20: 473–480.

10. Huiart L, Ernst P, Suissa S. Cardiovascular morbidity and mortality in COPD. Chest, 2005; 128: 2640–2646.
11. Schuit KW, Sleijfer DT, Meijler WJ et al. Symptoms and functional status of patients with disseminated cancer visiting outpatient departments. J Pain Symptom Manage, 1998; 16: 290–297.
12. Teunissen SC, Graeff A, Haes HC, Voest E. Prognostic significance of symptom of hospitalised advanced cancer patients. Eur J Cancer, 2006; 42: 2510–2516.
13. Vitetta L, Kenner D, Kissane D, Sali A. Clinical outcomes in terminally 111 patients admitted to hospice care: diagnostic and therapeutic interventions. J Palliat Care, 2001; 17: 69–77.
14. Vigano A, Bruera E, Suarez-Almazor ME. Terminal cancer syndrome: myth or reality? J Palliat Care, 1999; 15: 32–39.
15. Palatini P, Benetos A, Grassi G et al. Identification and management of the hypertensive patient with elevated heart rate: statement of a European Society of Hypertension Consensus Meeting. J Hypertens, 2006; 24: 603–610.
16. Fox K, Ford I, Steg PG et al. Ivabradine for patients with stable coronary artery disease and left-ventricular systolic dysfunction (BEAUTIFUL): a randomised, double-blind, placebo-controlled trial. Lancet, 2008; 372: 807–816. doi: 10.1016/S0140-6736(08)61170-8.
17. Mizia-Stec K, Gościńska A, Mizia M et al. Anthracycline chemotherapy impairs the structure and diastolic function of the left ventricle and induces negative arterial remodelling. Kardiol Pol, 2013; 71: 681–690. doi: 10.5603/KP.2013.0154.
18. Clarke MJ. Tamoxifen for early breast cancer. Cochrane Database Syst Rev, 2008; 8: CD000486. doi: 10.1002/14651858.
19. Buzdar A, Chlebowski R, Cuzick J et al. Defining the role of aromatase inhibitors in the adjuvant endocrine treatment of early breast cancer. Curr Med Res Opin, 2006; 22: 1575–1585.
20. Braithwaite RS, Chlebowski RT, Lau J et al. Meta-analysis of vascular and neoplastic events associated with tamoxifen. J Gen Intern Med, 2003; 18: 937–947.
21. The CONSENSUS Trial Study Group. Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). N Engl J Med, 1987; 316: 1429–1435.
22. The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. N Engl J Med, 1991; 325: 293–302.
23. Powe DG, Voss MJ, Zänker KS et al. Beta-blocker drug therapy reduces secondary cancer formation in breast cancer and improves cancer specific survival. Oncotarget, 2010; 1: 628–638.
24. Berenstein EG, Oritz Z. Megestrol acetate for the treatment of anorexia-cachexia syndrome (review). Cochrane Database Syst Rev, 2005; 2: CD004310.
25. Chen YX, Wang Y, Fu CC et al. Dexamethasone enhances cell resistance to chemotherapy by increasing adhesion to extracellular matrix in human ovarian cancer cells. Endocr Relat Cancer, 2010; 17: 39–50. doi: 10.1677/ERC-08-0296.

**Cite this article as:** Rydzek J, Gąsior ZT, Dąbek J et al. Assessment of risk factors for mortality in patients with cardiovascular disease and a history of treatment for malignancy. Kardiol Pol, 2015; 73: 730–739. doi: 10.5603/KP.a2015.0071.

# Ocena czynników ryzyka zgonu pacjentów z chorobami układu sercowo-naczyniowego i współistniejącym nowotworem złośliwym po przebytym leczeniu onkologicznym

Jarosław Rydzek[1, 2], Zbigniew T. Gąsior[3], Józefa Dąbek[3], Jerzy Wojnar[4], Michał Skrzypek[5]

[1]Świętokrzyskie Centrum Kardiologii, Kielce
[2]Wojewódzki Szpital Zespolony, Częstochowa
[3]Katedra i Klinika Kardiologii, WNoZ, Śląski Uniwersytet Medyczny, Katowice
[4]Katedra i Klinika Chorób Wewnętrznych i Chemioterapii Onkologicznej, WLK, Śląski Uniwersytet Medyczny, Katowice
[5]Katedra Epidemiologii i Biostatystyki, Zakład Biostatystyki, WFzOML, Śląski Uniwersytet Medyczny, Katowice

## Streszczenie

**Wstęp:** Pacjenci z zaawansowanym nowotworem po przebytej terapii onkologicznej coraz częściej są hospitalizowani na oddziałach kardiologicznych z powodu schorzeń układu sercowo-naczyniowego. Ważnym elementem przygotowania chorego do procedur inwazyjnych jest racjonalna ocena ryzyka jego zgonu. Wadą stosowanych w kardiologii skal ryzyka jest nieuwzględnianie choroby nowotworowej. Prawidłowe oszacowanie prognozowanego czasu przeżycia pacjentów z chorobami układu sercowo-naczyniowego i zaawansowaną chorobą nowotworową dotyczy około 20% pacjentów.

