Trends of Incidence and Mortality with Pathological Description of Colorectal Cancer

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ABSTRACT

Colorectal cancer (CRC) represents the most common malignant tumor of the gastrointestinal tract, it is the third most common malignant disease. The objective of this study was to determine the trends in CRC incidence, mortality and its pathological description. The incidence and mortality of CRC were obtained from data analysis sources, International Agency for Research on Cancer (IARC), centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS) and histopathological cases were obtained from pathology laboratory, Faculty of Medicine, SEGi University. The estimated of overall incidence prevalence of CRC was 1360,000 cases worldwide in 2012. The CRC incidence was in men (10.0%) and in women (9.2%) of the total cancer cases worldwide. Almost, 55% of the cases occurred in more developed regions, the highest estimated rates being in Australia/New Zealand (44.5) and Europe (39.5-34.5), while the lowest showed the Western Africa (4.5 and 3.8 per 100,000) in both men and women respectively. Mortality was showed the highest estimated rates in both sexes in Central and Eastern Europe (20.3 per 100,000 for men, 11.7 per 100,000 for women), and the lowest was in Western Africa (3.5 and 3.0 for men and women respectively). The colorectal cancer is less variability in mortality rates worldwide was six-fold in men and four-fold in women. In all ages of female and male, the highest incidence was in Australia and New Zealand (38.3), and Europe (31.4-26.6), while the lowest showed in the Africa (7.3-6.1). The highest mortality of CRC in Europe was (14.9-10.0) especially in the central and eastern areas (14.9), while the lowest mortality showed in the western Africa (3.0). In conclusion, the highest incidence of CRC cases was occurred in more developed regions. There is a wide geographical variation in the incidence of CRC across the world, and the geographical patterns are very similar in both men and women, while incidence rates vary ten-fold in both sexes worldwide.

Keywords: Incidence, Mortality, Pathology, Colorectal Cancer
INTRODUCTION
Colorectal cancer (CRC) represents the most common malignant tumor of the gastrointestinal tract, it is considered the third most common malignant disease, and the second most common cause of death in both genders. It has been reported that the disease frequency correlates with the industrial development of certain countries (Ellen and Fredric, 2010). According to the data from the Cancer Registry of the Croatian National Institute of Public Health, CRC is the second most common cancer form in men and women, second to lung and breast cancer, respectively, with prevalence of 15% in males, and 13% in females, in relation to the total number of all diagnosed malignant diseases. The highest incidence rates of CRC were registered in the USA, the CRC is the third most commonly diagnosed cancer and the third leading cause of cancer death in both men and women in the United States. The American Cancer Society estimates that 136,830 people diagnosed with colorectal cancer and 50,310 people might die from the disease in 2014 (Corporate Center, 2014). The incidence of CRC varies over 10-fold worldwide. The highest incidence rates are in Australia and New Zealand, Europe and North America, and the lowest rates are found in Africa and South-Central Asia. These geographic differences appeared to be attributable to differences in dietary and environmental exposures that are imposed upon a background of genetically determined susceptibility (Jemal et al., 2011). Colorectal cancer usually develops slowly over a period of 10 to 15 years. The tumor typically begins as a noncancerous polyp. A polyp is a growth of tissue that develops on the lining of the colon or rectum that can become cancerous. Certain kinds of polyps called adenomatous polyps or adenoma are the most likely to become cancers, though fewer than 10% of adenomas progress to cancer. However, adenoma is common and estimated one-third to one-half of all individuals that eventually developed one or more adenomas (Levine and Ahnen 2006). About 96% of colorectal cancers are adenocarcinomas, which evolved from glandular tissue. The great majority of these cancers arise from an adenomatous polyp, which is visible through a scope or on an X-ray-like image using double contrast barium enema. The information on early detection of the adenomas is most relevant to this type of cancer (Stewart et al., 2006). The objective of this study was to determine the trends in colorectal cancer (CRC) incidence and mortality with its pathological description of international regions.

