Epidemiology and care of surgical cancers in Sri Lanka.

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Introduction
Rising burden of cancer is a major challenge in the developing world. Cancer burden is estimated mainly by the incidence of cancer within a defined population while considering economic, social and emotional impact it causes. In Sri Lanka, the newly diagnosed cancer cases has increased by two fold over the last 3 decades with a concomitant rise in deaths related to cancer. Breast cancer is the commonest cancer in Sri Lanka. Other commonly prevalent cancers such as oropharyngeal, laryngeal, lung, oesophageal, gastric and colorectal malignancies also demonstrate a rising trend in incidence.

Due to the effective public health network and universal health care across the country, Sri Lanka is known for its commendable achievements in health outcomes compared to other neighbouring low middle income countries. While this success is laudable, Sri Lanka should enhance the existing health resources to cater the cancer epidemiological transitions. Quantification of the trends of the incidence of cancers is essential for the policy makers for the distribution of resources. Therefore, this oration is aimed to describe the trends and patterns of the incidence of common surgical cancers in Sri Lanka supported by additional data from cohort studies regarding the clinical patterns and outcomes.

Methods
The analysis was conducted among selected common surgical cancers in Sri Lanka with high incidence. Specifically, cancers of the breast, thyroid, oropharynx, gastrointestinal tract (oesophagus, stomach and colorectum), hepatopancreaticobiliary system (liver, pancreas and biliary), urological system (prostate, bladder and kidney) were analysed. Details of specific cancers between 2001-2019 were extracted from the Sri Lanka Cancer Registry. The specific ICD-10 coding system was used to define the anatomical regions of cancer. The data on age, sex and histology type were analysed and WHO age standardized rates of specific cancers per 100,000 population were calculated for each year by sex, using the WHO age standardized populations.

The trends and patterns in the incidence of specific cancers were analysed and quantified by Joinpoint regression software version 4.3 which discerns points where a statistically significant change in the trend has occurred. The estimated annual percentage change (EAPC) was quantified for each curve.

Additional findings from cohort studies including individual cancer patients from National Hospital of Sri Lanka (bladder cancer) and Apeksha Hospital (National Cancer Institute) (breast and colorectal cancers) was used to back arguments and support recommendations. Ethical clearance was obtained from the Ethics Review Committee of the Faculty of Medicine, University of Colombo and the relevant institutions.

Results
Incidence and trends of common surgical cancers in Sri Lanka
Breast cancer
Out of 53000 patients with newly diagnosed primary invasive

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Incidence 2019</th>
<th>EAPC (Male/Female)</th>
<th>Average age male</th>
<th>Average age female</th>
<th>Highest incidence (Male/Female)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>19.8</td>
<td>4.7* (2.7*/6.9*)</td>
<td>59</td>
<td>54.5</td>
<td>75+*/60-64</td>
</tr>
<tr>
<td>Thyroid</td>
<td>11.7</td>
<td>6.5* (10.3*/4.5*)</td>
<td>47</td>
<td>43</td>
<td>35-39</td>
</tr>
<tr>
<td>Oral</td>
<td>12.2</td>
<td>4.3* (6.7*/2.3)</td>
<td>62.6</td>
<td>60.4</td>
<td>70-74</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>3.5</td>
<td>8.4* (9.7*/2.4)</td>
<td>60.3</td>
<td>59.2</td>
<td>70-74</td>
</tr>
<tr>
<td>Gastric</td>
<td>2.9</td>
<td>6.8* (8.2*/9.9*)</td>
<td>60.9</td>
<td>60.5</td>
<td>70-74</td>
</tr>
<tr>
<td>Colorectal</td>
<td>11.2</td>
<td>9.1* (8.5*/10*)</td>
<td>60.7</td>
<td>59.6</td>
<td>70-74</td>
</tr>
<tr>
<td>Liver</td>
<td>2.4</td>
<td>7.6* (8.0*/7.4*)</td>
<td>61.4</td>
<td>56.7</td>
<td>70-74</td>
</tr>
<tr>
<td>Biliary</td>
<td>1.1</td>
<td>6.5* (7.5*/5.8*)</td>
<td>59.9</td>
<td>59.8</td>
<td>70-74</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.0</td>
<td>5.3* (5.2*/5.6*)</td>
<td>58.6</td>
<td>57.1</td>
<td>70-74</td>
</tr>
<tr>
<td>Bladder</td>
<td>3.0</td>
<td>12.1* (13.5*/11.5*)</td>
<td>64.6</td>
<td>63.0</td>
<td>70-74</td>
</tr>
<tr>
<td>Kidney</td>
<td>2.8</td>
<td>8.1* (8.4*/11.7*)</td>
<td>55.1</td>
<td>49.4</td>
<td>70-74</td>
</tr>
<tr>
<td>Prostate</td>
<td>10.8</td>
<td>11.4*</td>
<td>69.3</td>
<td>-</td>
<td>75+*</td>
</tr>
</tbody>
</table>

* implies p<0.05
breast cancer, around 97.2% were females. The WHO age standardized incidence in Sri Lanka has increased from 9.2 to 19.8 per 100,000 from 2001-2019 with an estimated annual percentage change (EAPC) of 4.7 (p<0.05).

