© Wydawnictwo UR 2017
ISSN 2544-1361
doi: 10.15584/ejcem.2017.1.3

http://www.ejcem.ur.edu.pl/en/
European Journal of Clinical and Experimental Medicine
Eur J Clin Exp Med 2017; 15 (1): 18–23

ORIGINAL PAPER

Konrad Klekot [1(ABCDFG)], Barbara Zubelewicz-Szkodzińska [2(ADF)]

Bioactive food components in the diet of patients diagnosed with cancer

[1] Institute of Nursing and Health Sciences, Faculty of Medicine, University of Rzeszow
[2] Department of Nutrition-Related Disease Prevention, School of Public Health in Bytom, Medical University of Silesia in Katowice, Poland

ABSTRACT

Introduction. Cancer, after cardiovascular disease, is the second most common cause of death both in Poland and Europe, so it is important to investigate and search for dietary components with anti-cancer properties. Components which can modulate different stages of carcinogenesis through epigenetic process are called bioactive food components.

Aim. The aim of this study was to evaluate nutritional habits of patients diagnosed with cancer in terms of level of bioactive food components consumption.

Material and methods. A group of 123 patients diagnosed with cancer were enrolled the study. The study was conducted by means of an anonymous questionnaire on diet history prepared by the authors. Statistical analysis was performed using IBM SPSS software, statistical significance was adopted at the level of $p < 0.05$.

Results. Based on the results of the questionnaires, major risk factors that increase the prevalence of cancer disease were age (above 55 years) and increased BMI (the score indicated overweight or obesity). Additionally, it was observed that cancer diagnosis resulted in change of eating habits in approx. 61.8% of the participants. Enrolled patients mostly consumed inadequate amounts of green vegetables, legumes, green tea and whole grains before the diagnosis. Moreover, patients with breast and colorectal cancer were found to be more likely to consume more red meat in comparison to others.

– Both non-modifiable factors: age and modifiable ones: body weight and lifestyle influence morbidity.

– Most participants ate incorrectly before cancer diagnosis; diagnosis of the disease changed their eating habits.

Key words. cancer, bioactive food components, diet, nutrigenomics, epigenetics

Corresponding author: Konrad Klekot, Faculty of Medicine, University of Rzeszów, al. mjr. W. Kopisto 2 a, 35-310 Rzeszów, Polnad, tel. 601 884 116, e-mail: konrad.klekot@gmail.com

Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 30.12.2016 | Accepted: 14.03.2017
Publication date: June 2017

Klekot K, Zubelewicz-Szkodzińska B. *Bioactive food components in the diet of patients diagnosed with cancer*. Eur J Clin Exp Med. 2017;15 (1):18–23. doi: 10.15584/ejcem.2017.1.3

Introduction

Cancer, after cardiovascular disease, is the second most common cause of death both in Poland and Europe. According to the estimates of the European database – Health for All, cancer morbidity and mortality amount to 379 cases and 168 deaths per 100,000 people respectively.[1] In the coming years they are predicted to become the leading cause of death before the age of 65 in women and men.[2]

Recent scientific findings suggest that improper diet and lack of regular physical activity may contribute to 30-40% of diagnoses, therefore, apart from promotion of an active way of spending free time, dietary components that have anti-cancer properties are searched.[3,4] Food components that can affect the individual stages of carcinogenesis are referred to as bioactive food components. The best-known bioactive food components with potential anti-cancer properties include: isothiocyanates contained in cruciferous vegetables, diallyl disulfide derived from allium vegetables, catechins found in green tea, soy isoflavones, and certain vitamins and minerals.[5,6] It is believed that bioactive food components can prevent the onset of cancer by overlapping mechanisms of action such as oxygen free radical scavenging, inhibition of cellular proliferation, expression of oncogens and induction of suppressor gene expression, regulation of gene expression, cell cycle and induction of apoptosis, modulation of detoxifying enzymes, stimulation of immune system, regulation of hormone metabolism, angiogenesis, and antiviral, and antimicrobial activity.[7] A recent review claims that their protective action may be related to epigenetic modifications, i.e. changes in the genes functioning that are not accompanied by changes in the DNA sequence itself. Major mammalian epigenetic control mechanisms include DNA methylation, histone protein modifications, and RNA interference (RNAi).[8]

