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REVIEW PUBLIC HEALTH

Cancer in the elderly

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ABSTRACT

Ageing is a fundamental biological process in all living beings. Nowadays as a result of developments in preventive and therapeutic medicine, and improvements in the quality of life, ageing of the population is one of the most important demographic issues. In the elderly, cancer is one of the predominant causes of mortality and morbidity, and its incidence increases with ageing. Sixty percent of all cases with cancer, and 70% of cancer-related deaths occur in patients aged 65 years and over. For optimal care, and treatment of elderly cancer patients a multidisciplinary approach consisting of physical, psychological, and tumor-related assessments should be pursued. Because of increased incidence of cancer caused by demographic changes in Turkey and in the world, an increase in the burden of cancer in the population is expected. In the years to come, this expectation will also lead to an increase in cancer-related health expenses.

Key words: Ageing; cancer; cancer incidence.

Ageing is a universal process seen in every living creature which begins mainly from intrauterine life, and continues up to death, and induces changes in physiological functions of organs, and systems under the influence of many factors. Nowadays, thanks to possibilities brought by scientific, and technological developments, disease, and mortality rates have decreased, birth rates have dropped, and environmental conditions improved which all of them have contributed to the prolongation of life span, and the relatively higher number of elder people in overall population. Based on estimates reported by The World Health Organization (WHO), people aged 65 years and over will be expected to reach 800 million in the year 2025 [1].

Ageing is defined as irreversible structural, and functional changes in molecules, tissues, organs, and systems of the organism which become apparent with advanced age. Senescent period has been classified from the biological, sociological, economical, and chronological perspectives. WHO defines old age as the period of life starting from 65 years of age. According to this chronological definition, age ranges of young old (65-74 yrs), middle old (75-84 yrs), and very old (≥85 yrs) have been defined [2]. One of the predominant causes of mortality, and morbidity is cancer whose incidence increases with

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age. Although cancer effects each age group, when it is seen from a global perspective, nearly 60% of the cases diagnosed as cancer, and 70% of the cancer-related mortalities occur in individuals aged 65 or older [3].

Based on the report released by WHO, and International Cancer Research Institute in the year 2012, approximately 14 million new cases were seen in the whole world, while this figure will be expected to rise to 22 million within the next 20 years leading to an increase in the global cancer burden. As a consequence of growing, and ageing population, an important part of this increase is predicted to concern developing countries. Because of limitations in the application of screening programs, early diagnosis, and access to treatment, further increases in the incidence of cancer, and cancer-related mortality rates have been foreseen [4, 5].

Incidence of cancer in Turkey demonstrates similarities with other developing countries. According to cancer statistics of the year 2009 performed in Turkey, in our country every year nearly 98.000 men, and 63.000 women are contracting cancer [6].

As is seen in the world, and in our country, cancer is a public health problem with increasing importance. Prolongation of overall lifetime leads to increase in the older population in our country. According to 2013 data of Turkish Statistical Institute (TÜİK) the percentage of the elder population was determined as 7.7 percent [7]. The percentage of the population aged 65 years and over is predicted to increase to 10.2% in the year 2023, and to 20.8% in 2050 [6]. In our country, 27% of the patients diagnosed as cancer are aged 65 years and over [3]. In the United States of America more than 60% of the cancer cases are seen in old individuals aged 65, and over [8].

Prolonged exposure to carcinogenic agents, DNA damage accumulation, tumor suppressor gene defects, impairment of cellular repair mechanisms, oncogenic activation, and attenuation of immunity have been held responsible for higher incidence of cancer in older individuals [3]. Since carcinogenesis is a very long process, emergence of cancer in advanced ages is a natural event.

Most frequently seen cancer types in elder people

Nowadays, nearly half of the cases with diagnosis of cancer constitute people aged 70 years and older [9]. Directorate of Cancer Department of Public Health Agency of Turkey reported the statistics of the most frequently seen cancer types in older female, and male population aged 70 years, and over (Figures 1, and 2) [6]. As is seen, the most frequently seen cancer types in population over 70 years are lung cancer, and prostate cancer in men, and breast cancer, and colorectal cancers in women.

