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Is mortality-to-incidence ratio associated with health disparity in pancreatic cancer? A cross-sectional database analysis of 57 countries

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ABSTRACT

Objective The colorectal cancer mortality-to-incidence ratio (MIR) can reflect healthcare disparities. However, a similar association has not yet been established between the MIR of pancreatic cancer and healthcare disparities.

Methods In this study, the incidence and mortality rates of pancreatic cancer were obtained from the GLOBOCAN 2012 database. The WHO rankings and total expenditures on health/gross domestic product (e/GDP) were obtained from a public database. Linear regression was performed to determine correlations between the variables.

Results 57 countries met the inclusion criteria according to the data quality. Developed regions (Europe and the Americas) had high pancreatic cancer incidence and mortality rates. The MIRs were over 0.90 in all regions. No significant correlation was found between MIRs and the WHO rankings, e/GDP or per capita total expenditure on health for analysis in the 57 countries, indicating no association between MIRs and cancer care disparities for pancreatic cancer.

Conclusions The MIR variations for pancreatic cancer do not correlate with healthcare disparities among countries. Further investigation is necessary to confirm this observation with secondary analysis of databases.

Strengths and limitations of this study

- This is a large observational study with secondary analysis of databases using a global database containing 184 countries.
- Only countries with relatively good data quality are included in further analysis.
- This study did not explore the clinical diversity of patients.
- This is not a cohort study; therefore, the mortality and incident cases might not represent the same patients.
- No information about survival time and survival rate was provided in this analysis.

INTRODUCTION

Pancreatic cancer is a highly lethal disease, and most cases are usually detected in the advanced stages, after metastasis.[1] The incidence rates are currently increasing in the USA,[2] as well as in European countries, highlighting a rising trend worldwide for this disease that might be associated with improved diagnosis methods.[3 4] However, patients with advanced pancreatic cancer have limited treatment options, and fewer than 20% are candidates for surgery.[5 6] Consequently, the prognosis is poor for patients diagnosed with pancreatic cancer.

Many cancers differ in their incidence and mortality rates in specific countries, regions and continents across the globe, which raises the possibility that these differences could reflect regional healthcare disparities.[7–10] The aim of the present study was to use the mortality-to-incidence ratio (MIR) as a parameter for evaluating pancreatic cancer in different countries. The MIR is a measurement that compares the relationship between mortality and incidence, and its value can serve as a proxy for 1–survival.[11 12] Achieving low MIR values depends on adequate cancer screenings, early diagnosis and effective treatments by the healthcare system.[13] For example, Sunkara and Hebert, in their study on colorectal cancer, described the MIR as a useful indicator for cancer screening and care in patients with colorectal cancer, as they found a positive correlation between the MIR values and the healthcare system rankings for different countries.[10]

Pancreatic cancer, unlike colorectal cancer, is difficult to detect and lacks routine screening policies.[1 5 14 15] No evidence yet supports an association between cancer health disparities and the MIR of patients with this cancer. The objective of our study was therefore to evaluate the relationships

between the incidence and mortality rates of pancreatic cancer and healthcare parameters, such as total expenditures on health/gross domestic product (e/GDP) and WHO rankings.

MATERIALS AND METHODS

Data acquisition

Cancer epidemiological data were obtained from the GLOBOCAN 2012 database maintained by the International Agency for Research on Cancer (https://www.iarc.fr/). The WHO ranking for these countries was obtained from the World's Health Systems, maintained by WHO. The e/GDP, per capita total expenditure on health and life expectancies for 2012 were obtained from the World Health Statistics 2015, which is an annual compilation of health-related data for its 194 member states. In total, 184 countries were screened in the GLOBOCAN 2012 database. Among these, 25 countries were excluded since no matching data existed in the WHO database. We also excluded 102 countries according to the availability level rankings of the mortality and incidence data in the GLOBOCAN 2012 database; these excluded countries had availability level rankings of E–G for incidence or 4–6 for mortality. In total, 57 countries were ultimately analysed. The crude rate was defined as rate every 100 000 persons. The MIR, in the present study, was defined as the ratio of the crude rate of mortalities and the crude rate of incidences.[10]

Patient and public involvement

This study analysed GLOBOCAN 2012 database. Therefore, we did not inform or disseminate the patients about the research question, outcome measures and results. Patients did not involve in the study, including design, recruitment and conduct of the study. There was no patient adviser for contributorship statement.

