RESEARCH ARTICLE

The Colorectal Cancer Mortality-to-Incidence Ratio as a Potential Cancer Surveillance Measure in Asia

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Abstract

Background: The cancer mortality-to-incidence ratio (MIR) has been established as an important measure of health disparities in local and global circumstances. Past work has corroborated a linkage between the colorectal cancer MIR and the World Health Organization (WHO) Health System ranking. The literature further documents many Asian countries having incomplete cancer registries and a lack of comprehensive colorectal cancer screening guidelines. Materials and Methods: The colorectal cancer MIR values for 23 Asian countries were calculated from data obtained from the 2012 GLOBOCAN database. The 2000 World Health Organization (WHO) Health System rankings were used as a proxy for health system infrastructure and responsiveness. A regression equation was calculated with the MIR as the dependent variable and the WHO Health System ranking as the independent variable. Predicted MIR values were next calculated based on the regression results. Actual MIR values that exceeded 0.20 from the predicted MIR were removed as 'divergent' points. The regression equation was then re-plotted. Goodness-of-fit for both regressions was assessed by the R-squared test. Results: Asian countries have a relatively wide colorectal cancer MIR range, from a minimum of 0.24 to a maximum of 0.86. For the full dataset, the adjusted R-squared value for this regression was 0.53. The equation was then used to calculate a predicted MIR, whereby two data points were identified as 'divergent' and removed. The adjusted R-squared for the edited dataset increased to 0.66. Conclusions: Asian countries have a marked range in their colorectal cancer MIR values and there is a strong correlationwith the WHO Health System ranking. These results corroborate the contribution of the MIR as a potentially robust tool in monitoring changes in colorectal cancer care for Asian nations.

Keywords: Colorectal cancer - incidence-mortaltiy ratio - Asia - WHO Health System - ranking

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Introduction

Colorectal cancer (CRC) has had a substantial detrimental effect on human health worldwide and is taking an increasing toll on medical and public health resources globally. In Asia, CRC has the sixth highest cancer incidence and seventh highest cancer mortality for both sexes (IARC, 2008). During the 2000s, the 5-year CRC survival in the region stayed relatively constant at 60%, despite substantial variability between countries. East Asia has higher CRC survival than South Asia, with a lack of early CRC detection and treatment being linked to these significant survivorship differences (Moghimi-Dehkordi and Safaee, 2012). Complicating the ability to understand the sources of these differences are unreliable cancer incidence and mortality statistics. Incomplete cancer registration in much of the region collectively pose a further serious barrier to understanding. Indeed, only Japan, Taiwan, South Korea, and Singapore have national guidelines for colorectal cancer screening. Most other Asian countries do not have these screening guidelines, or do not fund effective screening programs (Sung et al, 2008). Furthermore, incomplete cancer registration has generated substantial skepticism on the reliability of the cancer data that is available (Yeole, 2006; Song et al, 2007).

Without accurate data, there are serious limitations to assessing the quality and comprehensiveness of existent prevention and treatment services in the region. Nevertheless, multiple reasons exist for inconsistencies with the currently available data for Asia. Patients may go to different hospitals, and records may not be transmitted between these different facilities. This may be an especially important issue for countries in which registration is incomplete or where quality varies inter-regionally (e.g., in India) (Hebert et al, 2006; Sunkara and Hebert, 2015). Moreover, without formalized screening programs in place, the disease may not be caught until it is in an advanced stage when there are few clinical options outside of adjuvant care. An additional reason for data

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inconsistencies is that those individuals who pass away from complications related to CRC might not be properly counted due to incomplete death certification (Mohandas, 2011). The absence of accurate death certification leaves deceased individuals off the official records, and undercounts mortality tied to CRC. More broadly, there is a dearth of knowledge in the region on this disease entity, further complicating efforts to more completely record the epidemiology of CRC and to understand its etiology. Summarizing the lack of awareness of CRC in Asia, Sung and co-authors concluded: "In most Asian societies, public knowledge of CRC is poor and uptake of screening tests is expected to be low" (Sung et al, 2008).

The need to monitor cancer epidemiology is especially critical in regions where health infrastructure and knowledge are limited. However, it becomes further complicated to do so in places experiencing such limitations. The mortality-to-incidence ratio (MIR) has been used to assess disparities in cancer care in the United States and globally (Hebert et al, 2009; Wagner et al, 2012; Feletto and Sitas, 2015). In these investigations it is has been identified as a relatively robust and parsimonious statistic to track cancer epidemiology and compare the level of prevention and treatment between different groups. Indeed, our previous work demonstrated an association between the colorectal cancer MIR and the World Health Organization (WHO) Health System Rankings for nations in the Organisation for Economic Cooperation and Development (OECD) (Sunkara and Hebert, 2015). However, this relationship has not been examined for non-OECD nations. Assessing the generalizability of the MIR to other regions is an important step in identifying its potential usefulness as a surveillance tool for CRC. At the same time, the application of the MIR to Asian countries allows for a study of this statistic for nations which have a greater heterogeneity in their healthcare systems, but still can provide estimates of CRC incidence. It is in this context where resources are limited, that the further application of a robust and easily calculable statistic as the MIR might have significant benefit.