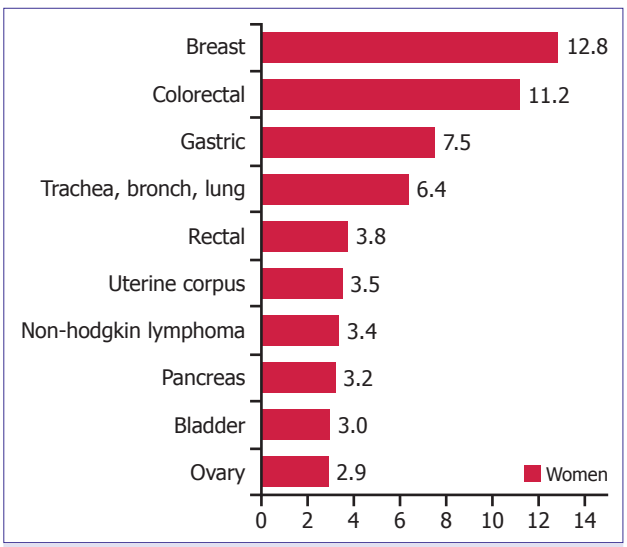

Figure 1. Distribution of some of the most frequently seen cancer types in women aged ≥70 years [6].

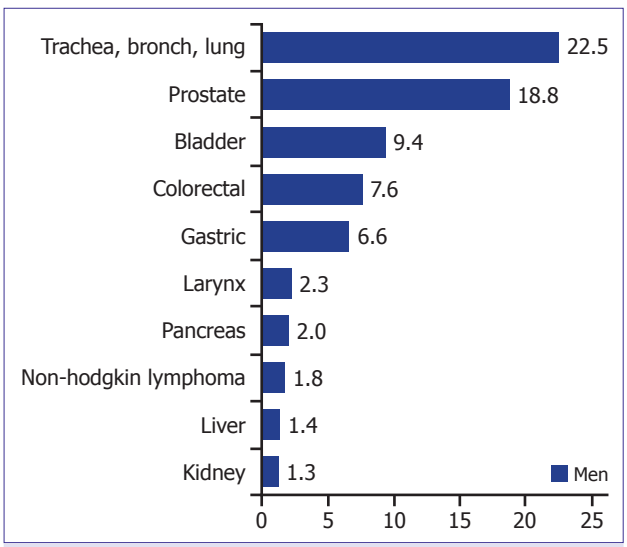

Figure 2. Distribution of some of the most frequently seen cancer types in men aged ≥70 years [6].

Lung cancer

Lung cancer has the shortest survival times among other cancer types, and takes the lead among cancer- related deaths in the whole world [6]. Half of the cases with lung cancer are diagnosed in the advanced stage [6]. More than 80% of the cases with lung cancer constitute non-small cell lung cancer (NSCLC). In the USA, median age of newly diagnosed cases with NSCLC is 68 years, while 40%, and 14% of these cases are over 70, and 80 years of age, respectively [10]. Less than 2% of all cases with the diagnosis of cancer are younger than 45 years of age. According to American Cancer Society (ACS) lung cancer is responsible from nearly 27% of all cancer-related deaths [8]. Owing to the decrease in the rate of smoking in Europe, and USA, decrease in incidence of lung cancer has been observed more frequently in men. Lung cancer -specific mortality rates between genders reflect smoking status, rates of quitting smoking, and historical differences within the last 50 years [11]. According to Globocan 2012 data published by International Cancer Agency, lung cancer ranks on top in men in Turkey, while in the European Union Countries, and in the USA it takes the second place [6]. In smokers the risk is higher relative to nonsmokers [12]. Smoking is the most important predictive risk factor which is responsible for nearly 70% of lung cancer-related mortality rates worldwide [13].

In Turkey lung cancer which is more frequently seen in men in Turkey, retains its updatedness as a public health problem. Therefore smoking quitting campaignes should be initiated, and maintained which will consequently lead to decrease in the incidence of lung cancer.

Breast cancer

Breast cancer is the most frequently seen malignancy among women aged 65 both in the world, and in our country. Incidence, and mortality rates of breast cancer increase with age (Figure 3) [6]. Among all types of cancer, incidence rates of breast cancer in women are 28% in the world, and 35.47% in Turkey [14].