Statistical analyses

Associations between the MIRs and variants among countries were analysed by linear regression as described previously.[7] R^2 changes and analysis of variance were analysed using SPSS statistical software version 15.0 (SPSS, Chicago, Illinois, USA). P values <0.05 of two-sided tests were considered statistically significant. Scatter plots were generated via Microsoft Excel 2010.

RESULTS

Rates of incidence/mortality and MIR of pancreatic cancer according to regions

The case numbers and rates of incidence and mortality for pancreatic cancer in different regions of the world are summarised in table 1. These regions were determined by

Table 1 Summary of the case numbers, rates and mortality-to-incidence ratio (MIR) of the incidence and mortality according to regions in pancreatic cancer

	Number		Crude rate		Age-standardised rate		
Region	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality	MIR*
World	337 872	330 391	4.8	4.7	4.2	4.0	0.98
Development							
More developed regions	187 465	184 429	15.0	14.8	7.2	6.8	0.99
Less developed regions	150 407	145 962	2.6	2.5	2.8	2.7	0.96
WHO region categories							
WHO Africa region	8324	8048	0.9	0.9	1.8	1.7	1.00
WHO Americas region	75 094	73 751	7.9	7.7	5.9	5.6	0.98
WHO East Mediterranean region	7686	7440	1.2	1.2	1.9	1.8	1.00
WHO Europe region	110 499	111 029	12.2	12.3	6.5	6.4	1.01
WHO South-East Asia region	23 210	21 638	1.3	1.2	1.5	1.4	0.92
WHO Western Pacific region	113 015	108 444	6.1	5.9	4.4	4.1	0.97
Continent							
Africa	12 101	11 704	1.1	1.1	2.0	1.9	1.00
Latin America and Caribbean	27 723	27 935	4.6	4.6	4.4	4.4	1.00
Northern America	47 371	45 816	13.5	13.1	7.4	6.9	0.97
Asia	143 363	137 251	3.4	3.2	3.2	3.0	0.94
Europe	103 845	104 554	14.0	14.1	6.8	6.6	1.01
Oceania	3469	3131	9.2	8.3	5.9	5.2	0.90

*The percentage in the ratio of the crude rate of mortalities and the crude rate of incidences.

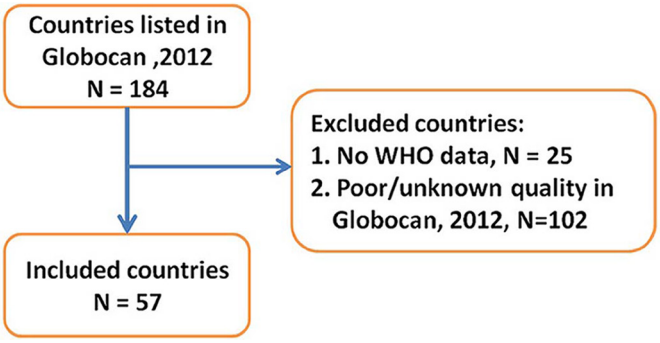

Figure 1 Diagram for data source selection.

three categories: development status, WHO region categories and continent. In this database, the incidence of pancreatic cancer is close in number (337 872 cases) to the number of mortalities (330 391 deaths). The world, as a whole, has a crude incidence rate of 4.8 and a crude mortality rate of 4.7. The age-standardised rates (ASRs) are 4.2 and 4.0 for incidence and mortality, respectively. The crude rates and ASRs of incidence and mortality are much larger in developed regions than in less developed regions (table 1). For the WHO region categories, the crude rates and ASRs of incidence and mortality are highest in the European region. Africa has the lowest crude rates and ASRs among the continents. The overall MIR is 0.98, and high MIRs occur in all regions (table 1).

