

RESEARCH COMMUNICATION

Pancreatic Cancer Mortality and Misclassification - Bayesian Analysis

Afsoon Taghavi¹, Zeinab Fazeli², Mohsen Vahedi³, Ahmad Reza Baghestani⁴, Mohammad Reza Zali², Mohamad Amin Pourhoseingholi^{2*}

Abstract

Background: Pancreatic cancer is a fatal cancer with a 5-year survival of only about 4% for all tumors. Mortality is a familiar projection to address the burden of cancers, but according to the Iranian death registry, about 20% of death statistics are still recorded in misclassified categories. The aim of this study was to estimate pancreatic cancer mortality for Iranian population, using a Bayesian approach in order to revise this misclassification. **Methods:** National Death Statistics reported by the Ministry of Health from 1999 to 2004, stratified by age group, sex and cause of death, were the basis for this analysis. Pancreas cancer [ICD-10; 25] were expressed as the annual mortality rates/100,000, overall, by sex and by age group (<50 and ≥50 years of age) and age standardized rate (ASR). The Bayesian approach to correct and account for misclassification effects in Poisson count regression was employed with a beta prior to estimate the mortality rate by age and sex group. **Results:** According to the Bayesian analysis, there were between 20 to 30 percent underreported mortality records in deaths due to pancreatic cancer and the rate decreased slightly during the years of the study. **Conclusion:** Our findings suggest a substantial undercount of pancreatic cancer mortality in the Iranian population. Therefore policy makers who determine research and treatment priorities should note these underreported data for death rates.

Key words: Pancreatic cancer - mortality - Bayesian analysis - under-reporting - Iran

Asian Pacific J Cancer Prev, 12, 2271-2274

Introduction

Gastrointestinal (GI) cancers are the most frequent category of cancer among Iranians (Pourhoseingholi et al., 2009a; 2009b; 2010a; 2010b; 2011). Pancreatic cancer is a rapidly fatal GI cancer (Ries et al., 2002; American Cancer Society, 1996) with a 25-30% five-year survival after surgery (Ryu et al., 2010) and there are currently no effective means of screening, early detection, or treatment (Coughlin, 2000). This cancer accounts for about 220,000 deaths annually and is the sixth major cause of cancer-related mortality due to its low survival (Lowenfels and Maisonneuve., 2005; Parkin et al., 2005) with the mortality approaching the incidence (Karanjawala et al., 2008).

Mortality is a familiar projection to address the burden of cancers (Burnet et al., 2005), but requires reliable death registry systems. Therefore analysis of death statistic subject to misclassification is a major problem in epidemiological analysis leading to biases

estimates, and underestimation of health risks (Stamey et al., 2008). According to the Iranian death registry, between 15% to 20% death statistics were recorded in misclassified categories such as septicemia, senility without mention of psychosis, unknown cancers and other ill-defined conditions (Naghavi, 2004).

In statistical literature two approaches are recommended for misclassification. First is using a small validation sample (Lyles, 2002) and the second is Bayesian analysis in which subjective prior information on at least some subset of the parameters is used to re-estimate death statistic (Whittemore and Gong, 1991; Spoto et al., 1992). Recently we developed a Bayesian model to estimate the burden of GI cancer and applied this model on colorectal cancer (Pourhoseingholi et al., 2009b), gastric cancer (Pourhoseingholi et al., 2010c) and liver cancer (Pourhoseingholi et al., 2010b).

The aim of the present study was to re-estimate pancreatic cancer mortality rate for Iranian population, using this Bayesian approach.

¹Department of Pathology, ²Health System Research, Research Center for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, ³Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, ⁴Department of Mathematic, Islamic Azad University - South Tehran Branch, Iran

*For correspondence: aminphg@gmail.com

Materials and Methods

We employed national death statistic to provide a trend analysis of pancreatic cancer. National death Statistic reported and published by the Ministry of Health and Medical Education (MOH&ME) from 1999 to 2004 (Naghavi, 2000; Naghavi, 2001; Naghavi, 2003; Naghavi, 2004; Naghavi, 2005; Naghavi, 2007) stratified by age group, sex, and cause of death (coded according to the 9th revision of the International Classification of Diseases [ICD-10]) are included in this analysis. Pancreas cancer [ICD-10; 25] were expressed as the annual mortality rates/100,000, overall, by sex and by age group (<50 and ≥50 years of age) and age standardized rate (ASR). The populations of Iran in 1999-2004 were estimated, using the censuses conducted by Statistics Centre of Iran and number of covered provinces in death registration data-base.