In our country breast cancer patients are old people aged 51-70 (40.7%), and ≥70 (8.2%) years. In men breast cancer is seen very rarely, and 5-10 years later than women [15]. Based on 2013 ACS statistics, cases with in situ, and invasive breast cancer, and their mortality rates are climbing [11].

Although limited number of studies have been performed on breast cancer in elder population, surgical, and medical approaches do not differ when compared with the younger population. However in

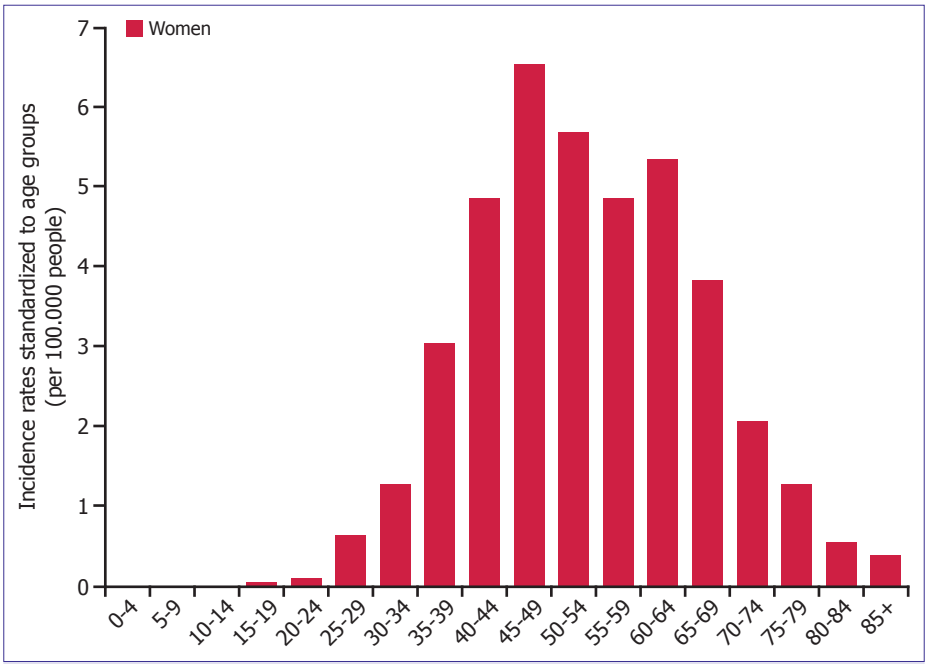

FIGURE 3. Distribution of age-specific incidence rates of breast cancer in Turkey [6].

patients aged 65 and over, presence of comorbidities, and performance status are preventing optimizaton of the treatment of breast cancer.

Within the frame of breast cancer screening program clinical breast examination, and mammographic methods have been used. ACS recommends annual mammographic controls beginning from 40 years of age on. In Turkey biannual mammographic screening is recommended up to 69 years of age [11]. Regular and organized population-based mammographic screening reportedly decreased breast cancer mortality at a rate of nearly 25-35% in women between 40-69 years of age [16]. In the whole world a total of 1.150.000 newly diagnosed cases in the year 2002 were observed, and in the year 2020 this figure will probably rise to 2.500.000 cases [17].

Cervical cancer

Both incidence, and mortality rates of invasive cervical cancer increases with age. Cervical cancer is a very costly disease which has a serious impact on health system, and population. In patients aged 65, and over cervical cancer has mortality rates ranging between 40, and 50%. However regular screening decreases cervical cancer risk at a rate of 80 percent [9]. Every year nearly 500.000 women are diagnosed as cervical cancer, and approximately 80% of them are seen in developing countries [18].

For the early diagnosis of cervical cancer, a very simple but highly sensitive, and specific Pap smear test has been used. Pap smear test which yields very successful outcomes in the early diagnosis of cervical cancer carries vital importance in the reduction, and prevention of mortality [19]. In the developed countries like USA, 85% of the women undergo Pap smear test at least once in their life time, while in the developing countries its rate drops to 5 percent. Only one negative Pap smear test decreases the risk of development of cervical cancer at a rate of 45 percent. Pap smear tests performed for 9 times during an individual's'life time decrease this risk at a rate of 99 percent [17]. According to ACS recommendations, screening tests for cervical cancer should be initiated within the first 3 years from the first sexual intercourse or at most at the age of 21. Every year obstetric examination and Pap smear test should be performed. If the last successive 3 screening test results are within normal limits, then screening tests can be done every 2-3 years.