Analysis of data from 2001-2010 showed only a modest rise in incidence among the younger (< 50 years) women with breast cancer (EAPC=2.3), while the rise was considerable among older women (50 years and older) (EAPC=5.5). However, analysis up to 2019 revealed that the incidence among younger women is also increasing at a greater rate (EAPC=3.0 compared with 4.7 among older women).

**Analysis from a cohort study**

Analysis of 5181 women with newly diagnosed breast cancer with a mean age of 56 years from Apeksha Hospital, Maharagama was conducted during the 5-year period from 2016 to 2020. Around two thirds of the breast cancers were diagnosed at an early stage (stage I & II). The ER / PR and HER-2 positivity rates were 72% and 22% respectively. Two thirds underwent mastectomy. Around 90% of females with node positive disease received chemotherapy while 77% of those indicated had received adjuvant radiotherapy. The rate of endocrine therapy was 88% among the eligible, while the rate of administration of trastuzumab was around 60% among eligible patients with HER2 positivity.

**Thyroid cancer**

Analysis of 25571 thyroid cancers over the 19-year study period (2001-2019) showed that majority were females (81%). The WHO age standardized incidence of thyroid cancer in Sri Lanka surged significantly from 2.44 to 11.7 per 100,000 from 2001-2019 (p<0.05 for trend). Although the increase was gradual over 2001-2012, thereafter it was variable with an overall increasing trend. The EAPC during the rise was 6.5 (95% CI 4.9-1.1).

**Oropharyngeal cancers**

**Oesophageal cancer**

From 2001-2019, 26 459 oesophageal cancers were diagnosed with a male predominance of 53%. The WHO age standardized incidence of oesophageal cancer has risen significantly from 5.78 to 8.46 per 100,000 from 2001 to 2019. This increase was prominent till 2016 and thereafter, showed a decreasing trend till 2019. During the rising period, the EAPC was 1.5. The magnitude of the rise in incidence was considerably higher for males.

**Gastric cancer**

From 2001-2019, 7914 gastric cancers were diagnosed with a male preponderance of 71%. The WHO age standardized incidence of gastric cancer in Sri Lanka has increased from 1.06 to 3.3 per 100,000 from 2001-2016, followed by a decreasing trend to 2.9 per 100,000 in 2019. Females showed a higher proportional increase in incidence (EAPC of 9.9 vs. 8.2).

**Colorectal cancer**

A total of 26 316 colorectal cancer (CRC) were diagnosed over the 19-year study period with an equal gender distribution (male: female: 1). The rectum was the commonest anatomical location (51.1%) and other common locations were sigmoid colon (12.1%) and recto sigmoid junction (4.8%). The WHO age standardized incidence of CRC was observed from 2.9 to 11.9 per 100,000 in from 2001-2017 (p < 0.05 for trend) followed by a decreasing trend to 11.2 per 100,000 in 2019 with an EAPC of 9.1 for the rising trend.

**Analysis from a cohort study**

Analysis of 1578 colorectal cancer patients (colon: 53% (n = 830) and rectum: 47% (n = 748) aged over 18 years (mean age: 61 years) was conducted at the Apeksha Hospital Maharagama from 2016-2020. Stage I, II, III and IV was observed among 13%, 28%, 46%, and 12% respectively. Adjuvant chemotherapy was administered to 82% of stage III colon cancer patients. Neoadjuvant chemoradiotherapy was delivered to only around 50% of patients with stage III rectal cancer.

Common cancers of the hepatopancreatobiliary system

**Liver cancer**
From 2001-2019, 5019 primary liver cancers were diagnosed with a male predominance of 72.7%. The WHO age standardized incidence rates of liver cancer has risen from 0.6 to 2.44 per 100,000 from 2001-2019 (p < 0.05 for trend), with an EAPC of 7.6.

Pancreatic cancer
Analysis over the 19-year period included 2331 pancreatic cancers with a male predominance (52.8%). From 2001-2019, the WHO age standardized incidence rates rose from 0.44 to 0.97 per 100,000 from 2001-2019 with an EAPC of 5.3. Females showed a higher proportional rise than males (EAPC: 5.6 vs. 5.2).

