Biuletyn Polskiego
Towarzystwa Onkologicznego
NOWOTWORY
2023, tom 8, nr 6, 484–485

ISSN: 2543–5248, e-ISSN: 2543–8077
www.nowotwory.edu.pl

VIA MEDICA

Edytorial / Editorial

Rak piersi / Breast cancer

Does an apple a day keep the doctor away? Cardiovascular prevention in breast cancer patients

Michał Jarząb

Breast Cancer Center, Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch, Gliwice, Poland

The aphorism "An apple a day keeps the doctor away", first in print coined as "Eat an apple on going to bed and you'll keep the doctor from earning his bread" as early as in 1866, has been tested by rigorous evidence-based approach [1]. Although the study was published on April Fool's Day in 2015 in JAMA Internal Medicine, it seriously tested the hypothesis that keeping to the rule above reduces the necessity of at least one visit per year. Unfortunately, the proverb did not pass the strict EBM threshold, although the study suggested that each-day-apple-consumers used fewer prescription medicines than the general population.

Dyrbuś et al. in this issue of *Nowotwory. Journal of Oncology* describe the variety of pharmacological preventive methods applied in contemporary cardio-oncology (*Pharmacological prevention methods in patients with cardiovascular disease with breast cancer – when, how, and for whom?*). The authors define when, how and for whom cardioprevention shall be applied; my insight here relates mainly to the question "Why?".

Since the beginning of cancer therapy, cardiotoxicity has been an issue of utmost importance. The first reports were related to post-anthracycline heart failure; the low magnitude of QRS complexes in ECG examination was the first considered, obviously not an early feature of this complication [2]. Polish oncological and cardiological community recognised the necessity of adequate patient monitoring. For example, Malinowski et al. analysed ECG data of patients treated by breast radiation between 1985 and 2002 and described the excess of ischemic features in patients with left-sided disease [3]. More recently, Kufel-Grabowska et al. studied the cardiotoxicity in patients treated with adjuvant trastuzumab after earlier anthracycline therapy [4]. The authors find significant differences in NT-proBNP concentrations at a post-treatment follow-up visit in patients with cardiotoxicity, while no such association for cardiac troponin levels. We have our Polish cardioprevention trials, both completed, e.g. ramipril study of Cracow team [5] or ongoing -- studies financed by Agency of Medical Research (EMPACT in Warsaw, MAINSTREAM in Zabrze, see clinicaltrials.gov).

In 2023 we can identify early signs of cardiotoxicity evoked by anti-cancer therapy and diminish its impact with effective preventive strategies. It was proven by some trials, which I refer to as "first generation". In second-generation studies, the population of patients for the intervention was selected by a marker of cardiotoxicity, with a defined population of high-risk patients eligible (see the review of Dyrbuś et al. for references). There comes a question – is the optimised management bringing benefit to patients' overall health? This issue is of raising importance, as last year European Society of Cardiology published comprehensive guidelines on cardio-oncology, developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). The document shows a complicated landscape of current cardio-oncology, with numerous procedures and classification schemes; many oncological practices and centres have problems fully implementing the algorithms into patient management pathways.

We urgently need the trials of "third generation", where biomarkers/imaging strategies and pharmacological preven-

Jak cytować / How to cite:
Jarząb M. ***Does an apple a day keep the doctor away? Cardiovascular prevention in breast cancer patients.*** *NOWOTWORY J Oncol* 2023; 73: 402–403.