Rates of incidence/mortality and MIR of pancreatic cancer according to countries

In total, 57 countries were included according to the criteria in this study (figure 1). Table 2 summarises the incidence and mortality according to country. The USA has the highest case number among the 57 countries. Four countries have a crude rate of incidence greater than 20: Japan (26.0), Finland (21.3), Germany (20.1) and the Czech Republic (20.0). These countries are also among the five that have crude mortality rates over 18, with the other one being Slovenia (18.3). The Czech Republic shows the highest ASR in both incidence and mortality (9.7 and 8.7, respectively).

The calculated MIRs are also presented in table 2. Malta has the lowest MIR among the 57 countries. Eighteen countries have MIRs greater than 1.00, with Sweden having the highest MIR. Eight countries have MIRs below 0.90, including Malta (0.80), Costa Rica (0.84), Bahrain (0.87), Bulgaria (0.85), Denmark (0.86), the Philippines (0.88), Ukraine (0.89) and Australia (0.89).

The associations between WHO ranking, e/GDP, per capita total expenditure on health and life expectancy among countries

The WHO ranking, e/GDP and life expectancy among the different countries are also listed in table 2. Linear regression confirms that countries with better WHO rankings have a high e/GDP (p=0.012, online supplementary figure S1A). A similar relationship is evident between the WHO ranking and life expectancy (p<0.001, online supplementary figure S1B). Countries with better WHO rankings are more likely to have higher e/GDP and a longer life expectancy.

The associations between crude rates and ASRs of incidence and mortality to the WHO ranking and to e/GDP are demonstrated in online supplementary figures S2 and S3. Countries with better WHO rankings are more likely to have higher incidence and mortality crude rates, but the ASR shows no statistical significance (online supplementary figures S2A–S2D). Countries with higher e/GDP also have higher incidence and mortality crude rates and ASRs (online supplementary figures S3A–S3D). Interestingly, no significant correlations are observed between WHO ranking, e/GDP and MIR (WHO ranking: R^2=0.001, p=0.818, e/GDP: R^2=0.006, p=0.553), as shown in figure 2. This is further confirmed via using per capita total expenditure on health for analysis. The list of per capita total expenditure on health of selected countries is shown in online supplementary table 1. As shown in figure 3, the MIR is not significantly correlated with per capita total expenditure on health.

DISCUSSION

To our knowledge, this is the first study to investigate the associations between the MIR of pancreatic cancer, the WHO ranking, life expectancy and e/GDP. We found no correlation between MIRs and WHO rankings or between MIRs and e/GDP. These findings differ from those reported previously for colorectal cancer, where a positive correlation was found between the healthcare system rankings and MIRs.[10] This discrepancy probably reflects the different characteristics and natural courses of these two cancers. Colorectal cancer is easier to screen with faecal immunochemical testing, fecal occult blood tests(FOBTs) or colonoscopy and it is a slowly developing cancer, taking years to develop from polyps.[16] The screening methods and long duration of cancer development allow early detection of the disease, as reflected by a higher worldwide incidence rate and an early diagnosis.[10] Pancreatic cancer, by contrast, has no efficient screening methods comparable with those available for colorectal cancer.[14 15 17] The sole screening method that is accessible to the public consists of the CA-199 biomarker, which, unfortunately, has a poor sensitivity and specificity since many non-malignant diseases also increase its level.[17 18]CT is also not sufficiently sensitive for detecting early pancreatic cancer.[19] The lack of screening and early detection strategies, even in highly developed regions, results in advanced cancer stage at diagnosis, with 55% of the cases being diagnosed at stage IV.[20] Consistently high MIRs across global regions are therefore inevitable, as approximately 95% of the cases die within 5 years after diagnosis.[20]