Data

Raw data on CRC mortality and incidence originates from the publicly available 2012 GLOBOCAN database. This database collects mortality, incidence, and prevalence statistics from 184 nations worldwide. Age-standardized colorectal cancer mortality and incidence statistics were aggregated for both sexes in Asia. A total of 23 countries were selected for investigation, including: India, China, Afghanistan, Bangladesh, Bhutan, Maldives, Nepal, Pakistan, Sri Lanka, Cambodia, Laos, Myanmar, Thailand, Vietnam, Japan, Mongolia, North Korea, South Korea, Malaysia, Brunei, Indonesia, Philippines, and Singapore. Likewise, the WHO Health System Rankings is a composite measure of health system infrastructure completed in 2000. It compiles multiple indices of health system quality and responsiveness and generates a ranking of all nations in the 190 country sample (Tandon et al, 2001). It is a comprehensive attempt at comparing nations in a systematic and quantitative way on the basis of their health infrastructure, and has been identified previously as a potential correlate of the MIR in the setting of OECD nations (Sunkara and Hebert, 2015). Countries present in the WHO ranking that are not in the GLOBOCAN database are primarily Oceania countries.

Materials and Methods

The colorectal cancer mortality-to-incidence ratio (MIR) was calculated for both sexes by dividing the age-standardized mortality rate for colorectal cancer by the age-standardized incidence rate for each nation in the sample. A regression equation was specified with the calculated MIR as the dependent variable and Health System Ranking as the independent variable: Colorectal MIR = $\beta 1$* Health System Ranking + Constant. The R-squared for the equation was calculated as a measure of goodness-of-fit. Next, a predicted MIR was calculated by multiplying the country ranking for each nation with the regression-calculated $\beta 1$ estimate. The difference between the actual MIR and predicted MIR was determined for all nations in the sample. Countries with an MIR difference $>|0.20|$ were removed as 'divergent'. The now-revised dataset was then re-assessed via the plotting of a second linear regression with the same identification approach: Colorectal $MIR_{revised}$ = $\beta 1$* Health System $Ranking_{revised}$ + $Constant_{revised}$.

Results

Table 1 provides a listing of each country's health system ranking, mortality and incidence statistics, and MIR. The range in colorectal cancer MIR is a low of 0.24 (South Korea) to a high of 0.86 (Afghanistan and Bhutan). The mean MIR is 0.64, which is considerably

Table 1. Cancer Statistics and Health System Rankings for Full Sample

	Health System Ranking	Mortality Rate	Incidence Rate	MIR
India	112	4.6	6.1	0.75
China	144	7.4	14.2	0.52
Afghanistan	173	4.2	4.9	0.86
Bangladesh	88	2.7	3.6	0.75
Bhutan	124	3	3.5	0.86
Maldives	147	4.3	5.8	0.74
Nepal	150	2.5	3.2	0.78
Pakistan	122	3	4	0.75
Sri Lanka	76	2.2	3.7	0.59
Cambodia	174	6.2	8.2	0.76
Laos	165	6.6	8.8	0.75
Myanmar	190	6.7	8.7	0.77
Thailand	47	7.3	12.4	0.59
Vietnam	160	7	10.1	0.69
Japan	10	11.9	32.2	0.37
Mongolia	145	4.2	6	0.7
North Korea	167	12	21.8	0.55
South Korea	58	10.7	45	0.24
Malaysia	49	9.4	18.3	0.51
Brunei	40	12	25	0.48
Indonesia	92	8.6	12.8	0.67
Philippines	60	7.8	13.1	0.6
Singapore	6	11.8	33.7	0.35

higher than what we observed in the OECD sample which ranged from 0.24 to 0.57 with a mean of about ½ of this Asian sample's mean (7).

In plotting the regression line for the full dataset, Figure 1 shows that for every 1 unit increase in the health system ranking, there is a 0.0021 proportionate increase in the colorectal cancer MIR. The R-squared value of 0.525 shows that 52.5 percent of the variance is explained by this model.

Table 2. List of Actual and Predicted MIR Values

	Actual MIR	Predicted MIR	Differential
India	0.75	0.64	0.11
China	0.52	0.71	-0.19
Afghanistan	0.86	0.77	0.09
Bangladesh	0.75	0.59	0.16
Bhutan	0.86	0.67	0.19
Maldives	0.74	0.71	0.03
Nepal	0.78	0.72	0.06
Pakistan	0.75	0.66	0.09
Sri Lanka	0.59	0.56	0.03
Cambodia	0.76	0.77	-0.01
Laos	0.75	0.75	0
Myanmar	0.77	0.8	-0.03
Thailand	0.59	0.5	0.09
Vietnam	0.69	0.74	-0.05
Japan	0.37	0.43	-0.06
Mongolia	0.7	0.71	-0.01
North Korea	0.55	0.76	-0.2
South Korea	0.24	0.53	-0.29
Malaysia	0.51	0.51	0.01
Brunei	0.48	0.49	-0.01
Indonesia	0.67	0.6	0.07
Philippines	0.6	0.53	0.06
Singapore	0.35	0.42	-0.07

