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Changing trends in gastrointestinal malignancy in Indonesia: The Jakarta experience

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Abstract

Aims: To identify changing trends in gastrointestinal cancer incidence in Indonesia according to age, gender, histopathology, and cancer location. *Methods:* We examined retrospectively the demography, cancer location, and pathological characteristics of 295 consecutive gastrointestinal cancer patients admitted to Cipto Mangunkusumo National General Hospital in 2002–2006. We compared these data with data from 343 gastrointestinal cancer patients admitted in 2007–2011. The data were analyzed by chi-square, analysis of variance, Kolmogorov–Smirnov, and Mann–Whitney U tests using SPSS 21.0. *Results:* The most prevalent gastrointestinal cancers in 2002–2006 and 2007–2011 were colorectal cancer (76.3% and 71.4%), followed by gastric cancer (15.6% and 14.9%), esophageal cancer (7.4% and 7.6%), and duodenal cancer (0.7% and 6.1%).There was an increase in esophageal adenocarcinoma prevalence from 36.4% to 69.2% (p = 0.023). The mean age at diagnosis of esophageal cancer decreased from 53.02 ± 13.12) to 50.43 ± 11.93) years (p = 0.031). The percentage of patients with gastric cancer aged 30–60 years increased from 60.9% to 82.4% (p = 0.018) and the percentage of patients aged > 60 years decreased from 34.8% to 13.7% (p = 0.015). In the histopathological analysis of gastric cancer, the prevalence of adenocarcinoma increased from 58.7% to 78.4% (p = 0.036), whereas the prevalence of signet ring cell carcinoma decreased from 21.7% to 5.9% (p = 0.022). The prevalence of gastric cancer lesions extending to >1 location increased from 2.2% to 27.5% (p = 0.001).The frequency of duodenal cancer among women increased non significantly from 0% to 52.4% (p = 0.261). The demography, histopathology, and location of colorectal cancers did not change between the two periods. *Conclusions:* Our study shows some changing trends in gastrointestinal malignancy in Indonesia in terms of demography, histopathology, and the location of cancers from 2002–2006 to 2007–2011.

Keywords: changing trends; gastrointestinal cancer; esophageal cancer; gastric cancer; duodenal cancer; colorectal cancer; Indonesia

Introduction

Gastrointestinal cancer is one of the most frequent cancers in the world and the second leading cause of cancer-related death. Colorectal, esophageal, gastric, and pancreatic cancer account for more than 214,000 cancer deaths in the USA annually [1]. Even though the highest incidence of gastric cancer has been reported in the Asia-Pacific region, some studies have shown a decrease in gastric cancer incidence in several countries [2, 3]. By contrast, the incidence of colorectal cancer has been increasing in Asia and is approaching that in Western countries [4]. A report from Iran showed that the incidence of gastric, esophageal, and colorectal cancer increased with age. However, the trends differed between the different types of gastrointestinal malignancy; that is, the total incidence of gastric and esophageal cancer decreased but that of duodenal and colorectal cancer increased [5].

Esophageal cancer is the eighth most frequent malignancy worldwide and the sixth most common cause of cancer-related mortality [6]. The disease is diagnosed more frequently in males than in females with an approximate

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ratio of 3.5:1 [7]. Esophageal cancer comprises two types of primary tumors, adenocarcinoma and squamous cell carcinoma. The most frequent histological type is squamous cell carcinoma, especially in developing countries with low socioeconomic status, such as in several Asian and African regions [8]. There has been a clear shift, in that the incidence of esophageal adenocarcinoma has been increasing rapidly whereas the incidence of squamous cell carcinoma has been decreasing. The percentage of adenocarcinoma prevalence increased from 3.5% in 1985 to 17% in 2000 [7].

In Western countries, adenocarcinoma has become the dominant histological type of esophageal cancer. The incidence of esophageal adenocarcinoma in Western Europe and the USA is almost 50% among all types of esophageal cancer [7, 9]. Data collected between 1998 and 2003 in the USA by the Centers for Disease Control and Prevention showed that the incidence of esophageal adenocarcinoma increased by 2.1% per year, whereas squamous cell carcinoma of the esophagus decreased by 3.6% per year [10]. Gastroesophageal reflux disease (GERD), obesity, and decreasing prevalence of *Helicobacter pylori* infection are factors related to the development of adenocarcinoma of the esophagus [9]. When classified according to the location of tumors, adenocarcinoma of the esophagus occurs in the distal third of the esophagus, whereas squamous cell carcinoma can occur in any part of the esophagus, although most tumors occur in the distal third of the esophagus [11].