Conversely, we found negative correlations between the WHO ranking and the e/GDP, life expectancy and incidence and mortality crude rates for pancreatic cancer, meaning that the numbers for these categories would

Table 2 Summary of WHO rankings, total expenditure on health/gross domestic product (GDP), life expectancy, pancreatic cancer incidence, mortality and mortality-to-incidence ratio (MIR) of selected countries

Country	Ranking	Total expenditure on health/ GDP (%)	Life expectancy	Number		Crude rate		Age-standardised rate		MIR*
				Incidence	Mortality	Incidence	Mortality	Incidence	Mortality	
France	1	11.6	82	9149	9588	14.4	15.1	6.9	6.5	1.05
Italy	2	9.2	83	10688	10637	17.5	17.4	6.7	6.4	0.99
Malta	5	8.7	81	75	60	17.9	14.3	8.1	6.6	0.80
Singapore	6	4.2	83	404	451	7.7	8.6	5.1	5.6	1.12
Spain	7	9.3	83	6367	5720	13.6	12.2	6.3	5.5	0.90
Oman	8	2.7	76	35	36	1.2	1.2	2.2	2.3	1.00
Austria	9	11.1	81	1585	1486	18.8	17.6	8.2	7.3	0.94
Japan	10	10.3	84	32899	31046	26.0	24.6	8.5	7.7	0.95
Norway	11	9.3	82	735	696	14.8	14.0	7.2	6.6	0.95
Portugal	12	9.9	81	1225	1268	11.4	11.9	5.0	4.9	1.04
Iceland	15	9.0	82	29	29	8.8	8.8	5.0	5.0	1.00
Luxembourg	16	7.2	82	67	67	12.8	12.8	6.1	6.0	1.00
Netherlands	17	12.7	81	2141	2489	12.8	14.9	6.3	6.7	1.16
UK	18	9.3	81	8747	8406	13.9	13.4	6.3	5.9	0.96
Ireland	19	8.9	81	510	488	11.1	10.7	6.6	6.2	0.96
Switzerland	20	11.4	83	1172	1080	15.2	14.0	6.5	5.8	0.92
Belgium	21	10.9	80	1293	1596	12.0	14.8	5.7	5.9	1.23
Colombia	22	6.8	78	1643	1617	3.5	3.4	3.8	3.7	0.97
Sweden	23	9.6	82	964	1640	10.2	17.3	4.8	7.0	1.70
Cyprus	24	7.3	82	77	88	6.8	7.8	4.3	4.9	1.15
Germany	25	11.3	81	16451	16188	20.1	19.7	7.9	7.3	0.98
Israel	28	7.4	82	862	867	11.2	11.3	7.6	7.3	1.01
Canada	30	10.9	82	4472	4293	12.9	12.4	6.4	5.9	0.96
Finland	31	9.1	81	1151	1052	21.3	19.5	8.7	7.8	0.92
Australia	32	8.9	83	2864	2537	12.5	11.1	6.6	5.6	0.89
Chile	33	7.3	80	1152	1246	6.6	7.2	4.8	5.2	1.09
Denmark	34	11.0	80	1023	877	18.3	15.7	8.5	7.1	0.86
Costa Rica	36	10.1	79	210	178	4.4	3.7	4.1	3.5	0.84
USA	37	17.0	79	42885	41509	13.6	13.1	7.5	7.0	0.96