DNA methylation involves the addition of methyl groups to the nitrogen-containing base of nucleotides most often in position 5 of cytosine, which is possible thanks to specialized enzymes – DNA methyltransferases (DNMT). This process plays an important role in regulation of gene expression, since methylation in the promoter area (mainly CpG dinucleotides) prevents the attachment of transcriptional proteins, but also other transcription machinery components.[9,10]

Another control mechanism is histone modification, connected with post-translational changes of amino acid residues of histones, which are the alkaline proteins belonging to the nucleoprotein complex called chromatin. In the construction of histones such features can be distinguished as: the globular domain, C-carboxylic and N-amino acids end groups, which may be subject to various post-translational modifications e.g. methylation, acetylation, and phosphorylation. Such changes contribute to the formation of transcriptionally inactive heterochromatin or active euchromatin. Thanks to precise regulation, it is possible to inhibit and activate certain fragments of DNA. The best known post-translational histone modifications include acetylation carried out by histone acetyltransferase (HAT) with acetyl-CoA. As a result, the interaction of histone proteins with DNA is impaired and DNA groove becomes uncovered. Proteins that enable access of the transcription device can attach to the groove. The reverse process - deacetylation of histones is caused by histone deacetylase (HDAC) and leads to chromatin condensation and prevents the transcription device from functioning.[11]

The last least understood process is RNA interference (RNAi) in which small double-stranded RNA molecules (dsRNA) can initiate post-transcriptional gene inactivation. One type of small RNA molecule is the microRNA (miRNA). Scientific studies have demonstrated that mutations and disorders of miRNA expression occur in some cancers in humans, therefore, more and more attention is paid to them in the pathogenesis of neoplasms.[12,13]

In 2004, the complete human genome sequence was published. This discovery contributed to the development of nutrigenomics – a field of science exploring the influence of individual food components on regulation of gene expression. This regulation takes place by means of the epigenetic modifications described above, in which bioactive food components are involved.[14] Currently, they are believed to play an important role in the prevention and treatment of cancer.

Aim of the study

The aim of this study was to evaluate nutritional habits of patients diagnosed with cancer in terms of bioactive food components consumption. In order to meet this goal, the relationship between the frequency of consumption of products rich in bioactive food components and the Body Mass Index (BMI) (according to WHO, World Health Organization), sex, age and diagnosed cancer were also assessed. The questionnaire on dietary history was designed to assess the nutritional habits of patients before cancer diagnosis. In addition, the study attempted to assess the impact of cancer diagnosis on the change in eating habits.

Material and methods

123 patients (98 women and 25 men) who were diagnosed with cancer in the last 12 months were enrolled in the study. Questionnaires were collected in the Silesian Province (University Center for Ophthalmology and Oncology in Katowice, Starkiewicz Specialist Hospital in Dąbrowa Górnicza - Zagłębie Center of Oncology) and Podkarpackie Province (Markiewicz Podkarpackie Oncology Center in Brzozów). The inclusion criteria were as follows: cancer diagnosed in the last 12 months, clinical status allowing to complete the questionnaire, sufficient patient memory in terms of eating habits before cancer

diagnosis, and patient's informed consent to participate in the study.

The study was conducted using the anonymous dietary history questionnaire prepared by the authors, which contained 26 closed questions about the frequency and amount of bioactive food components consumed prior to cancer diagnosis. The questionnaire was validated prior to a proper survey.

For the purpose of this paper, the following tests: V Kramera (tables 2x3, 4x5, etc.), Phi (2x2 tables) were used for the questions on nominal scales to verify the hypotheses. In case of questions in measurement scales, Tb - Kendall or Tc - Kendall tests were used – the first one for tables 2x2, the second one 2x3, 4x5, etc. In case the crosstab consisted of the nominal and order scale, statistics were read at the lower level.[15] All measures of relationship strength were normalized in order to be represented by the values in the range of 0–1, therefore, 0–0.29 was a weak relationship, 0.30–0.49 – a moderate relationship, 0.5–1 – a strong relationship respectively.[16] Statistical analysis was performed using the SPSS software and relationships were assumed statistically significant when $p < 0.05$.

Results

The age structure of the examined patients indicated that 90% of them were above the age of 55, while the patients aged 55 to 64 accounted for 50% of all respondents.