METHODS
Detailed methods and describing the analysis of incidence and mortality data sources in 2012 of CRC were obtained from Data Sources and Methods of International Agency for Research on Cancer in 2012 (GLOBOCAN 2012). Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012 (Ferlay et al., 2014). The data from US Census Bureau and the Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS). The
histopathological data were obtained from pathology laboratory, Faculty of Medicine, SEGi University. According to the AJCC (2010), Grading systems differ depending on the type of cancer. In general, tumors are graded as 1, 2, 3, or 4, depending on the amount of abnormality. In Grade 1 tumors, the tumor cells and the organization of the tumor tissue appear close to normal. These tumors tend to grow and spread slowly. In contrast, the cells and tissue of Grade 3 and Grade 4 tumors do not look like normal cells and tissue. Grade 3 and Grade 4 tumors tend to grow rapidly and spread faster than tumors with a lower grade. If a grading system for a tumor type is not specified, the following system is generally used: GX: Grade cannot be assessed (undetermined grade). G1: Well differentiated (low grade). G2: Moderately differentiated (intermediate grade). G3: Poorly differentiated (high grade). G4: Undifferentiated (high grade).

RESULTS

The analysis of incidence, mortality and death prevalence of CRC worldwide in 2012 showed the overall of incidence was 1360,000 cases. The CRC is the third most common cancer in men were 746000 cases which represent 10% of the total cancers) was 746,000 cases as a 10.0% of the total cancers worldwide. Almost 55% of the cases occur in more developed regions. There is wide geographical variation in incidence across the world and the geographical patterns are very similar in men and women, whereas the incidence rates vary ten-fold in both sexes worldwide (Table 1).

<table>
<thead>
<tr>
<th>*Estimated numbers (thousands)</th>
<th>Cases</th>
<th>Men Deaths</th>
<th>5-year prev.</th>
<th>Cases</th>
<th>Women Deaths</th>
<th>5-year prev.</th>
<th>Cases</th>
<th>Both sexes Deaths</th>
<th>5-year prev.</th>
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<td>374</td>
<td>1953</td>
<td>614</td>
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<td>175</td>
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<td>338</td>
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<td>966</td>
<td>737</td>
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*Estimated age-standardized rates (World) per 100,000, International Agency for Research on Cancer WHO
The results of this study on the colorectal cancer in male of all ages showed highest incidence in Australia and New Zealand (44.5) and Europe (39.5-34.5), while the lowest showed in the Africa (8.5-4.5). On another hand, the highest mortality of CRC was in the Europe (20.3-15.4) especially in the central and eastern areas (20.3), while the lowest motility showed also in the Africa (5.6-3.5) (Fig. 1). The colorectal cancer in female of all ages showed highest incidence in Australia and New Zealand (32.2), and Europe (25.3-21.7), while the lowest showed in the Africa (6.9-3.8). The highest mortality of CRC was in the Europe (11.7-9.1) especially in the central and eastern areas (11.7), while the lowest mortality showed also in the Western Africa (3.0) (Fig. 2).

The colorectal cancer in both female and male of all ages showed highest incidence in Australia and New Zealand (38.3), and Europe (31.4-26.6), while the lowest showed in the Africa (7.3-6.1). The highest mortality of CRC was in the Europe (14.9-10.0) especially in the central and eastern areas (14.9), while the lowest mortality showed also in the Western Africa (3.0) (Fig. 3). The highest incidence and mortality in both of female and male in the Australia and New Zealand, and more developed regions, while the lowest showed in less developed regions. However, the overall of CRC incidence and mortality worldwide showed male 21.0 and female 10.5, and male 10.0 and female 7.0 respectively (Fig 4).

![Figure 1: Showing the incidence and mortality of colorectal cancer in male of all ages.](image-url)
Figure 2: Showing the incidence and mortality of colorectal cancer in female of all ages.

Figure 3: Showing the incidence and mortality of colorectal cancer in female and male of all ages.
Figure 4: Showing the incidence and mortality of colorectal cancer in female and male of all ages.