There has been a downward trend in the incidence of gastric cancer. The prevalence of gastric cancer increased significantly throughout the 19th century, but the number of cases has decreased abruptly over the past five decades in most parts of the world [2, 12]. The most frequent gastric cancer type is adenocarcinoma, which accounts for 90–95% of adenocarcinoma cases, and the remaining 5–10% are carcinoma of nonepithelial origin [13]. According to Lauren's classification [14], there are three types of gastric adenocarcinoma: intestinal type (tubular, mucinous, and papillary adenocarcinoma), diffuse type (signet ring cell carcinoma and other poorly cohesive carcinomas), and indeterminate type or mixed carcinoma (squamous cell carcinoma, adenosquamous carcinoma, and other epithelial carcinomas). The frequency of each type is 54%, 32%, and 15%, respectively [15]. The decreasing number of *H. pylori* infections also contributes to the decline in the incidence of the intestinal type of gastric cancer because gastric cancer is associated with *H. pylori* infection and chronic gastritis. The rate of diffuse type gastric carcinoma increased from 0.3 cases per 100,000 population in 1973 to 1.8 cases per 100,000 population in 2000. An increase in the incidence of diffuse type gastric cancer and a decrease in intestinal-type gastric cancer was reported for males and females, African-Americans and whites [16]. The most common stomach cancer location in the world is non-cardia gastric cancer, although its incidence has been declining in developed regions. However, non-cardia gastric cancer remains common in many geographic regions, including China, Japan, Eastern Europe, and Central/ South America. By contrast, the incidence of adenocarcinoma of the cardia, which is triggered by reflux disease, has been rising in Europe and North America over the past two decades [3].

Small intestine cancer is a rare type of tumor that accounts for < 5% of primary gastrointestinal tumors originating in the small intestine. A review of 144 cases of small intestine cancer showed that 64% of patients were men, with a median age of 55.7 years, and that the four most common types of small intestine cancer are adenocarcinoma (47%), carcinoid (28%), sarcoma (13%), and lymphoma (12%) [17]. A study from Sweden reported that, from 1960 to 2009, the incidence of small intestine cancer increased from 14.2 to 19.7 per million per year. The incidence of duodenal cancer increased more than threefold from 1.6 to 5.4 per million per year, and the incidence of adenocarcinoma of the duodenum increased from 0.7 to 4.2 per million per year. Malignant tumors of the small bowel with unspecified anatomical locations increased slightly from 7.0 to 7.9 per million, but the incidence of small bowel tumor in other locations and of other histological types was more stable [18].

Global Cancer Statistics - 2008 stated that colorectal cancer is the third most common cancer in males and second most common in females [19, 20]. Several studies have reported that the incidence of colorectal cancer has been increasing in Asian countries [5, 21]. By contrast, the incidence of colorectal cancer has remained stable in most developed countries and has shown decreased trends in the USA [4, 22]. Some studies have shown that colorectal cancer affects a younger population in some regions in Asia, Canada, Australia, North America, and some European countries. In the USA, colon cancer incidence in younger patients (20-40 years) increased by 17%, while rectal cancer incidence rose by 75% in the period 1973-1999 [23]. By contrast, some studies have claimed that this was not a consistent trend or was a temporary trend only in particular areas. In China, the proportion of colorectal cancer patients aged < 50 years decreased from 54.1% in 1960 to 27.3% in 2008 while patients aged > 60 years diagnosed with colorectal cancer increased over time. A shift in the typical location of colorectal cancers has also occurred. In China, from year 2000 to 2008 the proportion of patients with sigmoid colon cancer increased from 13.8% to 20.7%, and that of patients with rectum cancer decreased from 63.3% to 54.4% [20]. By contrast, Gomez et al. found no shift in the location of colorectal cancers; the distribution by which 69% of colorectal cancers were left sided and 31% were right persisted [24]. Similar data were also reported by Effendi et al. who found 74.6% of colorectal cancers were located in the rectum [25].

The aim of this study was to identify the latest trends in the demography, histopathology, and location of gastrointestinal malignancies in patients admitted to

Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia. This hospital is a national referral hospital in Indonesia, to which most patients with malignancy, especially those from Jakarta's surrounding cities are referred.