Exceeded norm of BMI was found in 67.5% of the studied patients. BMI score in 41.5% of the subjects indicated overweight and in 26% obesity. Statistical analysis showed no statistically significant difference ($p = 0.09$) between sexes (male, female) and BMI (underweight, normal weight, overweight, obesity), and no statistically significant difference ($p = 0.37$) between the type of diagnosed cancer (breast cancer, colorectal cancer, other cancer) and BMI score (Table1).

More than a half of the respondents (51%) were diagnosed with breast cancer, while the second most commonly diagnosed cancer in the group of the respondents was colorectal cancer (24%). Lung cancer (6%), pancreatic cancer (5%) and cancer of other organs (14%) were much less frequent.

Diagnosis of cancer disease affected dietary habits in 61.8% of the patients, however, statistical analysis showed no statistically significant difference ($p = 0.24$) between sex and the influence of cancer diagnosis on changes in eating habits (Table 2).

At the next stage of the study, the frequency of consumption of individual products rich in bioactive food components was analyzed. There was a correlation between the consumption of cauliflower ($p = 0.007$), cabbage ($p = 0.03$), onion ($p = 0.01$) and BMI. The obese consumed these vegetables before diagnosing the cancer more often than the rest. There was no statistically significant relationship between the frequency

Table 1. BMI score in the group of men and women

			Sex		Total
			Female	Male	
BMI	Underweight	N	1	2	3
		%	1.0%	8.0%	2.4%
	Normal weight	N	27	10	37
		%	27.6%	40.0%	30.1%
	Overweight	N	42	9	51
		%	42.9%	36.0%	41.5%
	Obesity	N	28	4	32
		%	28.6%	16.0%	26.0%
Total		N	98	25	123
		%	100.0%	100.0%	100. 0%
		p = 0.09			

Table 2. The influence of cancer diagnosis on the change of eating habits with respect to the sex

			Sex		Total
			Female	Female	
Did the diagnosis of the disease affect the change in eating habits?	YES	N	58	18	76
		%	59.2%	72.0%	61.8%
	NO	N	40	7	47
		%	40.8%	28.0%	38.2%
Total		N	98	25	123
		%	100.0%	100.0%	100.0%
		p = 0.24			

of consumption of individual products and the diagnosis of cancer.

Statistical analysis showed that among the respondents, women were more likely to eat healthy products before diagnosis of the disease than men ($p = 0.009$). These products included brassica, alliaceous, legumes vegetables, green tea and whole meal products.

In addition, it was found that 46% of the respondents never or very seldom consumed green tea. Of all patients, only 15% declared drinking it at least once a day.

A half of the respondents (50%) declared red wine consumption several times a month, while 5% consumed it several times a week. Among the patients who consumed red wine, the majority (71%) consumed one glass (150 ml).

Products containing the bioactive components which were most commonly consumed by the patients before the diagnosis of the disease include cabbage, onion, garlic and leek. At least once a week the cabbage was eaten by 53%; onions 77%; garlic 56%; 49% and cauliflower 34%.

Vegetables such as spinach, broccoli and legumes were less popular: 14, 27 and 20% of the respondents respectively ate them at least once a week. Kale and asparagus were the least frequently consumed, as they were absent from the diet, of 88% and 72% of the patients respectively.

Discussion

It is believed that one of the non-modifiable factors increasing the risk of cancer is age. Data from Cancer Research UK - one of the world's largest organizations advocating cancer research and awareness suggests that in the United Kingdom between 2010 and 2012, an average of 80% of breast cancer cases were diagnosed in women over 50 years of age, with about one in four diagnosed in the UK after the age of 75. According to statistics on colorectal cancer of the same organization in 2010–2012, as many as 95% of diagnosed cases of this disease occurred in people over 50 years of age and 43% over 75 years of age.[17] Our results reflect the data presented, since the age structure of the respondents shows that as many as 90% of them are over 55, which confirms the fact that age is an important non-modifiable factor increasing the risk of cancer.

Another factor that positively correlates with the increase in incidence of certain types of cancer (e.g. breast, colon, ovarian, and pancreatic cancer) is BMI.[3] Some publications claim that the predicted increase in the risk of these types of cancers due to exceeded BMI ranges between 3% and 10% for the growth of this indicator.[18] In 2015, Lancet Oncology published a paper which estimated that in 2012 around 481,000 new cases of cancer in people over 30 in the world were caused by elevated BMI. In the group of the most vulnerable people are women and people living in developed and highly developed countries.[19] Our report indicated that BMI was above the norm in 67.5% of the respondents on the day of the survey, which may indicate BMI as a risk factor for the cancer.

