



New primary non-breast malignancies after breast cancer: ten years single institution follow-up

NATALIJA DEDIĆ PLAVETIĆ^{1,2}
MARINA BARIĆ¹
PAULA PODOLSKI¹
TANJA BADOVINAC-ČRNJEVIĆ¹
DAMIR VRBANEC^{1,2}

¹ Department of Medical Oncology, University Hospital Center Zagreb, Croatia

² University of Zagreb, School of Medicine, Croatia

Correspondence:

Marina Barić, MD
Department of Medical Oncology
University Hospital Center Zagreb
Kišpatićeva 12, HR- 10 000 Zagreb, Croatia
E-mail: marina.baric11@gmail.com

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Abstract

Background and Purpose: Breast cancer is the most common cancer in Croatian women. Due to improved diagnostic and treatment options women with breast cancer now live longer, which increases their risk of developing new primary malignancies. The aim of this study was to establish incidence of new primary non-breast malignancies after breast cancer diagnosis.

Material and Methods: In the study cohort that included 215 consecutive patients treated for early breast cancer at University Hospital Center Zagreb, Croatia, 12 patients (5.58%) have developed new primary non-breast malignancy within nearly ten year follow-up.

Results: Although the majority of studies found gynecological cancers to be the most common cancer site of new primary non-breast malignancies after breast cancer diagnosis, in our study most patients developed colorectal cancer.

Conclusion: This is particularly interesting if you take into account that after breast cancer colorectal cancer is the second most common cancer in Croatian women. In order to stratify the risk for the development of new primary tumors it is necessary to further investigate the interaction of various factors that are thought to influence the evolution of tumors.

INTRODUCTION

According to the data provided by Croatian National Cancer Registry for 2011, there were 2094 new cases of breast cancer in Croatia. That number represents 22% of all newly diagnosed cases making it most common cancer site in women (1). Advances in early detection and improved treatment modalities in the developed countries led to the fact that nearly 90% of women diagnosed and treated for breast cancer live more than 5 years after the initial diagnosis. Longer life expectancy of the patients with breast cancer also increases the risk of development of new primary non-breast malignancies.

The purpose of this study was to determine incidence of new primary non-breast malignancies after breast cancer diagnosis.

PATIENTS AND METHODS

The study cohort included 215 consecutive patients treated for early breast cancer at University Hospital Center Zagreb, Croatia, from September of 2002 until September of 2003, evaluated prospectively. Annotated clinical follow-up information was available for all patients. The

TABLE 1

New primary non-breast cancers in 215 breast cancer survivors – distribution by cancer site.

New primary by site	Number	Share %	Time after breast cancer diagnosis, range in months (mean value)
Colorectal cancer	7	58.3	20–120 (73)
Ovarian cancer	2	16.7	21–102 (61.5)
Non-Hodgkin lymphoma	2	16.7	59–61 (60)
Other*	1	8.3	15 (15)
Total	12	100	15–120 (64)

* parotid gland malignancy

median follow-up was 117 months (9.8 years), ranging from 7.8 to 129 months. Over 75% of studied patients received adjuvant chemotherapy, mostly anthracycline based, and over 65% hormonal therapy.

RESULTS

In the study population, 12 patients (5.58%) have developed new primary non-breast malignancy within nearly ten year follow-up. This result is very similar to other studies with data that one of twenty women with breast cancer will develop a new primary non-breast malignancy within 10 years from the diagnosis.

Colorectal cancer was the most common new primary cancer accounting for 58.3% (7 of 12) of all new primary non-breast cancers, followed by ovarian cancer with a share of 16.7% (2 of 12) and non-Hodgkin lymphoma also with a share of 16.7% (2 of 12). There was one case of parotid gland tumor, with a share of 8,3%.

DISCUSSION

A significant number of studies found gynecologic cancers to be the most common new primary tumor in breast cancer survivors (2, 3, 4). For example, Dogan et al study found ovarian cancers as the most frequently occurred in a greater study cohort, but shorter follow-up period (3.6 years) (5). It should be noted that median age of breast cancer diagnosis in our study was 56 years, compared to median age of 49 in Dogan's study. We find this difference important, considering that Denmark study on 14151 patient has shown that both age and menopausal status at breast cancer diagnosis are important predictors of site of new metachronous primary, with significantly elevated risk for endometrial and ovarian cancers in premenopausal women (6). Younger cohort age in Dogans study was concordant with higher frequency of ovarian cancer.

However, the fact that we found colorectal cancer to be the most common second malignancy is consistent with epidemiological data for whole population in Croatia. According to Croatian National Cancer Registry, in 2011 colorectal cancer was the second common cancer site in Croatian women population, representing 13% of all new

cancer cases (1). It's interesting that this high incidence is also confirmed in our study in the population of breast cancer survivors. This is in contrast with some earlier studies where large risk reduction was seen for colorectal cancer. It was explained by the fact that adjuvant chemotherapy regimens frequently comprised fluorouracil, cytotoxic drug also effective in colon cancer treatment. Further studies on larger breast cancers survivor cohorts are needed to determine if there is also an excess risk for colorectal cancer in comparison to risk of general women population in Croatia.

Close follow-up of breast cancer survivors population requires a multidisciplinary approach. With respect to the current findings, physicians should pay careful attention to gynecological, gastrointestinal, and urinary tract symptoms. In order to stratify the risk for the development of new primary tumors it is necessary to further investigate the interaction of various factors that are thought to influence the evolvement of tumors, such as genetics, environment and unwanted side effects of breast cancer treatment.

REFERENCES

1. Croatian National Cancer Registry, Croatian Institute For Public Health, accessed 6.5.2014. Available from: http://hzjz.hr/wp-content/uploads/2013/11/rak_2011.pdf
2. MOLINA-MONTES E, POLLÁN M, PAYER T, MOLINA E, DÁVILA-ARIAS C, SÁNCHEZ MJ 2013 Risk of second primary cancer among women with breast cancer: a population-based study in Granada (Spain). *Gynecol Oncol* 130(2): 340-5
3. YADAV B S, SHARMA S C, PATEL F D, GHOSHAL S, KAPOOR R, KUMAR R 2009 Nonbreast second malignancies after treatment of primary breast cancer. *Int J Radiat Oncol Biol Phys* 73(5): 1489-92
4. YI M, CORMIER J N, XING Y, GIORDANO S H, CHAI C, MERIC-BERNSTAM F, VLASTOS G, KUERER H M, MIRZA N Q, BUCHHOLZ T A, HUNT K K 2013 Other primary malignancies in breast cancer patients treated with breast conserving surgery and radiation therapy. *Ann Surg Oncol* 20(5): 1514-21
5. DOGAN E, AKSOY S, DIZDAR O, DEDE D S, ARSLAN C, OZISKI Y, ALTUNDAG K 2010 Other malignancies in patients with breast cancer: a single institute experience. *Med Oncol* 27(4):1434-5
6. LANGBALLE R, OLSEN J H, ANDERSSON M, MELLEM-KJÆR L 2011 Risk for second primary non-breast cancer in pre- and postmenopausal women with breast cancer not treated with chemotherapy, radiotherapy or endocrine therapy. *Eur J Cancer* 47(6): 946-52