Methods

This cross-sectional retrospective study was based on medical records collected consecutively from January 1, 2002, to December 31, 2011. The subjects were patients diagnosed with esophageal cancer, gastric cancer, duodenal cancer, and colorectal cancer based on endoscopy reports from the Gastrointestinal Endoscopy Center, Cipto Mangunkusumo National General Hospital.

The variables analyzed in this study were age, gender, histopathology, and location of the cancers. The data were analyzed using analysis of variance, independent t test, chi-square test, or Fisher–Kolmogorov–Smirnov test using SPSS 21.0 to compare the demography, histopathology, and location patterns between the intervals 2002–2006 and 2007–2011.

Results

There were 295 and 343 gastrointestinal cancer patients data analysed during 2002–2006 and 2007–2011, respectively (Table 1) and Among all, 61.7% male and 38.3% female patients during 2002 – 2006 and 59.7% males and 40.3% females during in 2007–2011 period were analysed, out of which most patients were aged 30–60 years.

Table 1 Demography of gastrointestinal cancer patients.

Variable	*2002–2006, n (%)*	*2007–2011, n (%)*	*Total, n (%)*
Total number	295	343	638
Age			
<30 years	12 (4.1%)	27 (7.9%)	39 (6.1%)
30–60 years	201 (68.1%)	229 (66.8%)	430 (67.4%)
>60 years	82 (27.8%)	87 (25.4%)	169 (26.5%)
Gender			
Male	182 (61.7%)	199 (58%)	381 (59.7%)
Female	113 (38.3%)	144 (42%)	257 (40.3%)

The most prevalent gastrointestinal cancers throughout the decade were colorectal cancer (76.3% and 71.4% in 2002–2006 and 2007–2011, respectively), followed by gastric cancer (15.6% and 14.87%), esophageal cancer (7.4% and 7.6%), and duodenal cancer (0.67%% and 6.1%) (Table 2).

Table 2 Incidence of types of gastrointestinal cancer.

Variable	*2002–2006, n (%)*	*2007–2011, n (%)*	*Total, n (%)*
Esophageal cancer	22 (7.4%)	26 (7.6%)	48 (7.5%)
Gastric cancer	46 (15.6%)	51 (14.9%)	97 (15.2%)
Duodenal cancer	2 (0.7%)	21 (6.1%)	23 (3.6%)
Colorectal cancer	225 (76.3%)	245(71.4%)	470 (73.7%)
Total	295 (100%)	343 (100%)	638 (100%)

Esophageal cancer

Demography of esophageal cancer: There was no statistically significant change in the demography of esophageal cancer between the two periods (Table 3). However the prevalence was higher in males as compared to females during both periods.

Table 3 Demography of esophageal cancer patients.

Variable	*2002–2006, n (%)*	*2007–2011, n (%)*	*p-value*
Total number	22	26	
Age, mean	53.32 ± 11.07	51.50 ± 10.32	0.811
< 30 years	0 (0%)	1 (3.8%)	1
30–60 years	20 (90.9%)	21 (80.8%)	0.674
> 60 years	2 (9.1%)	4 (15.5%)	0.674
Age ≤ 60 years vs > 60 years			
≤ 60 years	20 (90.9%)	22 (84.6%)	0.674
> 60 years	2 (9.1%)	4 (15.4%)	
Gender			
Male	16 (72.7%)	16 (61.5%)	0.413
Female	6 (27.3%)	10 (38.5%)	

Histopathology of esophageal cancer: There was a shift in the pattern of the histopathology of esophageal cancer (Table 4). The percentage of squamous cell carcinoma cases were decreased from 2002–2006 to 2007–2011 (54.4% vs 26.9%, p = 0.051) whereas the percentage of adenocarcinoma cases increased from 36.4% to 69.2% (p = 0.023).

Location of esophageal cancer: Overall, there were no changes in the location of esophageal cancers (upper esophagus, lower esophagus, middle esophagus, and diffuse) between the periods (Table 5). There was a nonsignificant increase in the percentage of cases with a diffuse location from 0% to 15.4% (p = 0.112).

Table 4 Histopathology of esophageal cancer.

Histopathology	*2002–2006, n (%)*	*2007–2011, n (%)*	*p-value*
Squamous cell carcinoma	12 (54.4%)	7 (26.9%)	0.051
Adenocarcinoma	8 (36.4%)	18 (69.2%)	0.023
Mucinous adenocarcinoma	1 (4.5%)	1 (3.8%)	1
Adenosquamous carcinoma	1 (4.5%)	0 (0%)	1
Total	22 (100%)	26 (100%)	

Table 5 Location of esophageal cancers.