One of the bioactive food ingredients that are responsible for modulating epigenetic processes at the level of DNA methylation and modification of histone protein are polyphenols. Gallus epigallocatechin (EGCG), found in green tea, belongs to polyphenols with well-known antioxidant and antitumor properties – especially in vitro and in animal models.[20] The conclusions of the review and meta-analysis are no longer so clear. In a Cochrane Library review published in 2009, which reviewed 23 cohort studies, 27 case studies and one randomized clinical trial, it was found that current scientific data are insufficient and contradictory to form binding recommendations for green tea consumption in the prevention of cancer. However, it has been further added that the indicated green tea intake is between 3 and 5 cups per day (up to 1200 ml), which provides 250 mg of catechins.[21] Although most current scientific research seem to support previous assumptions, it should be noted that ambiguous epidemiological results may be due to the fact that dietary polyphenols intake is relatively low compared to doses used in in vitro or in animal models. In addition, cancerogenous agents differ between populations, and green tea consumption may affect carcinogenesis only in specific cases.[22] Referring to the above-mentioned publications, it was observed that, despite ambiguous scientific evidence on the effect of green tea on the reduction of cancer risk, the group of the respondents was characterized by its very low consumption, only 15% of the patients consumed it once a day. In addition, the subjects who consumed green tea most often drank one cup a day.

One of the questions in our questionnaire focused on the consumption of red dry wine as a source of resveratrol in patients before the diagnosis of cancer. Only 5% of the patients consumed it several times a week, while half of the respondents declared red wine consumption several times a month. The patients identified the consumption of this alcoholic beverage with pro-health effects. Scientists believe that one of the most bioactive components found in red wine is a polyphenol-resveratrol compound. Although its role in the prevention of the cardiovascular diseases is well known, the impact on cancer prevention is no longer so clear. Current scientific evidence points to the chemopreventive effect of resveratrol in colorectal cancer which was evaluated in in vitro and in vivo studies. Animal models have also been shown to reduce the number of pre-cancerous lesions and some papers claim that preclinical studies also appear promising.[23] However, further research are required to increase the bioavailability and pharmacological properties of resveratrol, despite high absorption (75% of the administered dose), it is characterized by very low bioavailability (<1%) due to rapid metabolism in the intestines and the liver.[24] In addition, Advances in Nutrition published in 2016 a review which determined 1g as a therapeutic dose of resveratrol for a day. Such a dose can be found in about 505 liters of good

quality red wine, 2857 kg of dark chocolate, 2500 kg of apples or 795 kg of dark grapes. The quantities presented are impossible to be supplied with food.[25] Alcohol itself is considered to be a carcinogen. There is extensive scientific evidence that it increases the risk of oral, larynx, esophagus and liver cancers. However, red dry wine due to the increased content of bioactive food components is often treated as an alcoholic drink with health benefits. It should be remembered that patterns of consumption and changes in alcohol consumption are difficult to estimate. In addition, people who consume wine often lead a healthier lifestyle, and the effect of alcohol on health may in some studies be attributed to other interfering factors.[26] Based on the literature data, our data may suggest that low consumption of red wine among the respondents may be associated with worse eating habits in these people. On the other hand, bearing in mind that excessive alcohol consumption increases the risk of certain types of cancer, it may be concluded that the patient's eating habits were correct given only red wine consumption.