If 3 separate or 10 successive Pap smear tests performed for women aged 70 and over yield normal results, cervical screening tests can be discontinued. According to National Cervical Cancer Screening Standards, smear, and HPV tests should be performed at every 5 years beginning from 30 years of age. If the last 2 tests yield negative results, screening should be stopped when the patient reaches 65 years of age. Screening tests may not be performed in patients who had undergone hysterectomies [11].

Colorectal cancers

Colorectal cancer (CRC) ranks among the first five most frequently seen cancer types in our country in both genders [6]. Prevalence, and mortality rates of CRC increase in individuals aged ≥50 years [9]. Incidence of CRC is 6 –times higher in the 65-84 year age group when compared with the younger individuals [3]. In our country it is most frequently seen in men rather than women (Figure 4). Its incidence rates per one hundred thousand individuals is 21 in men, and 13.4 in women [6]. In the whole world the highest incidence of CRC is found in Northern America, Australia, Northern, and Western Europe, and while in developing countries of Asia, and Africa its incidence is relatively lower [20]. It has been reported that the annual incidence of CRC in individuals aged 50 years and over in the USA decreased at a rate of 3.7%, while in the young population its annual incidence increased, at a rate of 1.8 percent [11].

Even recently developed surgical techniques, and adjuvant treatments could not drop 5-year mortality rates of CRC patients below 50 percent [21]. Ninety percent of newly diagnosed CRC cases, and 93% of CRC-related deaths are seen in patients 50 years and older [8].

According to ACS recommendations all women, and men from 50 years of age should participate in one of the screening programs. Annual fecal occult blood test (FOBT), and at 5–year intervals, sigmoidoscopy, sigmoidoscopy plus annual fecal occult blood tests, barium colonography, and at 10-year intervals colonoscopy have been recommended [11]. In our country CRC Screening program of Ministry of Health is initiated at 50, and terminated at 70 years of age. FOBT at alternate years, and colonos-

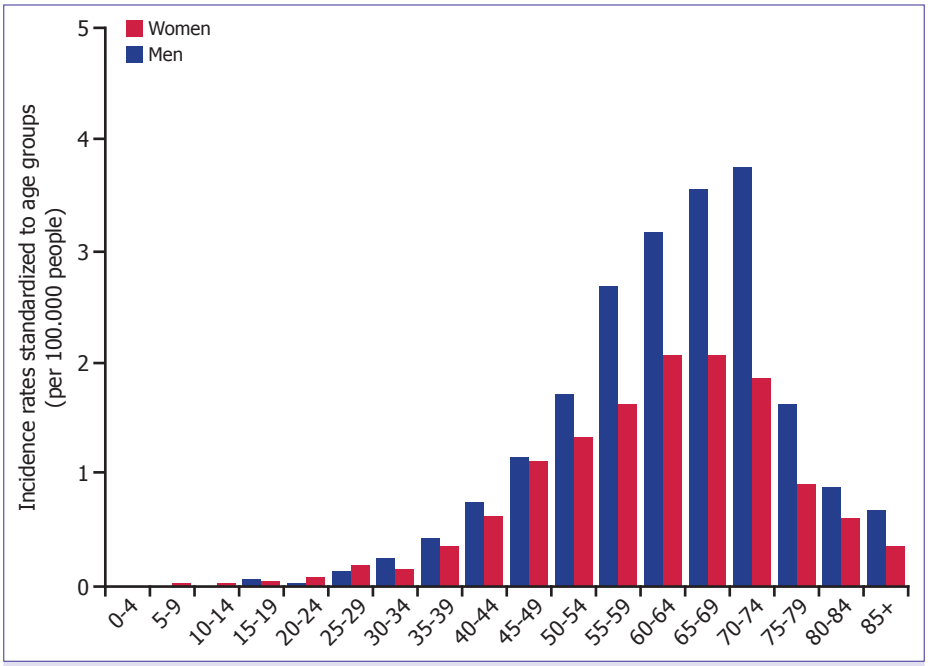

FIGURE 4. Distribution of age-specific incidence rates of colorectal cancer in men, and women in Turkey [6].

copy at every 10 years are recommended. As indicated, for cessation of screening in women, and men aged 70 years, fecal occult blood tests should yield negative results [21].