**Cel:** Zasadniczym celem pracy była ocena wpływu wybranych parametrów klinicznych na czas przeżycia u pacjentów z chorobą układu sercowo-naczyniowego oraz rakiem płuca lub piersi po przebytym leczeniu onkologicznym. Celem dodatkowym była identyfikacja chorych z dużym prawdopodobieństwem przeżycia roku w dobrym stanie ogólnym.

**Metody:** Badaniem objęto 326 pacjentów z rozpoznaną chorobą układu sercowo-naczyniowego i rakiem piersi lub płuca (drobnokomórkowy, niedrobnokomórkowy), wyselekcjonowanych z grupy 7818 chorych, będących w latach 2008–2012 pod opieką częstochowskiego hospicjum ,,Palium''. Otrzymane dane zebrano w arkuszu kalkulacyjnym i poddano analizie statystycznej.

**Wyniki:** Najsilniejszymi czynnikami zwiększającymi ryzyko zgonu pacjentów z chorobą sercowo-naczyniową oraz zaawansowanym rakiem piersi lub płuca po przebytej chemio- i/lub radioterapii były: rodzaj nowotworu, zaawansowanie choroby nowotworowej, stopień upośledzenia sprawności wg ECOG oraz obecność wyniszczenia. Istotny wpływ na skrócenie czasu przeżycia miały również: zaawansowanie objawów niewydolności serca wg NYHA, znaczne zmniejszenie frakcji wyrzutowej lewej komory, obecność choroby niedokrwiennej serca, obecność przewlekłej obturacyjnej choroby płuc, hiperglikemia na czczo, znaczne osłabienie, nudności i ból. W analizie wpływu zastosowanej farmakoterapii na czas przeżycia badanych chorych istotnie dłuższe przeżycie zaobserwowano u pacjentów stosujących inhibitory konwertazy angiotensyny (ACE), natomiast przyjmowanie diuretyków i steroidów wiązało się z krótszym czasem przeżycia. Największe szanse na roczne przeżycie w stosunkowo dobrym stanie funkcjonalnym wśród analizowanych chorych wykazywały pacjentki z rakiem piersi w III stopniu zaawansowania klinicznego, bez kacheksji, bez choroby niedokrwiennej serca i uporczywych dolegliwości somatycznych oraz poddane terapii tamoksyfenem, inhibitorem ACE i octanem megestrolu.

**Wnioski:** Wykonana analiza jest pierwszym badaniem oceniającym jednoczesny wpływ na przeżycie kardiologicznych i onkologicznych czynników ryzyka u pacjentów z współistniejącym schorzeniem układu sercowo-naczyniowego oraz nowotworem złośliwym po radio- i/lub chemioterapii. Porównując trzy grupy chorych na nowotwory o zróżnicowanym rokowaniu, wykazano odmienny wpływ poszczególnych czynników zależny od choroby podstawowej. Analiza potwierdziła istotność ryzyka skumulowanego. W niniejszej pracy pokazano istotne aspekty zastosowania czynników prognostycznych przeżycia we współczesnej kardiologii wśród pacjentów z nowotworem, jak również potrzebę przeprowadzenia dalszych badań w celu pełniejszego wyjaśnienia omawianych zagadnień.

**Słowa kluczowe:** nowotwory, choroby układu sercowo-naczyniowego, prognozowanie, terapia

Kardiol Pol 2015; 73, 9: 730–739

**Adres do korespondencji:**
prof. dr hab. n. med. Zbigniew T. Gąsior, Katedra i Klinika Kardiologii, WNoZ, Śląski Uniwersytet Medyczny, ul. Ziołowa 45, 40–635 Katowice, e-mail: zgasior@sum.edu.pl
**Praca wpłynęła:** 22.10.2014 r. **Zaakceptowana do druku:** 23.02.2015 r. **Data publikacji AoP:** 25.03.2015 r.