Location	*2002–2006, n (%)*	*2007–2011, n (%)*	*p-value*
Upper	2 (9.1%)	3 (11.5%)	1
Middle	6 (27.3%)	4 (15.4%)	0.48
lower	14 (63.6%)	15 (57.7%)	0.798
Diffuse	0 (0)	4 (15.4%)	0.112
Total	22 (100%)	26 (100%)	

Gastric cancer

Demography of gastric cancer: The mean age at diagnosis of gastric cancer was 52.02 ± 13.12) years in 2002–2006, and this was decreased to 50.43 ± 11.93) years in 2007–2011 (p = 0.031) (Table 6). This shift in age was also apparent in the different age groups: the percentage of patients aged 30–60 years increased from 60.9% in 2002–2006 to 82.4% in 2007–20011 (p = 0.018), and the percentage of patients aged > 60 years decreased from 34.8% to 13.7% during the same time (p = 0.015). More patients were male in both periods.

Table 6 Demography gastric cancer patients.

Variable	*2002–2006, n (%)*	*2007–2011, n (%)*	*p-value*
Total number	46	51	
Age, mean	52.02 (±13.12)	50.43 (±11.93)	0.031
<30 years	2 (4.3%)	2 (3.9%)	1
30–60 years	28 (60.9%)	42 (82.4%)	0.018
>60 years	16 (34.8%)	7 (13.7%)	0.015
Gender			
Male	29 (63%)	40 (78.4%)	0.095
Female	17 (37%)	11 (21.6)	

Histopathology of gastric cancer: Adenocarcinoma comprises intestinal, diffuse, and indeterminate types. In this study, the intestinal type comprised tubular, papillary, and mucinous adenocarcinoma. The diffuse type comprises signet ring cell carcinoma, and the indeterminate type comprises adenosquamous carcinoma [15]. Nonepithelial tumors comprise gastrointestinal stromal tumor (GIST), composite glandular endocrine tumor, mucosa-associated lymphoid tissue lymphoma, lymphoma, leiomyosarcoma, and mesenchymal tumor. The intestinal type of adenocarcinoma was the most frequent type of gastric cancer in both periods (Table 7). The histopathology pattern of gastric cancer showed that the percentage of the diffuse type of adenocarcinoma decreased from 21.7% in 2002–2006 to 5.9% in 2007–2011 (p = 0.022).

Table 7 Histopathology of gastric cancer.

Variable	2002–2006 (%)	2007–2011 (%)	p-value
Intestinal type of adenocarcinoma	27 (58.7%)	38 (74.5%)	0.098
Diffuse type of adenocarcinoma	10 (21.7%)	3 (5.9%)	0.022
Indeterminate type of adenocarcinoma	0 (0%)	2 (3.9%)	0.496
Nonepithelial carcinoma	9 (19.6%)	8 (15.7%)	0.616
Total	46 (100%)	51 (100%)	

Location of gastric cancer: The percentage of cases with an unclassified location or where the tumor extended more than one location increased from 2.2% in 2002–2006 to 27.5% in 2007–2011(p = 0.001) (Table 8).

Table 8 Location of gastric cancers.

Location	2002–2006	2007–2011	p-value
Proximal	18 (39.1%)	15 (29.4%)	0.313
Body	19 (41.3%)	13 (25.5%)	0.098
Distal	8 (17.4%)	9 (17.6%)	0.974
Extended	1 (2.2%)	14 (27.5%)	0.001
Total	46 (100%)	51 (100%)	

Abbreviations: Proximal = cardia to fundus; Distal = antrum to pylorus.

Duodenal cancer

Demography of duodenal cancer: There was a significant (10-fold) increase in the incidence of duodenal cancer from 2002–2006 to 2007–2011 (Table 9). There were no significant demographic changes in duodenal cancer over this interval, and most patients were aged 30–60 years at both times. The percentage of female duodenal cancer patients increased non significantly from 0% in 2002–2006 to 52.4% in 2007–2011.

Table 9 Demography of duodenal cancer patients.