In the USA, it has been estimated that with CRC screening programs, CRC was prevented at a rate of 58-80%, when treated effectively [22]. Limited number of studies have demonstrated the impact of FOBT on the incidence of CRC. In a cohort study lasting for 22 years screened group was compared with a non-screened group, and incidence, and mortality rates of CRC were observedly decreased in the screened group at a rate of 40, and 64%, respectively. It has been suggested that in FOBT positive cases when these findings were combined with complete colonoscopic follow-up, annual FOBT control can be an effective approach [23].

Prostate cancer

Prostate cancer is one of the most frequently seen malignancies especially in the older male population. Majority (75%) of male patients diagnosed as prostate cancer are ≥65-years-old [24]. In the USA 64% of newly diagnosed cases are elder people aged ≥65 years. It has been estimated that the incidence of prostate cancer will continue to increase in line with a continual rise in the number of elder population [9].

Patients aged 65 years and over have not been included in drug trials performed in many oncological survey studies. This approach presents difficulties in determining the impact of treatment on an elderly patient. To avoid demographic bias, every age group should be included in prostate cancer survey studies. Recently new agents used in the treatment of prostate cancer patients have widened the spectrum of treatment, and supportive therapy alternatives of prostate cancer patients in every age group [11].

As prostate cancer screening tests, routine use of digital rectal examination (DRE), and prostate-specific antigen tests are recommended. ACS recommends screening programs for prostate cancer including PSA test and DRE to be performed beginning from the age of 50, In patients with higher risk (presence of prostate cancer in one or more than one younger first-degree relatives) these tests should be initiated at an early age. In individuals with very high risk for prostate cancer, tests should be performed at an age of 40, and if normal test results are obtained, then annual tests can be carried on after the age of 45 [11].

In the USA between the years 2006 and 2010, incidence of prostate cancer decreased at an annual rate of 2.0 percent. The number of newly diagnosed cases will be estimated to rise to 233.000 in the year 2014 [11].

General approach to cancer therapy

Ageing is an important risk factor for contracting cancer. However age really represents only number of years. Ageing is a both biological, and chronological phenomenon. Biological ageing begins with fertilization, and progesses all life long, and plays a role in the performance status, and concomitant diseases of the individual. In cancer therapies, biological, rather than chronological age should be taken into consideration. Health state, level of functionality, and expectation from study will differ between individuals. As a consequence, age should not be the only factor to be considered in the determination of cancer treatment alternatives. Other concomitant health problems of elder individuals (cardiovascular diseases, diabetes etc) can effect treatment decisions. Presence of these medical problems, chemotherapy, radiotherapy, and surgery can increase the risk of post-treatment complication rates. Other additional factors as life expectancy, and drug interactions should be also taken into account [8].

International Association of Geriatric Oncology emphasizes the importance of Comprehensive Geriatric Evaluation in old patients [25]. Comprehensive Geriatric Evaluation determines functional state, comorbidities, mental state, nutritional status of the patients, and drugs used by them. It can be used to present treatment alternatives, and in the prevention of treatment complications. In every stage of the treatment, multidisciplinary approach encompassing physical, psychological, and oncological assessments should be pursued for optimal care, and treatment of the elder people with cancer.

As a consequence of physiological changes seen in old age, under the influence of cellular, and vascular factors glomerular filtration rate (GFR) slows down, and renal functions deteriorate. At the same time, hepatic metabolism, intestinal motility, and immunity attenuate. Age-related physiological changes, and presence of comorbidities can increase toxicity of chemotherapy, and also interfere with the effectiveness of the treatment dose. Chemotherapy-related serious complications increase in old people. Myelosuppression, mucositis, nausea, and vomiting in late stages, cardiomyopathy, peripheral neuropathy, and neurotoxicity are more frequently seen. For old people exposure to adverse effects of chemotherapy is the greatest threat to their quality of life Therefore treatment should be individualized. Comprehensive Geriatric Evaluation can identify patients with high risk as for predictive factors for their life expectancies, and chemotherapeutic complications This approach allows for making standard or palliative treatment decisions.