Continued

Table 2 Continued

Country	Ranking	Total expenditure on health/ GDP (%)	Life expectancy	Number		Crude rate		Age-standardised rate		MIR*
				Incidence	Mortality	Incidence	Mortality	Incidence	Mortality	
Slovenia	38	9.4	80	383	374	18.8	18.3	8.8	8.1	0.97
Cuba	39	8.6	78	895	944	8.0	8.4	4.6	4.7	1.05
New Zealand	41	10.2	82	486	476	10.9	10.7	5.9	5.6	0.98
Bahrain	46	4.4	77	21	18	1.5	1.3	2.9	2.7	0.87
Thailand	47	4.5	75	1920	1722	2.7	2.5	2.1	1.8	0.93
Czech Republic	48	7.5	78	2118	1928	20.0	18.2	9.7	8.7	0.91
Malaysia	49	4.0	74	594	774	2.0	2.6	2.4	3.2	1.30
Poland	50	6.8	77	5004	4846	13.1	12.6	6.9	6.6	0.96
Jamaica	53	5.6	74	104	104	3.8	3.8	3.3	3.5	1.00
Republic of Korea	58	7.6	82	5379	5086	11.1	10.5	6.7	6.2	0.95
Philippines	60	4.4	69	1682	1476	1.7	1.5	2.6	2.4	0.88
Slovakia	62	8.1	76	881	815	16.1	14.9	9.4	8.5	0.93
Egypt	63	4.9	71	2347	2268	2.8	2.7	3.4	3.3	0.96
Uruguay	65	8.6	77	454	480	13.4	14.2	7.7	7.9	1.06
Trinidad and Tobago	67	5.5	71	93	88	6.9	6.5	6.1	5.8	0.94
Belarus	72	5.0	72	809	836	8.5	8.8	5.0	5.1	1.04
Lithuania	73	6.7	74	480	458	14.6	13.9	7.4	6.9	0.95
Argentina	75	6.8	76	3988	4330	9.7	10.5	6.7	7.2	1.08
Estonia	77	5.9	77	191	229	14.3	17.1	7.0	7.5	1.20
Ukraine	79	7.5	71	4728	4168	10.5	9.3	5.9	5.3	0.89
Mauritius	84	4.8	74	60	78	4.6	5.9	3.9	5.1	1.28
Fiji	96	4.0	70	17	17	1.9	1.9	2.1	2.2	1.00
Bulgaria	102	7.4	75	1236	1052	16.7	14.2	8.0	6.7	0.85
Latvia	105	5.9	74	371	366	16.6	16.4	8.1	7.4	0.99
Ecuador	111	6.4	76	458	522	3.1	3.5	3.2	3.6	1.13
Brazil	125	9.5	75	9871	9879	5.0	5.0	4.6	4.5	1.00
Russian Federation	130	6.5	69	14512	16371	10.2	11.5	6.0	6.7	1.13
South African Republic	175	8.9	60	1830	1768	3.6	3.5	4.7	4.6	0.97

*The percentage in the ratio of the crude rate of mortalities and the crude rate of incidences.

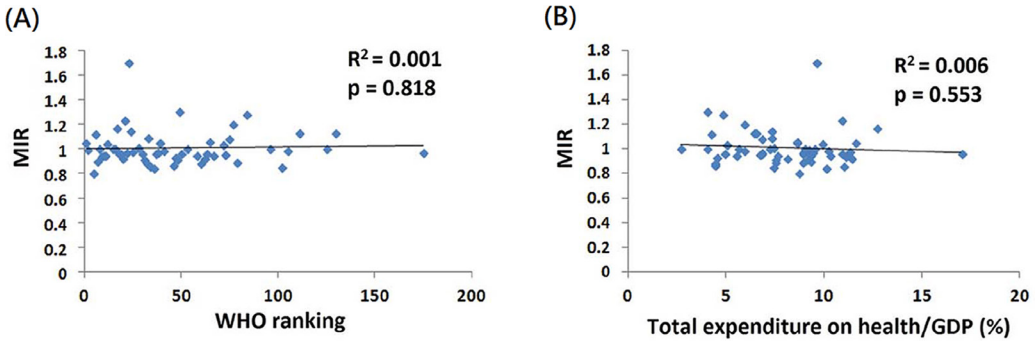

Figure 2 The (A) WHO rankings and (B) total expenditures on health/gross domestic product (GDP) were not associated with the mortality-to-incidence ratio (MIR) of pancreatic cancer.