Biliary cancers
Analysis was performed from 2006-2019. During the 14-year study period, 2144 biliary tract cancers were diagnosed with a female preponderance of 54.5%. The incidence of biliary cancer has risen from 0.53 to 1.06 per 100,000 from 2006-2019 (p < 0.05 for trend), with an EAPC of 6.5. The steady increase in incidence was observed among both genders with a higher EAPC among males (7.5 vs. 5.8).

Common cancers of the urological system
Bladder cancer
A total of 7,349 newly diagnosed bladder cancers were documented (males = 80.9%, male: female = 4.24: 1) from 2001-2019. The Joinpoint analysis showed that the incidence of bladder malignancies has surged from 0.88 to 3.9 per 100,000 population from 2001 to 2017; with an EAPC of 12.1 (p<0.05 for trend) with a subsequent decline in incidence (2.97 per 100,000 in 2019).

Analysis from a cohort study
A retrospective analysis of 314 newly diagnosed primary bladder malignancies (mean age = 65.4; males=245, 84.8%) from 2007-2017 at a Urology Unit and National Hospital of Sri Lanka was performed. Of the 289 (92%) urothelial cancers, around 64% had non-muscle invasive cancers (pTa: 30.1%; pT1: 34.3%) and the rest (36%) were muscle invasive. The majority were high grade tumours (n=156, 54%). Around 17.5% had pT1 high grade (pT1-HG) tumours . Of the 55(17.5%) women with bladder cancer, 80% had urothelial cancers. Women had a disproportionately higher proportion of non-urothelial cancers (20% vs.5.4%, p<0.001) and muscle invasiveness (45.5% vs. 33.5% (82/245) than in men .

Prostate cancer
Analysis was performed from 2006 to 2019. A total of 9695 prostate cancers were diagnosed over the 14-year study period. The WHO age standardized incidence observed for prostate cancer has been increasing from 2006 to 2016 from 4.4 to 12.3 per 100,000 population with an EAPC of 11.4 (p<0.05). Thereafter, the rate was static till 2019 to 10.8 per 100,000 with an EAPC of -1 (p>0.05).

Renal cancer
Analysis was performed from 2006-2019. During the 14-year study period, 3833 renal cancers were diagnosed with a male preponderance of 70.4%. The incidence of renal cancer in Sri Lanka has increased from 0.8 to 2.8 per 100,000 from 2006-2019 (p < 0.05 for trend), with an EAPC of 8.1. The steady increase in incidence was observed among males (EAPC: 8.1), whereas females showed a varying trend.

Discussion
Summary of findings
Analysis of data from 2001-2019, revealed a steadily rising trend in the incidence among breast, liver, biliary, oral and renal cancers and variable trends in other cancers. These trends are likely due to the combination of better reporting and diagnosis and true increase in incidence. Analysis of a cohort of breast, colon and bladder cancer patients showed that the diagnosis of malignancy was at a more advanced stage. Furthermore, the concordance with the treatment guidelines was suboptimal.

Primary prevention for common surgical cancers
Tobacco use, chewing of betel quid, alcohol and obesity as a result of unhealthy diet and physical inactivity are some of the major preventable causes. It is commendable that tobacco smoking in public places and advertisements were banned. However, smokeless tobacco and betel chewing is a major predisposing factor for oropharyngeal and upper gastrointestinal cancers in Sri Lanka and there are cultural barriers in banning it completely. Measures should be taken to ban smokeless tobacco to prevent upper aerodigestive cancers.

Minimising exposure to carcinogens is given priority in prevention. However, much greater importance is essential to manage metabolic risk factors that include dietary factors, physical inactivity and obesity. Encouraging a healthy lifestyle by mass education using various media is therefore imperative.

Screening
The NCCP delivers screening programmes for selected malignancies such as breast and oral cancers. Sri Lanka lacks
enough mammography machines to offer nationwide community based mammographic screening for breast cancer. Although clinical breast examination is readily offered in well-women clinics, such facilities are underutilised. Based on age distribution of incidence, women over 40 years may be advised to undergo at least a clinical screening for breast cancer annually.

Similarly, community based screening centres for oropharyngeal cancers are conducted islandwide. However, the compliance and adherence to screening seems suboptimal. Screening should be offered to older individuals with exposure to carcinogenic risk factors including areas where smokeless tobacco consumption is prevalent.