The microscopic growth pattern of tumor is depending on the presence and volume of villous tissue. Adenomas also classified according to the grade of evident epithelial dysplasia: mild, moderate, or sever dysplasia. In mild dysplasia, the nuclear to cytoplasmic ratio is low and the nuclei are elongated, crowded, and stratified. In severe dysplasia, the nuclei are enlarged, ovoid, or round, hyperchromatic and often contain prominent nucleoli (Fig 5). Adenocarcinoma is divided into three grades according to differentiation, well, moderately and poorly differentiated microscopically. The cellular changes according to the tumor differentiation comprise well-formed glands in which nuclei are uniform in the size, shape and retain a basal location. In moderately differentiated tumor, where 60% of glands are less regular but remain easily recognized and the nuclei are large with lack of basal location. In the poorly differentiated adenocarcinoma, the cells and glands appeared in small, highly irregular clusters and difficult to discern (Figure 6).
Discussion

The global burden of cancer continues to increase largely because of the aging and growth of the world population alongside an increasing adoption of cancer-causing behaviors, particularly smoking, in economically developing countries (Center et al., 2009). However, The estimated of incidence, mortality and death prevalence of CRC worldwide in 2012 showed the overall incidence was the third most common cancer in men (10.0% of the total) and the second in women (9.2% of the total) worldwide. Almost 55% of the cases and 64% of the deaths occurred in the economically developing world. Mortality rate is the lowest in the Middle Africa and South-Central Asia and highest in Central and Eastern Europe with a six-fold variation in male and a five-fold variation in female mortality rates between the regions of the world (Ferlay et al., 2010; Ferlay et al., 2014) Although, overall cancer incidence rates in the developing world are half those seen in the developed world in both sexes, the overall cancer mortality rates are generally similar. Cancer survival tends to be poorer in developing countries, most likely because of a combination of a late stage at diagnosis and limited access to timely and standard treatment. A substantial proportion of the worldwide burden of cancer could be prevented through the application of existing cancer control knowledge and by implementing programs for

Figures of histopathology of CRC: 5) Adenomas tubulovillous shows elongated, crowded, and stratified and irregularities crypts (arrow), X 10 H&E. 6) Adenocarcinoma shows the glands are less regular but remain easily recognized. The nuclei are large (arrowhead) and lack a basal location (arrow), X 40 H&E.
tobacco control, vaccination, and early detection and treatment, as well as public health campaigns promoting physical activity and a healthier dietary intake (Jemal et al., 2011). The highest incidence and mortality in both of female and male in the Australia and New Zealand, and more developed regions, while the lowest showed in less developed regions. However, the overall of CRC incidence and mortality in the worldwide showed male more than female. Low socioeconomic status (SES) is also associated with an increased risk for the development of colorectal cancer; one study estimated the CRC risk to be about 30 percent increase in the lowest as compared to the highest SES quintile. Unhealthy but potentially modifiable behaviors such as physical inactivity, unhealthy diet, smoking, and obesity are thought to account for substantial proportion estimates of one-third to one-half of the socioeconomic disparity in risk of new onset colorectal cancer (Stewart et al., 2006). It was also found that colorectal cancer of adenocarcinomas was the highest incidence in the sigmoid part of the colon among the IBD and chronic gastrointestinal tract cases (Al-Jashamy et al., 2010). The body mass index and obesity increases the risk of colon cancer death and that the relation is stronger and more linear in men than in women (Murphy et al., 2000). Individuals in many regions had a higher burden of CRC and stable or increasing CRC mortality. An understanding of the factors driving these regional disparities could offer critical insights for prevention and control programs (David et al., 2014).