Definitely the most popular products containing bioactive food components among the patients were typical Polish dishes such as cabbage, onion, garlic or leeks. Brassicas besides vitamins (C, E, K, folate) and minerals contain substances called glucosinolates, which are sulfur-containing chemicals.[27] During the food processing, chewing and digestion, glucosinolates are decomposed to biologically active compounds, i.e. indoles, nitriles, thiocyanates and isothiocyanates. The most bioactive are indol-3-carbinol and sulforaphane. In animal models of breast, colon, lung, liver or stomach cancer, these two compounds protected cells from DNA damage, inactivated carcinogens, acted anti-inflammatory, antibacterial, antiviral, induced apoptosis, inhibited angiogenesis and metastasis.[28] As in above mentioned studies, the results of the study involving people are not unequivocal but promising. The meta-analysis and systematic review published in 2014 analyzing epidemiological studies describing the association between crucifers consumption and colon cancer development indicate that crucifers consumption is inversely correlated with the risk of colorectal cancer (OR = 0.84). The researchers have found that broccoli, which were less popular among the respondents, is particularly effective.[29] However, they underline that due to the low number of studies, strong conclusions cannot be formulated.[30] It is suspected that increased consumption of brassica vegetables may also reduce the risk of pancreatic, ovarian or prostate cancer.[31-33] Despite promising findings in literature, our study results showed that the consumption of cabbage ($p = 0.03$) and cauliflowers ($p = 0.007$) was significantly associated with obesity. This unexpected relationship may be, in our opinion caused by the traditions of Polish cuisine, where the vegetables are consumed with added fat or fatty foods. Such habits can contribute to overweight and obesity.

Allium family including onion, garlic, leek or chives are rich in bioactive components, among which scientists focus primarily on sulfur compounds. In recent years, some interesting papers have been published that assess the relationship between allium vegetables consumption and the risk of gastrointestinal cancer. Galeone et al. (2006) assessed the effect of Allium vegetables on the etiology of different types of cancer. Using data from Italian and Swiss clinical and control studies on onion and garlic consumption, the odds ratio was estimated using the multivariate regression model. The researchers found that the consumption of garlic and onions prevented colorectal cancer. The highest consumption of onions (≥7 servings a week) was associated with a reduction in the risk of colorectal cancer from OR 0.44. Moderate and high garlic consumption were also associated with a decrease in the risk of colorectal cancer, respectively from OR 0.88 and 0.74.[34] Despite unclear evidence, current literature reports indicate that intake of these vegetables may be particularly helpful in the prevention of gastrointestinal cancers. This information may be confirmed by randomized study.[35] As in the case of brassica family vegetables, our results showed that obese people more often than those with underweight, normal weight and overweight consumed onions before diagnosing cancer ($p = 0.01$). These results may suggest that apart from taking care of the proper content of bioactive food components in our diet, attention should be paid to its energy value.

Limitations

The authors are aware that the paper has some limitations. They include: a small and heterogeneous group of the respondents and lack of a control group, so it is advisable to continue research in this direction. The control group could be elderly people in the risk group but without cancer. The results of such studies would not only allow assessing the differences in the amount of bioactive food components between groups, but also help to determine the optimal dosage of compounds that affect epigenetic modifications.

Conclusion

— The incidence of cancer can depend on non-modifiable factors: age and modifiable: body weight, lifestyle.
— Most of the subjects before diagnosis of cancer had an improper diet; and diagnosis of the disease in most cases affected the change in eating habits.

Compliance with ethical standards

Conflict of interest: The authors declare that they have no conflicts of interest.