Establishment of endoscopic screening has been established in high-come countries with a high prevalence of cancers of the upper and lower gastrointestinal tract. Currently, similar screening programmes are not established in Sri Lanka due to resource constraints. Owing to rising incidence of colorectal oesophageal and gastric cancers, opportunistic screening via endoscopy/ faecal testing should be offered to symptomatic individuals aged over 40 years based on the incidence patterns. As the majority of cancers are found in the left colon (approximately 70%), screening with sigmoidoscopy can be considered as an alternative for colonoscopy in the context of limited resources.

Prostate cancer showed a rising trend in the incidence and has become the fifth commonest cancer among Sri Lankan males. Although there is no established screening program, prostate specific antigen (PSA) based opportunistic screening should be encouraged among older men with lower urinary tract symptoms.

**Diagnosis and Treatment**

Although, facilities for medical oncology has been established in every district general hospital in Sri Lanka, there is a lack of radiation oncology facilities in the country. Restriction of radiation oncology facilities to a few hospitals leads to increased waiting time, and default rate. As most of above cancers need radiotherapy in the form of adjuvant or neoadjuvant therapy, increasing the radiation oncology facilities is an urgent need.

Cancer care with a multidisciplinary approach is less commonly practised in Sri Lanka. Currently, there are no dedicated breast and endocrine cancer centres despite these being the top two cancers in Sri Lanka. Currently, there are no centralised and dedicated cancer centres for hepatopancreaticobiliary and urological cancers which need specialised expertise and resources. Thus establishing specialised dedicated centres with formal referral pathways is a timely need.

Due to the rising incidence, enhancing the resources for ancillary services such as minimally invasive radiology, immunohistochemistry and molecular diagnostics is an urgent need.

Most cancers in Sri Lanka are treated based on globally accepted guidelines formulated by developed nations. More evidence should be generated to enrich the local guidelines to suit the local setting. The cohort analyses of breast and colorectal cancers revealed considerable lapse in the concordance with the guidelines in terms of administration of neoadjuvant and adjuvant chemoradiotherapy. Establishing nationally accepted local guidelines may reduce such discrepancy.

**Cancer research and improvement of cancer registry**

In Sri Lanka, the National Cancer Registry is the most extensive database for cancer incidence. However, there are challenges of obtaining data related to mortality. Obtaining nationwide cancer mortality data will give important insight to mitigate the increasing burden of cancer in Sri Lanka.

It is documented that characteristics of cancers in this region of the world may be dissimilar to established literature from the developed world. Furthermore, the effects on quality of life and psychological impact are different due to the sociocultural variations. Thus original studies from Sri Lanka in these aspects are a timely necessity.

**Palliative care**

In Sri Lanka, palliative services are established only in selected tertiary care hospitals and community based palliative care is lacking. According to the analysis of incidence most patients with cancer are diagnosed at an age above 70 years. Such patients with comorbidities may not be suitable for major resections despite resectability and will need palliative care. With the increasing population of the elderly in Sri Lanka, the number of patients needing palliative care is expected to rise exponentially. Thus establishment of both tertiary care and community based palliative cancer services is an urgent need in Sri Lanka.

**Health literacy and public education of cancer**

Education of the public and health literacy is imperative for primary prevention, participation in screening and compliance to treatment. Credible information should be
provided by the experts without inducing unnecessary anxiety among the healthy public. In this era, the public seek information from the internet which may be of suboptimal quality and lack updated information. Furthermore, due to issues in readability, the information may be difficult to comprehend or may be misinterpreted. Publishing online information for common cancers is a welcome initiative by the NCCP. However, more focussed information on common malignancies compiled by local experts based local practices in relation to treatment will be useful.

Limitations
The technological advancements over the years would have caused an increase in the diagnosis and data collection which might have contributed to reported increase of cancers. Incomplete and missing data was noted in the treatment modalities and adjuvant therapy among breast and colorectal cancer cohort and considerable lost to follow up among bladder cancers. However, such limitations would have negligible influence on the reporting of disease characteristics and staging which is more relevant to this analysis.

Conclusions
An overall rising incidence of surgical cancers has been observed. These trends are likely due to the combination of better reporting and true increase in incidence. Regardless, more robust community based screening programmes for selected cancers should be considered. Expansion of the coverage of Sri Lanka Cancer Registry is needed in terms of cancer related mortality. With the rise in surgical cancers, more facilities for curative surgical services, radiation oncology and ancillary services are needed. Establishing nationally accepted local guidelines may reduce the discordance with guidelines however, further studies are needed to study other factors that may have led to this observation. A lack of tertiary care and community based palliative care facilities is a major concern in Sri Lanka and should be addressed urgently.

References