Several studies have demonstrated that most of the cancer patients have been represented in clinical cancer studies, while health state of cancer patients aged 65 years and over has not been adequately revealed [8]. Limited number of studies performed also influence chemoprevention alternatives for the elderly.

Financial burden of cancer

In the years to come cancer burden of the nations is expected to rise in line with the increase in the incidence of cancer as a consequence of demographic change in the whole world, and Turkey. This expectation also points out to an increase in cancer-related healthcare expenditures. National Disease Burden, and Cost-Effectiveness Study conducted in Turkey supports these outcomes.

Financial burden of cancer within the frame of healthcare finance can be calculated with the procurement of effective epidemiological data. Establishment of reliable cancer registration systems is extremely effective in the acquisition of epidemiological data. When Turkey is compared with European countries, it ranks 6th among countries with the highest cancer-related healthcare expenditures. Since incidence of cancer increases with age, average cancer burden per individual aged over 45 also increases [17]. Anticancer drugs are respondible for 3.8, and 7.2% of all drug expenditures in the years 2003, and 2010, respectively [26].

According to 2014 World Cancer Report, increasing financial burden of cancer are even challenging for economies of countries with higher annual income. Total annual financial burden of cancer in the year 2010 reached to 1.6 trlllion US dollars. According to WHO data 40% of the cases

with cancer can be prevented. Increasing incidence of cancer cases is an important obstacle for the development, and prosperity of human beings in the whole world [4]. Lowering incidence rates of cancer will contribute greatly to expenditures incurred by malignant diseases.

In studies performed a marked increase in survival times of breast cancer patients with effective screening programs has been seen, while early diagnosis has apparently directly decreased disease-related treatment costs Cervical cancer screening programs included in routine screening programs decrease financial burden of cancer in that these tests do not require advanced technology with their advantages of effectiveness and lower cost. In our country cancer –related morbidities are responsible for nearly 11% of healthcare expenses for the year 2006 17].

Because of the impact of cancer on healthcare expenses, implementation of reliable registration systems should specify srategies for early diagnosis, and screening. As a consequence of ageing in the population an increase in the incidence of cancer is predicted. Population-based effective screening methods enable establishment of early diagnosis, and increase the chance of cure. This approach will have favourable reflections on cancer therapy.

Cancer prophylaxis

Prophylaxis seems to have the utmost importance in decreasing cancer burden in society. General opinion in cancer prophylaxis involves taking measures to improve nutrition, physical activity, and also prevent obesity. World Cancer Research Foundation estimates that one-third of the cancer cases in developed countries are overweight or obese which are related to physical inactivity or insufficient nutrition. Recommendations of ACS for cancer prophylaxis are as follows:

- Maintain a healthy body weight,
- Restrict intake of processed meat or red meat,
- Daily intake of at least 2 ½ servings of vegetables and fruits
- Prefer wholewheat bread rather than refined cereal products,
- Restrict alcohol intake,
- Avoidance of using tobacco products
- Regular engagement in physical activities
- Restriction of sedentary life style [11].

Even if we brought nutritional status, physical activity, and other environmental factors completely under control, it is not possible to keep away from cancer by all means. Together with physiological ageing process, mechanisms which control proliferation of cells weaken, repair mechanisms slows down, and cellular destructive changes accumulate. Within this context, even if healthy individuals have not any complaint, cancer screening tests are performed for early diagnosis of cancer so as to increase chances of cure. Early detection of the disease yields better outcomes for its treatment, and care.

Conclusion

Sixty percent of cancers originate from etiological factors related to ageing. Treatment, and care for older patients with cancer should be individualized rather than focusing on age of the patient. With comprehensive geriatric evaluation, risks, and benefits of the available treatment alternatives should be properly determined. Early diagnosis, treatment, and screening programs will also lessen cancer burden imposed on communities thanks to decreasing incidence rates of cancer in elderly.

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