tive approaches are linked to the tailoring of cancer therapy. There are many ways to adjust the intensity of cancer treatment, either adapting it to the response/toxicity or trying to make a perfect fit a priori, before initiating therapy. In breast cancer, we could easily avoid anthracyclines in HER2-positive patients (however, sometimes for a price of excess fatigue or non-cardiac toxicity), we may try to spare from cardiac burden patients with luminal cancers (although avoiding radiation or chemotherapy is not as straightforward, especially in premenopausal patients, where the potential long-term toxicity might be of utmost importance). Finally, in triple-negative individuals, where we usually apply relatively aggressive chemotherapy, we could add anti-PD-L1 immunotherapy or leave the patient without this additional cardiac risk factor. However, we deeply do not understand, what is the survival impact of every one of these decisions on patient survival. When decreasing the intensity of oncological therapy will provide a net benefit due to better cardiac health? Cardiologists sometimes joke that it is easier to fix the heart than cure cancer; however, we all know from epidemiological data that the death toll of late cardiac toxicity among cancer survivors is substantial. It holds true not only for the old cytotoxic chemotherapy but also for many novel targeted treatments [6].

I invite the readers of the article prepared by colleagues from Zabrze to get acquainted with cardiopreventive strategies and to apply them as broadly as possible, with benefit to the cardiac health of our patients. There shall also be a time for reflection, how is cardiology shaping oncology nowadays? Will cardiac specialists fix our failures or instead provide a critical selection gateway to the treatment? It is evident that merging both approaches is potentially the most effective; how to test it in clinical trials? And last but not least, it is critically vital that trials of oncological therapies will be open for wisely selected high-risk cardiac patients; only then we could learn whether in such a setting modifying the oncological treatment in parallel with maximal cardioprotection and effective rescue strategies provide a net health benefit.

And coming back to the role of a healthy lifestyle. There will be a time for fourth-generation trials, comparing pharmacological interventions with proactive exercise, diet, psychotherapy, education approach and testing which patients benefit, as well as providing rational advice on how to mix these strategies and provide patient compliance.

Article information and declarations

Conflict of interest

None declared

Michał Jarząb
Maria Sklodowska-Curie National Research Institute of Oncology
Gliwice Branch
Breast Cancer Center
Wybrzeże Armii Krajowej 15
44-102 Gliwice, Poland
e-mail: michal.jarzab@gliwice.nio.gov.pl

Received: 17 Oct 2023
Accepted: 18 Oct 2023

References

1. Davis MA, Bynum JPW, Sirovich BE. Association between apple consumption and physician visits: appealing the conventional wisdom that an apple a day keeps the doctor away. JAMA Intern Med. 2015; 175(5): 777–783, doi: 10.1001/jamainternmed.2014.5466, indexed in Pubmed: 25822137.
2. Lefrak EA, Pitha J, Rosenheim S, et al. A clinicopathologic analysis of adriamycin cardiotoxicity. Cancer. 1973; 32(2): 302–314, doi: 10.1002/1097-0142(197308)32:2<302::aid-cncr2820320205>3.0.co;2-2, indexed in Pubmed: 4353012.
3. Malinowski Z, Skowrońska-Gardas A, Jodkiewicz Z, et al. Preliminary risk assessment of radiation-induced cardiac sequelae in breast cancer patients receiving adjuvant radiotherapy after breast conserving therapy. Nowotwory. 2004; 54(2): 108–113.
4. Kufel-Grabowska J, Katarzyński S, Szmit S, et al. Cardiotoxicity in patients with early breast cancer treated with adjuvant trastuzumab. Nowotwory. Journal of Oncology. 2022; 72(5): 288–293, doi: 10.5603/njo.a2022.0047.
5. Słowik A, Jagielski P, Potocki P, et al. Anthracycline-induced cardiotoxicity prevention with angiotensin-converting enzyme inhibitor ramipril in women with low-risk breast cancer: results of a prospective randomized study. Kardiol Pol. 2020; 78(2): 131–137, doi: 10.33963/KP.15163, indexed in Pubmed: 31995035.
6. Jagielska B, Tałasiewicz K, Czachowska A, et al. Are molecular target therapies limited by cardiotoxicity — causes and symptoms of cardiovascular damage. Nowotwory. Journal of Oncology. 2017; 67(1): 34–40, doi: 10.5603/njo.2017.0005.