The Bayesian approach which considered here derived from models proposed by Stamey et al to correct and account for misclassification in a Poisson regression (Stamey et al., 2008). Stamey's technique extended the model recently proposed to overcome the problem of misclassification in cancer data (Whittemore and Gong, 1991; Spoto et al., 1992) and Pourhoseingholi et al developed this technique to estimate mortality rate of colorectal cancer (Pourhoseingholi et al., 2009b), gastric cancer (Pourhoseingholi et al., 2010c) and liver cancer (Pourhoseingholi et al., 2010b). The misclassification probability estimate which is proposed in prior distribution was based on Iranian

Table 1. Age Standardized Rate (per 100,000) for Pancreas Cancer Mortality, by Sex Group Before and after Adjusting for Misclassification with the Bayesian Model

Year	Male		Female		Total	
	FR	BR	FR	BR	FR	BR
1999	1.54	1.81	0.77	0.91	1.16	1.37
2000	1.25	1.46	0.70	0.82	1.03	1.20
2001	1.22	1.49	0.86	1.05	1.05	1.28
2002	1.13	1.35	0.64	0.77	0.89	1.07
2003	1.10	1.29	0.70	0.82	0.90	1.05
2004	0.89	1.06	0.57	0.68	0.73	0.87

FR, Frequency Rate; BR, Bayesian Rate

Table 2. Age Specific Rate (per 100,000) for Pancreas Cancer Mortality Stratified by Sex Group Before and after Adjusting for Misclassification by Bayesian Model

Year	<50 Years		≥50 Years	
	FR	BR	FR	BR
1999	0.14	0.17	5.48	6.48
2000	0.13	0.15	4.84	5.66
2001	0.14	0.17	4.86	5.92
2002	0.10	0.12	4.21	5.05
2003	0.12	0.14	4.22	4.94
2004	0.11	0.13	3.38	4.02

FR, Frequentist Rate; BR, Bayesian Rate

death registration introduced up to 20% misclassified records in total deaths and a beta prior assumed to re-estimate death statistics from misclassified groups. All analysis performed by a Macro, developed in S-Plus.

Results

All death records due to pancreas cancer from 1999 to 2004 are included in this study. The rate of Pancreas cancer mortality classified by sex and age, generated from original database (Frequentist Rate) and their Bayesian corresponding projections (Bayesian Rate) appeared in Table 1 and Table 2. According to the Bayesian re-estimate there were between 20 to 30 percent underreported mortality records in death due to Pancreas cancer (Figure 1). The age standardized mortality rate showed that the mortality slightly

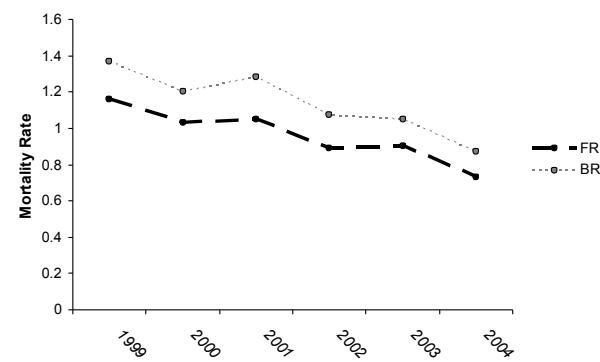


Figure 1. Trends of Pancreas Cancer Mortality During the Period 1999-2004

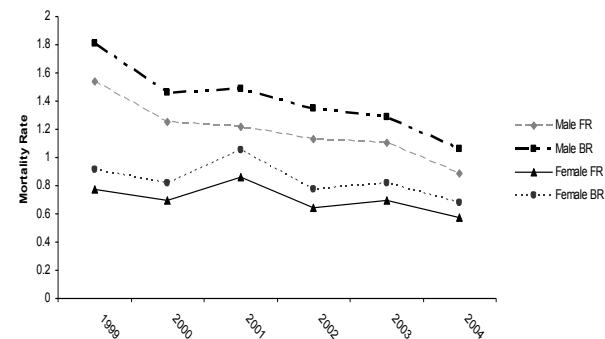


Figure 2. Trends of Pancreas Cancer Mortality During the Period 1999-2004 by Sex Group