Variable	*2002–2006, n (%)*	*2007–2011, n (%)*	*p-value*
Total number	2	21	
Age (year), mean	42.50 ± 3.536	50.14 ± 14.193	0.443
<30 years	0	2 (9.5%)	1
30–60 years	2 (100%)	13 (61.9%)	0.526
>60 years	0 (100%)	6 (28.6%)	1
Gender			
Male	2 (100%)	10 (47.6%)	0.261
Female	0 (0%)	11 (52.4%)	

Histology of duodenal carcinoma: There were no changes in the pattern of the histology of duodenal carcinoma from 2002-2006 to 2007-2011(Table 10). Adenocarcinoma was the most prevalent duodenal carcinoma at both periods.

Table 10 Histology of duodenal carcinoma.

Histopathology	*2002–2006*	*2007–2011*	*p-value*
Adenocarcinoma	2 (100%)	15 (71.4%)	1
Non adenocarcinoma	0 (0%)	6 (28.6%)	
Total	2 (100%)	21 (100%)	

Location of duodenal cancers: Similarly, No change was observed in the location of duodenal cancers in both periods (Table 11).

Table 11 Location of duodenal cancers.

Location	*2002–2006*	*2007–2011*	*p-value*
Bulb	1 (50%)	12 (57.1%)	1
Descending part	1 (50%)	9 (42.9%)	
Total	2 (100%)	21(100%)	

Colorectal cancer

Demography of colorectal cancer: The percentage of patients with colorectal cancer aged < 30 years increased from 4.4% in 2002–2006 to 9% in 2007–2011 (p = 0.051) (Table 12). However, the mean age of colorectal cancer incidence did not change significantly.

Histopathology of colorectal cancer: There was no change in the histopathology of colorectal cancer (Table 13) when compared between periods. Carcinoma was the most frequent colorectal cancer in both periods.

Location of colorectal cancers: There was no change in the location of colorectal cancers (Table 14).

Table 12 Demography of colorectal cancer.

Variable	*2002–2006, n (%)*	*2007–2011, n (%)*	*p-value*
Total number	225	245	
Age, mean	51.74 ± 14.012	52.09 ± 14.242	0.645
<30 years	10 (4.4%)	22 (9.0%)	0.051
30–60 years	151 (67.1%)	153 (62.4%)	0.291
>60 years	64 (28.4%)	70 (28.6%)	0.976
Gender			
Male	135 (60%)	133 (54.3%)	0.211
Female	90 (40%)	112 (45.7%)	

Table 13 Histopathology of colorectal cancer.

Histopathology	*2002–2006*	*2007–2011*	*p-value*
Carcinoma	212 (94.2%)	226 (92.2%)	0.395
Non epithelial	12 (5.3%)	19 (7.8%)	0.291
Carcinoid	1 (0.4%)	0 (0%)	1
Total	225 (100%)	245 (100%)	

Table 14 Location of colorectal cancers.

Location	*2002–2006*	*2007–2011*	*p-value*
Right	70 (31.3%)	74 (30.2%)	0.878a
Left	155 (68.9%)	171 (69.8%)	
Total	225	245	

Abbreviations: Right = cecum, ascending colon, hepatic flexure, and transverse colon; Left = descending colon, sigmoid, rectum, and anus.

Discussion

Cancer is the leading cause of death in economically developed countries and the second leading cause of death in developing countries [19]. Gastrointestinal malignancy is one of the most common malignancies in the world, and its incidence remains high, particularly in Asia [4].

The number of cases of gastrointestinal malignancy in Cipto Mangunkusumo National General Hospital was higher in 2007–2011 compared with 2002–2006 (343 and 295, respectively). Most patients were male: 61.4% vs 38.6% (men vs women) in 2002–2006 and 57.8% vs 42.1% in 2007–2011 and aged between 30-60 years. The incidence of gastrointestinal cancer in our hospital is similar to that reported in other countries. In general, we did not find any changing trends in the demography of gastrointestinal malignancy [19].

Esophageal cancer

Demography of esophageal cancer

Esophageal carcinoma is likely to occur in older people and is more frequent in males. A study from the Czech Republic found that the highest incidence of esophageal carcinoma occurred in people aged 50–70 years, with male-to-female ratio of 3.5:1 [7]. In our study, the highest incidence of esophageal cancer occurred in people aged 50–60 years, but the male-to-female ratio was 2:1. Even though the increase in the percentage of female patients did not change significantly between the two periods (27.3% to 38.5%, p = 0.413), we should be aware that this percentage appears to be increasing.

