Editorial

Cancer prevention from the perspective of global cancer burden patterns

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Cancer is the second leading cause of death worldwide behind cardiovascular disease (1). According to the Global Burden of Disease (GBD) 2015 Study, which was conducted as part of a comprehensive regional and global research program assessing the mortality and disability caused by major diseases, injuries, and risk factors and involving over 500 researchers representing over 300 institutions and 50 countries, cancer mortality decreased between 2005 and 2015 despite the global incidence rates of cancer increasing during this period (1). However, improvements in cancer survival rates due the use of precision medicine or immunotherapy have mainly occurred in high-income countries, whereas in low-income countries cancer prevention, education, and access to cancer screening tests as well as cancer treatment are inadequate (2,3). The potential of cancer prevention techniques, including vaccinations and smoking cessation programs, to reduce the incidence and mortality rates of cancer has not been sufficiently realized, and efforts are especially lagging in socioeconomically disadvantaged populations (4). This has led to worse cancer outcomes and higher incidence rates of cancer in certain low-income countries. Further advancement of cancer control requires the appropriate allocation of resources for cancer prevention, early diagnosis, and curative and palliative care.

The GBD 2015 study reported that the most common types of cancer are prostate, lung, and colorectal cancer in males and breast, colorectal, and lung cancer in females. On the other hand, the leading causes of cancer deaths are lung, liver, and gastric cancer in males and breast, lung, and colorectal cancer in females (1). In adolescents and young adults (age 15–39 years), for whom cancer prevention and early diagnosis are important, the most common cancers (at the global level) are breast and cervical cancer, and the main causes of cancer deaths are leukemia and liver cancer (1). All of the above lists are written in descending order.

To reduce the incidence of the abovementioned cancers, the prevention of carcinogenic infections and efforts aimed at lifestyle improvement are essential. In low-income countries, infection-related cancers are predominant. In contrast, in high-income countries lung, colorectal, and breast cancer, which are strongly associated with lifestyle-related risk factors, including cigarette smoking, alcohol consumption, and obesity, display high incidence rates. In addition, the prevalence of cancer-screening tests and the identification of high-risk patients, including those with inherited cancer syndromes, are important for improving survival.

The main carcinogenic pathogens include hepatitis B virus (HBV) and hepatitis C virus (HCV), human papilloma virus (HPV), *Helicobacter pylori*, Epstein-Barr virus, and human immunodeficiency virus. HBV- and HCV-related chronic hepatitis are the main causes of liver cancer, which exhibits high morbidity and mortality rates. Therefore, it is important to prevent and treat HBV and HCV. Immunizing individuals against HBV would lead to a reduction in the

incidence of liver cancer. The efficacy of HBV vaccination was verified in a randomized controlled trial in which 75,000 newborns were immunized with an HBV vaccine. After a median follow-up period of about 25 years, the ratio of the incidence of primary liver cancer in the vaccination-at-birth group to that in the control group was 0.16 [95% confidence interval (CI): 0.03–0.77] (5). In addition, blood banks test all donated blood for both HBV and HCV, which greatly reduces the risk of getting the virus from blood transfusions or blood products (6). Furthermore, liver cancer caused by non-alcoholic fatty liver disease, which is the hepatic manifestation of metabolic syndrome, is reported to account for 10–24% of liver cancer in developed countries (7), which indicates the importance of lifestyle improvements for preventing liver cancer.

HPV infections are associated with the development of cervical cancer, oropharyngeal cancer, and squamous cell carcinoma of the anus (8-10). A multicenter, double-blind placebo-controlled trial demonstrated that vaccinations against HPV-16/HPV-18 are effective at preventing HPV infections in HPV-naïve individuals and are associated with a reduced incidence of cervical cancer (11). Based on this evidence, HPV vaccination is universally recommended by health authorities. Vaccination against HPV was also shown to reduce the incidence of squamous cell carcinoma of the anus in another double-blind placebo-controlled trial (12), whereas there is no evidence that vaccination at a young age substantially reduces the risk of HPV-associated oropharyngeal cancer later in life.