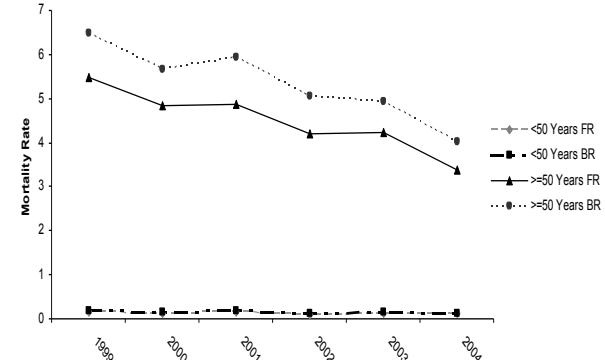


Figure 3. Trends of Pancreas Cancer Mortality During the Period 1999-2004

decreased during the years under study. Moreover Pancreatic cancer mortality was higher for male (Table 1 and Figure2) and older age (Table2 and Figure3). Also decreasing trend for older age in male was higher than female's (Table2). Age specific rate indicated that the mortality increased with age (Table 2 and Figure 3).

Discussion

Our results indicated that up to 20-30% of mortality due to pancreatic cancer remains underreported and suggested a substantial undercount of pancreatic cancer mortality in Iranian population. Also this study indicated that the trend of pancreatic cancer mortality was slightly decreased in the years under study. This declining trend is in contrast to western countries (Katanoda and Yako-Suketomo., 2010) and some Asian countries, such as South Korea and Singapore (Worldwide cancer mortality statistics, 2006) and China (Wang et al., 2003).

In Iranian Death Registration System, data on causes of death are collected from various sources and have been assessed to be about 80% complete (Khosravi et al., 2007). In spite of this, there is still up to 20% undefined death records categorized as misclassification.

Recently Bayesian approach received much attention in the case of misclassification. Whittemore and Gong used this approach to estimate cervical cancer mortality rates (Whittemore and Gong, 1991), Sparto et al developed this model to assess the effect of diagnostic misclassification on non-cancer and cancer mortality dose-response in A-bomb survivors (Sporto et al., 1992), Stamey et al used Bayesian approach in data consisting of the number of deaths due to cancer and non-cancer among residents of Hiroshima and Nagasaki, who were present during the atomic bombings in August of 1945 (Stamey et al., 2008) and we used this technique to estimate mortality rate of colorectal cancer (Pourhoseingholi et al., 2009b), gastric cancer (Pourhoseingholi et al., 2010c) and liver cancer (Pourhoseingholi et al., 2010b) according to Iranian death statistics.

In conclusion, this study provides comprehensive projection for burden of death due to pancreatic cancer based on the national death registry, suggested that the trend of this fatal cancer is still low and may be leveled off in recent years. The burden of disease was higher for male and older age. Besides there is a substantial undercount of pancreatic cancer mortality according to the Bayesian model. So healthcare policy makers who determine research and treatment priorities on death rates as an indicator of burden of disease should notice to this underreported data.

Acknowledgments

This study was sponsored by a grant from the National Elite Foundation, Iran.