Worldwide, both in high-and low-incidence areas for esophageal cancer, the percentage of the population younger than 30 years with esophageal cancer are 0.5–1%. Data from our hospital is in line with global incidence of esophageal cancer in the younger population aged <30 years. By contrast, a report from Tenwek Hospital, Bomet, Kenya found that the percentage of esophageal cancer in the population aged <30 years was 6.3%. [26]. This difference between studies may reflect genetic or environmental differences such as socioeconomic status, diet, use of traditional medicine or foods, and the presence of communicable diseases [22].

Histopathology of esophageal cancer

During the decade of this study, the number of adenocarcinoma cases increased and that of squamous cell carcinomas decreased. These results are similar to those of a study by Rozen et al. in Israel, which found that the incidence of squamous cell carcinoma of the esophagus decreased and that the incidence of adenocarcinoma increased [15]. Adenocarcinoma of the esophagus is associated with chronic GERD. A recent meta-analysis based on five studies showed that GERD patients without reflux symptoms or at least weekly symptoms had a nearly fivefold increased risk of adenocarcinoma of the esophagus (odds ratio (OR), 4.9; 95% confidence interval (CI), 3.9–6.2), whereas GERD patients with daily symptoms had a sevenfold increased risk of adenocarcinoma of the esophagus (OR, 7.4; 95% CI, 4.9–11.1) compared to normal population [27]. The mechanism for the increased risk could involve the chronic reflux of gastric contents into the esophagus, which irritates the lower part of the esophagus and leads to cell transversion and mutation [15, 28], and eventually to the premalignant lesions of Barrett's esophagus.

In addition to GERD, many studies have shown that obesity is also a risk factor for adenocarcinoma of the esophagus, particularly in men. Several authors have hypothesized that this is because a heavier abdomen tends to increase the pressure on the stomach, causing acid reflux into the esophagus [9]. The increased BMI has strong association with development of adenocarcinoma of esophagus. A recent meta-analysis based on 22 observational studies found that the risk ratio of adenocarcinoma of the esophagus was 2.7 (95% CI, 2.2–3.5) among persons with a BMI of 30 or more compared with those with a normal BMI (25 or less), while a pooled analysis of data from 12 studies comparing individuals with a BMI of 40 or higher with those with a BMI of less than 25 revealed a relative risk of 4.8 (95% CI, 3.0–7.7) [9].

The changing histological pattern of esophageal cancer in Indonesia is similar to that in other countries. The increased prevalence of GERD and obesity has become important factors in the development of adenocarcinoma of the esophagus. The prevalence of GERD in Indonesia has clearly increased in the last two decades. Syam et al. reported that the prevalence GERD in Cipto Mangunkusumo National General Hospital increased from 5.7% in 1997 to 25.2 in 2002 [29].

In addition to the increased prevalence of GERD, the high prevalence of overweight has also become an important factor underlying the changing histological pattern of esophageal cancer both worldwide and in Indonesia. Worldwide, the prevalence of overweight and obesity combined rose by 27.5% for adults and by 47.1% for children between 1980 and 2013 [30]. A study by Stevens et al reported that during 1998 to 2008, there was an increase prevalence of overweight from 24.6% to 34.4% while the obesity increased from 6.4% to 12% [31]. Data from the Ministry of Health, Republic of Indonesia, in the National Basic Health Research 2007 report showed that the percentages of Indonesian people with a BMI ≥ 25 kg/m^2 were about 30% for females and 19% for males in 2008 [32].

We predict that, in the future, adenocarcinoma of the esophagus will occur more often compare with squamous cell carcinoma because of the increase in the prevalence of GERD and obesity in Indonesia. These related factors seemed to be increasing because of dietary changes, especially fast food consumption, in our population. This is supported by the rapid increase in the number of fast food restaurants, which make remarkable profits in Indonesia [33].

Location of esophageal cancers

In this study, the most prevalent location was in the lower third of the esophagus, and adenocarcinoma was the most prevalent type of esophageal cancer. This location is affected by several risk factors, such as GERD and obesity [34]. There was no clear change in the locations of esophageal cancer between the two periods. This might relate to the location of squamous cell carcinomas, which are found in any part of the esophagus, whereas adenocarcinoma is found mainly in the distal third of the esophagus [11].