The microscopic growth pattern of tumor is classically described as tubular (gland like), tubulovillous or villous (finger-like projections), depending on the presence and volume of villous tissue (Bond, 2000). Tubules are lined by columnar epithelium, embedded with lamina propria where they proliferate by branching and villi comprise a covering of columnar epithelium and a core of lamina propria. By forming complex, cerebriform folds of epithelium, the surface area of a villous adenoma may be considerable and lead to significant loss of fluid and electrolytes. Tubulovillous adenomas combine both architectural patterns (Thieblemont et al., 1997). The cellular morphological changes that distinguish an adenoma from normal by the higher proportion of immature cells containing enlarged, hyperchromatic, stratified of nuclei. Mitotic activity is not limited to the basal zone and is often accentuated within the upper crypt and surface epithelium. The abnormal cytologic features that define dysplasia include nuclear characteristic like enlargement, hyperchromasia, elongation and relocation. Nuclear crowding and relocation create the impression stratification. With increasing severity, the cytologic changes are accompanied by increased nuclear pleomorphism, loss of nuclear polarity, atypical mitotic figures and decreased cytoplasmic mucincontent. The frequency of severe dysplasia increases with the size of the adenoma and in highest villous adenomas. Flat adenomas showed cytologic and glandular abnormalities, which are similar to those, observed in polypoid lesions. In addition, it has been shown that non-polypoid adenomas gradually enlarge by the formation of new crypts producing a circular lateral growth (Geboes et al., 2005). The crypts showed architectural irregularities, being coiled, branched, and crowded. Adenomas also classified according to the grade of evident epithelial dysplasia: mild, moderated, or sever dysplasia. In
mild dysplasia the nuclear to cytoplasmic ratio is low and the nuclei are elongated, crowded, and stratified. Mucus secretion is usually preserved, but may be reduced or absent in adenomas that include a high proportion of absorptive type cells within the epithelium. In severe dysplasia the nuclei are enlarged, ovoid, or round, hyperchromatic and often contain prominent nucleoli. The epithelial cells appeared undifferentiated and there is considerable architectural irregularity, including crowded, back to back glands (Thieblemont et al., 1997, Geboes et al., 2005).

Adenocarcinoma of the colon is common on two subtypes of adenocarcinoma (microscopic) include signet ring cell adenocarcinoma and mucinous adenocarcinoma. Signet ring cell adenocarcinomas are considered more aggressive than regular adenocarcinomas and are harder to be treated. The signet ring cell form is very uncommon and accounts for about 0.1 percent of all adenocarcinomas. Adenocarcinoma is divided according to well, moderately or poorly differentiated. Well-differentiated tumor (20%) comprises well-formed glands in which nuclei are uniform in size, shape and retain a basal location. In moderately differentiated tumor (60%), the glands are less regular but remain easily recognized. The nuclei are large and lack a basal location. In poorly differentiated tumor, the glands are highly irregular and difficult to discern (Al-Jashamy et al., 2009, Al-Jashamy, 2014).

Adenocarcinoma of the colon is common and often a fatal disease. It is the second most frequent diagnosed malignancy in the United States and the second most common cause of cancer deaths. The clinical presentation of colorectal carcinoma is variable and often depends on the size, site, and types of the tumor. It is a disease of the elderly, most frequently seen in patients older than 50 years of age, with a peak incidence at 60-70 years of age at the time of diagnosis. The incidence is slightly higher in men than women. Adenocarcinomas of the colon, especially those occurring on the right side, are often clinically silent for many years (Buetow et al., 1995). Virtually all carcinomas of the colon are adenocarcinomas. Almost all adenocarcinomas develop from a preexisting adenoma. Some adenocarcinomas of the colon, however, do not develop from preexisting adenomas but from a premalignant condition within flat mucosa called dysplasia. This condition may be partially responsible for the carcinoma seen in patients with the hereditary non-polyposis colon cancer syndrome (Buetow et al., 1995, Al-Jashamy 2014). In conclusion, the highest incidence of CRC cases occurred in more developed regions. There is wide geographical variation in incidence across the world, and the geographical patterns are very similar in men and women, incidence rates vary ten-fold in both sexes worldwide.

References