References

- American Cancer Society (1996). Cancer facts and figures, American Cancer Society.
- Burnet NG, Jefferies SJ, Benson RJ, et al (2005). Years of life lost (YLL) from cancer is an important measure of population burden – and should be considered when allocating research funds *Br J Cancer*, **92**, 241 -5.
- Coughlin SS, Calle EE, Patel AV, Thun MJ (2000). Predictors of pancreatic cancer mortality among a large cohort of United States adults. *Cancer Causes Control*, **11**, 915-23.
- Karanjawala ZE, Illei PB, Ashfaq R, et al (2008). New markers of pancreatic cancer identified through differential gene expression analyses: claudin 18 and annexin A8. *Am J Surg Pathol*, **32**, 188-96.
- Katanoda K, Yako-Suketomo H (2010).Comparison of time trends in pancreatic cancer mortality (1990-2006) between countries based on the WHO mortality database. *Jpn J Clin Oncol.*, **40**, 601-2.
- Khosravi A, Taylor R, Naghavi M, Lopez AD (2007). Mortality in the Islamic Republic of Iran, 1964–2004. *Bull WHO*, **85**, 607-14.
- Lowenfels AB, Maisonneuve P (2005). Risk factors for pancreatic cancer. *Cell Biochem*, **95**, 649-56.
- Naghavi M (2000). Death report from 4 provinces in Iran. 1st edition. Ministry of Health and Medical Education, Tehran, Iran.
- Naghavi M (2001). Death report from 10 provinces in Iran. 1st edition. Ministry of Health and Medical Education, Tehran, Iran.
- Naghavi M (2003). Death report from 18 provinces in Iran. 1st edition. Ministry of Health and Medical Education, Tehran, Iran.
- Naghavi M (2004). Death report from 18 provinces in Iran. 1st edition. Ministry of Health and Medical Education, Tehran, Iran.
- Naghavi M (2005). Death report from 23 provinces in Iran. 1st edition. Ministry of Health and Medical Education, Tehran, Iran.
- Naghavi M (2007). Death report from 29 provinces in Iran. 1st edition. Ministry of Health and Medical Education, Tehran, Iran.
- Parkin DM, Bray F, Ferlay J, Pisani P (2005). Global cancer statistics, 2002. *CA Cancer J Clin*, **55**, 74-108.
- Pourhoseingholi MA, Vahedi M, Moghimi-Dehkordi B, et al (2009a). Burden of hospitalization for gastrointestinal tract cancer patients - Results from a cross-sectional study in Tehran. *Asian Pac J Cancer Prev*, **10**, 107-10.
- Pourhoseingholi MA, Faghihzadeh S, Hajizadeh E, et al (2009b). Bayesian estimation of colorectal cancer mortality in the presence of misclassification in Iran. *Asian Pac J Cancer Prev*, **10**, 691-4.
- Pourhoseingholi MA, Faghihzadeh S, Hajizadeh E, Abadi A (2010a).Years of life lost due to colorectal cancer in Iran. *Gastroenterol Hepatol From Bed to Bench*, **3**, 187-9.
- Pourhoseingholi MA, Fazeli Z, Zali MR, Alavian SM (2010b). Burden of hepatocellular carcinoma in Iran; Bayesian projection and trend analysis. *Asian Pac J Cancer Prev*, **11**, 859-62.
- Pourhoseingholi MA, Faghihzadeh S, Hajizadeh E, Abadi A (2010 c). Bayesian Analysis of Gastric Cancer Mortality in Iranian Population. *Gastroenterol Hepatol Bed to Bench*, **3**, 15-8.
- Pourhoseingholi MA, Faghihzadeh S, Hajizadeh E, et al (2011). Trend analysis of gastric cancer and colorectal

- cancer mortality in Iran, 1995-2003. *Iran J Cancer Prev*, **1**, 38-43.
- Ries LAG, Eisner MP, Kosary CL, et al (2002). SEER Cancer Statistics Review, 1973-1999. Bethesda, MD, USA: National Cancer Institute.
- Ryu JK, Hong SM, Karikari CA, et al (2010). Aberrant MicroRNA-155 expression is an early event in the multistep progression of pancreatic adenocarcinoma. *Pancreatology*, **10**, 66-73.
- Sposto R, Preston DL, Shimizu Y, Mabuchi K (1992). The effect of diagnostic misclassification on non-cancer and cancer mortality dose-response in A-bomb survivors. *Biometrics*, **48**, 605-17.
- Stamey JD, Young DM, Seaman Jr JW (2008). A Bayesian approach to adjust for diagnostic misclassification between two mortality causes in Poisson regression. *Statist. Med*, **27**, 2440-52.
- Wang L, Yang GH, Lu XH, et al (2003). Pancreatic cancer mortality in China (1991-2000). *World J Gastroenterol*, **9**, 1819-23.
- Worldwide cancer mortality statistics (2006). [cited 2002-06]. Available form: URL: <http://www-depdb.iarc.fr/who/menu.htm>
- Whittemore AS, Gong G (1991). Poisson regression with misclassified counts: application to cervical cancer mortality rates. *Appl Statistics*, **40**, 81-93.