Gastric cancer

Demography of gastric cancer

The incidence of gastric cancer has been declining over several decades. Gastric cancer occurs most commonly

in males, with a male-to-female ratio of 2:1 to 3:2. The highest incidence occurs in people aged <65 years, and 70% of patients are aged <50 years [19, 35].

In this study, the male-to-female ratio for gastric cancer was 2:1, which is similar to the value reported in the Global Cancer Statistics [19]. In our study, the mean age of gastric cancer patients shifted to a younger age between the two time periods, and the percentage of patients aged 30–60 years increased whereas the percentage of patients aged >60 years decreased. The increased prevalence among the population aged 30–60 years may reflect an increased awareness of health, especially among dyspeptic patients, some of whom received an upper gastrointestinal endoscopy examination. This speculation is also supported by the increased number of doctors who are competent in gastrointestinal endoscopy procedures and the number of gastrointestinal endoscopy facilities in Indonesia during the past decades, which ensure that gastrointestinal cancer patients receive a proper examination in the early stage [36]. Another factor that contributes in the development of gastric cancer in young adults is *H. pylori* infection at a younger age [37]. Several studies have shown that, in addition to genetic factors, *H. pylori* infection plays a major role in the pathogenesis of gastric cancer in young adults [38].

Histopathology of gastric cancer

A report showed that the number of cases of intestinal-type of adenocarcinoma has decreased in Western countries because of declining numbers of cases of *H. pylori* infection [16]. However, in this study, intestinal adenocarcinoma was still the most frequent type of gastric cancer. This may reflect the high incidence of *H. pylori* infection and chronic gastritis in Indonesia. In the latest study of patients with dyspepsia who underwent endoscopic examination in five large cities in Indonesia, 52.3% of 310 samples were positive for *H. pylori* [39]. A study by Henson et al. found higher prevalence rates of *H. pylori* infections in developing Asian countries and lower rates in more industrialized and developed countries [16].

Even though several studies have claimed that the prevalence of *H. pylori* infection in Indonesia remains high, a study by Saragih et al., which collected data from one hospital in Jakarta, showed a gradual decrease in *H. pylori* infection prevalence from 1998 to 2005. The prevalence of *H. pylori* infection was 12.8% in 1998, 12.4% in 1999, 14.7% in 2000, 9.6% in 2001, 11.9 % in 2002, 3.8% in 2003, 2.3% in 2004, and 2.9% in 2005 [40]. Based on these data, we predict that in Indonesia, the intestinal type of gastric cancer will remain the most prevalent type of gastric cancer for the next few years but that the overall prevalence of gastric cancer will continue to decline because of the declining number of *H. pylori* infections.

Location of gastric cancers

Non-cardia gastric cancer was more frequent than cardia gastric cancer. *H. pylori* infection is an important etiological factor for the occurrence of non-cardia gastric adenocarcinoma [41] and the incidence of *H. pylori* infection remains high in Indonesia. Eventhough the incidence of cardia adenocarcinoma has been rising in Europe because of the increased incidence of GERD, in our study, the prevalence of adenocarcinoma with a cardial or proximal location did not change over the studied decade. However, the prevalence of GERD has clearly increased in Indonesia in the last two decades. Syam et al. reported that the prevalence GERD in patients admitted to Cipto Mangunkusumo National General Hospital increased from 5.7% in 1997 to 25.2% in 2002 [27]. Although the increase in the prevalence of GERD did not affect the number of cardia gastric cancer cases, its increase is consistent with the rising of prevalence of adenocarcinoma of the distal esophagus in Indonesia.

In this study, we found that the incidence of cancer with an extended or unclassified location increased from 2.2% to 27.5% (p = 0.001) from 2002–2006 to 2007–2011. Diffuse stomach cancer is an aggressive type of adenocarcinoma and develops more in young population with a family history of the disease or a genetic syndrome [42].

Duodenal cancer

Demography of duodenal cancer

Malignant tumors of the small intestine are rare throughout the world, with a global incidence of less than 1.0 per 100,000 population [43]. The incidence of duodenal cancer in Cipto Mangunkusumo National General Hospital has increased up to 10-fold over the past decade. A similar trend was reported by Lu et al., who claimed that the incidence of small intestine cancer has increased in the last four decades [18].

Lifestyle habits and diet play significant roles in the development of duodenal cancer. A high intake of carbohydrates, red meat, and salted and preserved food increases the risk of adenocarcinoma of the small intestine, whereas a high intake of coffee, fish, and vegetables seems to be protective against adenocarcinoma of the small intestine.