Funding: None

References

1. World Health Organization Web site. The European Health Report 2012: charting the way to well-being. http://

www.euro.who.int/__data/assets/pdf_file/0004/197113/EHR2012-Eng.pdf. Updated 2012. Cited 2013.
2. Potrykowska A, Strzelecki Z, Szymborski J, Witkowski J, ed. Cancer incidence and mortality versus the demographic situation of Poland. Warszawa:Rządowa Rada Ludnościowa;2014.
3. World Cancer Research Fund/American Institute for Cancer Research Web site. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington DC: AICR. www.aicr.org/assets/docs/pdf/reports/Second_Expert_Report.pdf. Updated 2007.
4. Tuorkey MJ. Curcumin a potent cancer preventive agent: Mechanisms of cancer cell killing. Interv Med Appl Sci. 2014;6(4):139-46.
5. Stefanska B, Karlic H, Varga F, et al. Epigenetic mechanisms in anti-cancer actions of bioactive food components---the implications in cancer prevention. Br J Pharmacol. 2012;167(2):279-97.
6. Supic G, Jagodic M, Magic Z. Epigenetics: a new link between nutrition and cancer. Nutr Cancer. 2013;65(6):781-92.
7. Liu RH. Dietary bioactive compounds and their health implications. J Food Sci. 2013;78(1):18-25.
8. Daniel M, Tollefsbol TO. Epigenetic linkage of aging, cancer and nutrition. J Exp Biol. 2015;218(1):59-70.
9. Busch C, Burkard M. et al. Epigenetic activities of flavonoids in the prevention and treatment of cancer. Clin Epigenetics. 2015;10(7):1:64.
10. Bal J. Biologia molekularna w medycynie. Elementy genetyki klinicznej. Warszawa:PWN;2013.
11. Kouzarides T. Chromatin modifications and their function. Cell. 2007;128(4):693-705.
12. Ross SA, Davis CD. MicroRNA, nutrition, and cancer prevention. Adv Nutr. 2011;2:472-85.
13. Su LJ, Mahabir S, Ellison GL, et al. Epigenetic Contributions to the Relationship between Cancer and Dietary Intake of Nutrients, Bioactive Food Components, and Environmental Toxicants. Front Genet. 2012;2:91.
14. Human Genome Sequencing Consortium. Finishing the euchromatic sequence of the human genome. Nature. 2004;5:931-45.
15. Bedyńska S. Brzezicka A. Statystyczny drogowskaz. Warszawa:SWPS Academica; 2007.
16. Nawojczyk M. Przewodnik po statystyce dla socjologów, Kraków:SPSS Polska;2002.
17. Office for National Statistics. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/cancerregistrationstatisticsengland/previousReleases. Requested 2016.
18. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008;371:569-78.
19. Arnold M, Pandeya N, Byrnes G, et al. Global burden of cancer attributable to high body-mass index in 2012: a population-based study. Lancet Oncol. 2015;16(1):36-46.
20. Yang CS, Fang M, Lambert JD, et al. Reversal of hypermethylation and reactivation of genes by dietary polyphenolic compounds. Nutr Rev. 2008;66(1):18-20.
21. Boehm K, Borrelli F, Ernst E, et al. Green tea (Camellia sinensis) for the prevention of cancer. Cochrane Database Syst Rev. 2009;8(3):CD005004.
22. Yuan JM. Cancer prevention by green tea: evidence from epidemiologic studies. Am J Clin Nutr. 2013;98(6):1676-81.
23. Juan ME, Alfaras I, Planas JM. Colorectal cancer chemoprevention by trans-resveratrol. Pharmacol Res. 2012;65(6):584-91.
24. Cottart CH, Nivet-Antoine V, Laguillier-Morizot C, Beaudeux JL. Resveratrol bioavailability and toxicity in humans. Mol Nutr Food Res. 2010;54:7-16.
25. Weiskirchen S, Weiskirchen R. Resveratrol: How Much Wine Do You Have to Drink to Stay Healthy? Adv Nutr. 2016;7(4):706-18.
26. Artero A, Artero A, Tarín JJ, Cano A. The impact of moderate wine consumption on health. Maturitas. 2015;80(1):3-13.
27. Hayes JD, Kelleher MO, Eggleston IM. The cancer chemopreventive actions of phytochemicals derived from glucosinolates. European Journal of Nutrition. 2008;47(2):73-88.
28. Hecht SS. Inhibition of carcinogenesis by isothiocyanates. Drug Metabolism Reviews. 2000;32(3-4):395-411.
29. Tse G, Eslick GD, Cruciferous vegetables and risk of colorectal neoplasms: a systematic review and meta-analysis. Nutr Cancer. 2014;66(1):128-39.
30. Liu X, Lv K. Cruciferous vegetables intake is inversely associated with risk of breast cancer: a meta-analysis. Breast. 2013;22(3):309-13.
31. Li LY, Luo Y, Lu MD, et al. Cruciferous vegetable consumption and the risk of pancreatic cancer: a meta-analysis. World J Surg Oncol. 2015;13:44.
32. Han B, Li X, Yu T. Cruciferous vegetables consumption and the risk of ovarian cancer: a meta-analysis of observational studies. Diagn Pathol. 2014;9:7.
33. Liu B, Mao Q, Cao M, Xie L. Cruciferous vegetables intake and risk of prostate cancer: a meta-analysis. Int J Urol. 2012;2:134-41.
34. Galeone C, Pelucchi C, Levi F, et al. Onion and garlic use and human cancer. The American Journal of Clinical Nutrition. 2006;84:1027-32.
35. Nicastro HL, Ross SA, Milner JA. Garlic and onions: their cancer prevention properties. Cancer Prev Res (Phila). 2015;8(3):181-9.