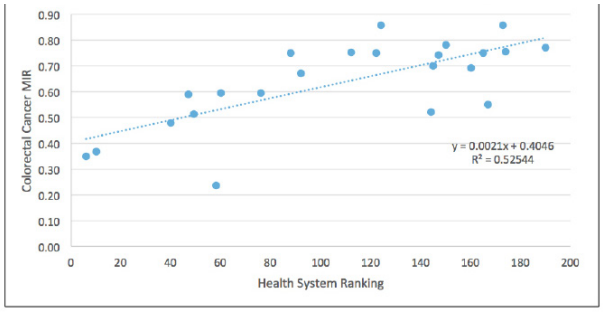

Figure 1. Colorectal Cancer MIR versus Health System Ranking

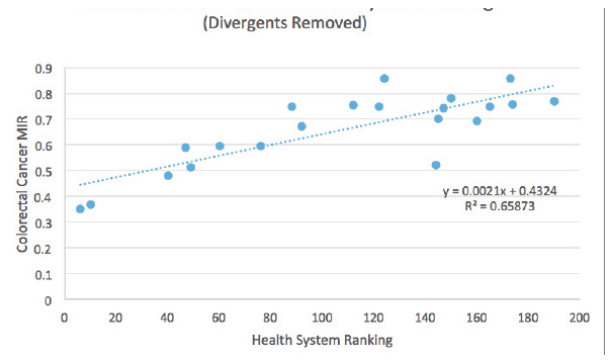

Figure 2. Colorectal Cancer MIR versus Health System Ranking after Removal of Divergent Items

Using the previous regression equation, the predicted MIR result was calculated for each nation. Table 2 shows the differential between the actual and the predicted MIR. There is a range of -0.20 to 0.29.

Any observations with a differential exceeding |0.20| were removed. In this case, 2 points were removed (North Korea and South Korea). On removing the divergent points, Figure 2 shows an increase in the R^2 to 0.66 for the now condensed dataset.

Discussion

The MIR has been gradually established as a useful indicator of disparities in cancer care. While the statistic has been applied predominantly within the United States, there is a growing literature that signals its importance for cancer care disparities across the world. Through its ease in being calculated as well as the ready access to cancer incidence and mortality data in some form across almost all countries, the potential for using the MIR are suspected to be extensive. The current investigation provides further evidence that the colorectal cancer MIR is correlated with measures of health infrastructure. In its extension to Asian countries, this work corroborates the robustness of the MIR in nations where there is wide heterogeneity in the prevention and treatment of colorectal cancer.

In particular, this work shows a strong association between the colorectal cancer MIR and Health System Rankings for Asian countries. The nations had a relatively high mean MIR value of 0.64 with a marked range in values of 0.24 to 0.86. This is reflective of the heterogeneity in the MIR for countries in the region, alongside of a right-skew to the MIR distribution.In contrast, the colorectal cancer MIR values for countries in the Organisation for Economic Cooperation and Development (OECD) had a mean of 0.39 and a more narrow range in values between 0.26 to 0.60. Given this this heterogeneity, it is noteworthy that the R2 value for the full dataset was 0.53. The fraction of data that exceeded the |0.20| cutoff was minimal, i.e., only two of 24 total countries (8.3%). Further, with two divergent observations removed, the R2 increased to 0.66. These findings extend to Asia previous results noting a connection between the MIR for colorectal cancer and healthcare infrastructure. While results from prior analyses were limited to OECD countries, the present work demonstrates this association holds for countries more heterogeneous, and generally much higher, MIR values.

While these results corroborate the use of the MIR for assessing disparities in colorectal cancer care, it also is important to recognize the limitations of this study. There is a time discrepancy between the WHO Health System Rankings and the 2012 GLOBOCAN data. While certain health infrastructure elements in a given country are not expected to change rapidly over time, an increasing time gap between the WHO rankings and the GLOBOCAN data collection will result in a variation in the relationship. The exact extent to which this relationship changes with increasing time is a subject relevant for further investigation. Furthermore, data collection methods varied by country in reliability and comprehensiveness. These

country-specific data also had variability in the timing of data collection.

Despite the limitations noted, it appears that the colorectal cancer MIR is a useful statistic to monitor healthcare infrastructure in both low-income and high-income resource settings in Asia. Further work that extends this research to other cancer types will be helpful to understand the extent that the MIR can be used as a monitoring tool. It is expected that there will be variability in its reliability based on the cancer type. However, the actual extent to which this is true has yet to be determined Cancer care is a extremely pressing concern worldwide, whose importance will increase in a manner commensurate with the aging of most populations. With this in mind, having additional surveillance tools in place to monitor potential disparities in care is a critical issue. Having previously shown the usefulness of the MIR in OECD countries, the extension of that work to Asia now provides further evidence that the MIR may potentially act as such a tool in selected cases. Based on that belief, it is hoped such work will contribute a firm foundation for the optimal application of the MIR for cancer surveillance purposes globally.

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