Data from the National Statistical Bureau of the Republic of Indonesia show that there was an increase in consumption of meat and prepared food in the last decade. The average daily per capita consumption of protein as meat increased from 1.33 g in 1999 to 2.75 g in 2010. A similar trend was observed for consumption of prepared food, in which the average daily per capita consumption of protein as prepared food increased from 4.62 g in 1999 to 9.01 g in 2011 [44]. We speculate that, in the near future, the incidence of intestinal cancer will increase because of these dietary changes of Indonesian people, who now prefer to eat more meat and prepared food.

Histology and location of duodenal cancers

Adenocarcinoma arises most commonly in the duodenum,

whereas carcinoid tumors and lymphoma predominate in the jejunum and ileum. Sarcoma distributes equally among all three segments of the small intestine [45].

There were no changes in the histology or location of small intestine cancers in the past decade [18]. Adenocarcinoma was the most prevalent type of duodenal carcinoma in both periods. This finding is consistent with the findings of other studies that found that adenocarcinoma accounts for almost 90% of all cancer of the duodenum. Adenocarcinoma is related to the pathology of cancer of the small intestine, where a high consumption of red meat, carbohydrate, and preserved food triggers the growth of duodenal adenocarcinoma [24].

Colorectal cancer

Demography of colorectal cancer

Colorectal cancer is the most frequent type of gastrointestinal cancer. The incidence and death rates for colorectal cancer increase with age. Overall, 90% of new cases and 94% of deaths occur in individuals 50 years and older. The incidence of colorectal cancer is more than 15 times higher in adults 50 years and older than in those aged 20 to 49 years [46]. In the USA, the rates of colorectal cancer are similar in men and women, although worldwide there appears to be a slight male predominance [47]. Our findings that colorectal cancer was more prevalent in patients aged 30–60 years and in men (3:2 male-to-female ratio) are consistent with these previous studies.

Histopathology of colorectal cancer

Adenocarcinoma counts for 96–98% of all colorectal cancer, and the remaining 2–4% is nonepithelial cancer, which includes neuroendocrine cancer (carcinoid), epidermoid carcinoma, lymphoma, and sarcoma (including GIST) [48]. In this study, the incidence of colorectal adenocarcinoma was >90% during both periods. This shows that colorectal adenocarcinoma was both the most frequent colorectal cancer and the most frequent gastrointestinal cancer.

Location of colorectal cancers

In this study, there was no change in the location of colorectal tumors between the two time periods. Some studies have reported increase in the incidence of colorectal cancer in the right side, which includes the cecum, ascending colon, hepatic flexure, transverse colon, and splenic flexure. However, several studies have also claimed that the data from these previous studies represented only temporary trends in particular areas.

A study by Cucino et al. found that the proportion of proximal lesions increased by 16% among white males and females and by 22% among black males aged over 30 years [49]. However, a study by Gomez et al. reported no significant change in the anatomical distribution of colorectal cancer in the past 10 years and found no significant changes in colorectal cancer locations when compared between ages at diagnosis and genders. Left-sided colorectal cancer accounted for 69% of cases and right-sided cancer for 31% [24].

Conclusion

We found several changing trends in the patterns of gastrointestinal malignancy in Indonesian patients. The histopathology of esophageal cancer changed and adenocarcinoma became more prevalent than squamous cell carcinoma in the second period (2007–2011). The mean age of gastric cancer patients shifted to a younger age, and the percentage of patients aged 30–60 years increased while the percentage of patients aged >60 years decreased. Analysis of the histopathology of gastric cancer showed a significant decrease in the percentage of patients with diffuse type gastric cancer. A new trend was also found in the location of gastric cancers, as shown by the increase in the number of extended lesions to >2 locations. However, this study found no changes in the percentages of cardia and non-cardia gastric cancers. Although several studies have found that the location of colorectal cancers shifted to the right side during this time, we found no such change. Several changing trends found in our study are similar to those reported in other regions of the world. Indonesia is a developing country where the incidence of gastrointestinal malignancy is influenced by a combination of environmental and lifestyle risk factors, including a high incidence of *H. pylori* infection and changes in the lifestyle and diet of the Indonesian population, which have triggered an increase in the incidence of GERD. Further epidemiological data with larger samples are needed to understand fully these changing trends in gastrointestinal malignancy in Indonesia.

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Conflict of interest

The authors declare no conflict of interest.

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