Helicobacter pylori infections are strongly associated with both the initiation and promotion of gastric cancer and gastric lymphoma (13,14). A meta-analysis of seven randomized studies, all of which were conducted in areas where the populations were at high-risk of gastric cancer (all but one were performed in Asia), suggested that the treatment of *Helicobacter pylori* might reduce the risk of gastric cancer [from 1.7% to 1.1%; relative risk (RR): 0.65; 95% CI: 0.43–0.98] (15). The International Agency for Research on Cancer (IARC) recommends that countries investigate whether population-based screening and treatment programs for *Helicobacter pylori* are indicated. However, there are few countries that have implemented population-wide screening programs exhibit high incidences of gastric cancer.

The prevention and treatment of the carcinogenic infections described above have the potential to reduce the future cancer burden and the incidence of associated diseases like cirrhosis in endemic areas. In the meantime, we should focus on risk factors associated with lifestyle, including cigarette smoking, alcohol consumption, and obesity.

Cigarette smoking causes many types of cancer, including cancer of the lung, oral cavity and pharynx, larynx, esophagus, bladder, kidneys, pancreas, stomach, uterus, and cervix, as well as acute myeloid leukemia (16). In particular, lung cancer is strongly associated with smoking (the most important risk factor for lung cancer). Compared with non-smokers, smokers experience a dose-dependent increase in their risk of developing lung cancer. Not smoking is the most effective measure for preventing lung cancer. The preventive effects of smoking cessation depend on the duration and intensity of prior smoking and the time since cessation. Compared with persistent smokers, a 30% to 50% reduction in the risk of lung cancer mortality is seen at 10 years after the cessation of smoking (17). Tobacco control is a crucial cancer control strategy since it has health benefits that extend far beyond cancer prevention.

Esophageal carcinoma, oropharyngeal cancer, colorectal cancer, and breast cancer are all associated with excess alcohol intake. In particular, the risk of esophageal carcinoma and oropharyngeal carcinoma is highest in people who both smoke heavily and consume large amounts of alcohol. A meta-analysis of eight studies showed that the cessation of alcohol consumption resulted in a significant (35%) reduction in the risk of head and neck cancer, relative to current drinkers, after ≥20 years (18).

Obesity is a risk factor for breast, colorectal, and ovarian cancer.

In the Cancer Prevention Study II, which was a large nationwide cohort study, people with body mass indices (BMI) of 30 to 34.9 had an adjusted RR for colorectal cancer mortality of 1.47 (95% CI: 1.30–1.66), and a statistically significant dose-response relationship was observed (19). In an observational study, obesity was also reported to increase the incidence of breast cancer among postmenopausal women (RR: 2.85, 95% CI: 1.81–4.49) who weighed more than 82.2 kg, compared with those who weighed less than 58.7 kg (20). Another cohort study showed that a high BMI during adolescence was associated with an increased risk of ovarian cancer (21). Many observational studies have revealed that regular physical activity is associated with decreased incidences of colorectal and breast cancer (22,23).

Even when population-wide primary prevention is employed in combination with programs against carcinogenic infections and lifestyle-related risk factors, it is impossible to prevent all cancer. Therefore, as secondary prevention

measures, cancer control strategies should also focus on early detection through the use of cancer-screening tests, including mammography for breast cancer; immunochemical fecal occult blood tests, computed tomographic colonography and colonoscopy for colorectal cancer; annual low-dose computed tomography of the chest for people that are at high risk of lung cancer due to a smoking history of at least 30 pack-years (24). Furthermore, to facilitate early diagnosis it is essential to identify people with inherited susceptibility to cancer, including those with BRCA1/2 mutations or Lynch syndrome, as the medical history of the patient's family is very important in such cases.

In the latest issue of *JAMA Oncology*, the Global Burden of Disease Cancer Collaboration group reported a systemic analysis of the GBD 2015 study. As a result, they identified global cancer burden patterns; revealed the widening disparity in cancer care between low-income and high-income countries; and highlighted the need for appropriate allocation of medical resources to aid cancer prevention, early diagnosis, and curative and palliative care. In particular, cancer prevention efforts are lacking in low-income countries. To aid cancer control, it is essential to promote cancer prevention measures, including tobacco control and vaccination programs, treatments for carcinogenic infections, and physical activity programs aimed at ensuring that individuals maintain an adequate weight.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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