increase as the WHO rankings improved. We also found positive correlations between the crude rates of mortality and incidence and the e/GDP.[7 21 22] One possible explanation for this latter finding is that this disease usually strikes the elderly, with most cases diagnosed at ages 60–80.[3] Our finding of a negative correlation between the WHO ranking and life expectancy, as shown in online supplementary figure S1, indicates that those countries with better WHO rankings, where the citizens are more likely to have longer life expectancies, also have a higher incidence of this cancer. Another explanation could be the variability in healthcare accessibility among countries with different WHO rankings. Countries with worse rankings are more likely to have poorer healthcare access. Thus, signs and symptoms of pancreatic cancer may be overlooked, thereby causing a decrease in the incidence rate relative to the total cases who die with undiagnosed pancreatic cancer. This will reduce the reported cases both in incidence and in mortality and result in misleading of apparently lower crude rates.

The MIR was calculated with the crude rate ratio of mortality and incidence. In total, 18 countries had MIR values greater than 1.00, which would not happen in a cohort study. However, the GLOBOCAN database, which provides contemporary estimates of the cancer incidence, mortality and prevalence, is not a cohort study. Other factors, such as control of the denominator time, underestimation of cancer incidence and database quality, might account for this issue.[23] Therefore, we excluded countries with poor or unknown availability data according to the ranking of GLOBOCAN 2012 to reduce the information and data bias.

Our study has a large sample size, but it still has some limitations. The GLOBOCAN database collected data from various countries to observe cancer epidemiology. The data were also scored according to the quality of data acquisition. We did not include those countries with poor or unknown availability of mortality/incidence data to reduce the bias, which leads to incompleteness of the data collection and reduces the generalisability of the results. Moreover, patients with early disease might not be diagnosed and not be included in this database. We also did not record the risk factors among countries, such as smoking percentage, long-term diabetes mellitus and chronic pancreatitis, and these risk factors may play important roles in determining the incidence and mortality rates among different countries and regions.[24–28] We also only collected cross-sectional data for 1 year, so the data may not accurately present the actual trend of the disease. Another limitation is the use of WHO ranking: this grading system was established in 2000, so it may not precisely reflect the current situation for healthcare systems among different countries, although the correlations with life expectancy and e/GDP assure some of its credibility. Despite these limitations, our study shows higher incidence and mortality rates of pancreatic cancer in more developed regions and countries with better WHO rankings. However, the MIRs

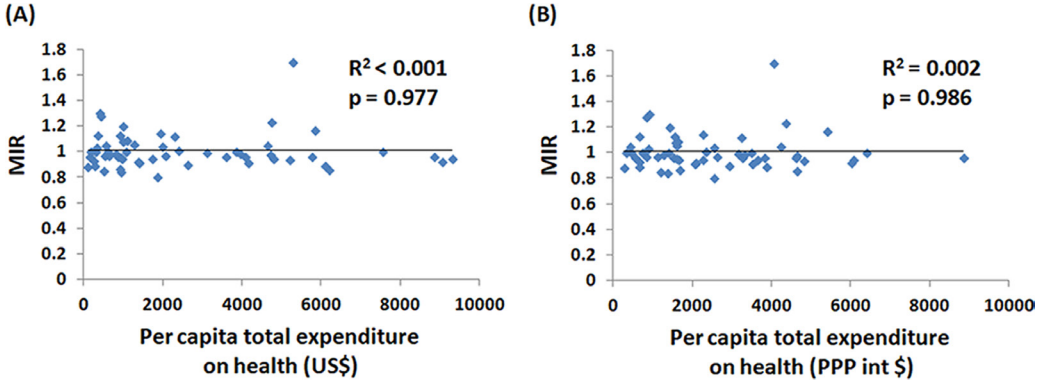

Figure 3 The per capita total expenditure on health in (A) US$ and (B) purchasing power parity at international dollar rate (PPP) were not associated with the mortality-to-incidence ratio (MIR) of pancreatic cancer.

of the countries seem to have no association with their WHO rankings and e/GDP.

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