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Research Article

Impact of COVID-19 on Management and Outcomes of Oncology Patients: Results of MENA COVID-19 and Cancer Registry (MCCR)

Abdul-Rahman Jazieh,[1] Adda Bounedjar,[2] Hikmat Abdel-Razeq,[3] Elif Berna Koksoy,[4] Jawaher Ansari,[5] Arafat H. Tfayli,[6] Emad M. Tashkandi,[7] Wasil A. Jastaniah,[8] Mohamed Osama Alorabi,[9] Amira D. Darwish,[10] Ahmed Magdy Rabea,[11] Ashwaq Al Olayan,[12] Fahad Ibnshamsah,[13] Hassan Errihani,[14] Mohammad Omar AlKaiyat,[15] Fazal Hussain,[16] Khaled Alkattan,[17,18] Suanna Steeby Bruinooge,[19] Elizabeth Garrett-Mayer,[19] Hani Tamim[6,17]

[1]Cincinnati Cancer Advisors, Cincinnati, OH, USA
[2]Université Blida 1 Laboratoire de Cancérologie, Faculté de Médecine, Blida, Algeria
[3]King Hussein Cancer Center, Amman, Jordan
[4]Ankara University Faculty of Medicine, Medical Oncology Department, Ankara, Turkey
[5]Tawam Hospital, Al Ain, United Arab Emirates
[6]American University of Beirut, Beirut, Lebanon
[7]College of Medicine, Umm AlQura University and Oncology Center, King Abdullah Medical City, Makkah, Saudi Arabia
[8]King Faisal Specialist Hospital & Research Center - Jeddah, Jeddah, Saudi Arabia
[9]Shefaa Al Orman Hospital and Clinical Oncology Department, Faculty of Medicine - Ain Shams University, Cairo, Egypt
[10]NCI Cairo University and Baheya Foundation for Early Detection and Treatment of Breast Cancer, Cairo, Egypt
[11]Shefaa Al Orman Hospital and National Cancer Institute Cairo, Cairo, Egypt
[12]Department of Oncology, King Abdulaziz Medical City, Ministry of National Guard - Health Affairs, Riyadh, Saudi Arabia
[13]King Fahad Specialist Hospital, Dammam, Saudi Arabia
[14]National Institute of Oncology, Mohammed V University, Rabat, Morocco
[15]Oncology Department, King Abdulaziz Medical City, Ministry of National Guard, Riyadh, Saudi Arabia
[16]University of Texas Health Science Center, San Antonio, TX, USA
[17]College of Medicine, Alfaisal University, Riyadh, Saudi Arabia
[18]King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia
[19]American Society of Clinical Oncology, Alexandria, VA, USA

Address correspondence to Abdul-Rahman Jazieh (Jaziehoncology@gmail.com).

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ABSTRACT

Introduction: Despite extensive studies of the impact of COVID-19 on patients with cancer, there is a dearth of information from the Middle East and North Africa (MENA) region. Our study aimed to report pertinent MENA COVID-19 and Cancer Registry (MCCR) findings on patient management and outcomes. **Methods:** MCCR was adapted from the American Society of Clinical Oncology COVID-19 Registry to collect data specifically from patients with cancer and SARS-CoV-2 infection from 12 centers in eight countries including Saudi Arabia, Jordan, Lebanon, Turkey, Egypt, Algeria, United Arab Emirates, and Morocco. The Registry included data on patients and disease characteristics, treatment, and patient outcomes. Logistic regression was used to assess associations with mortality. **Results:** Between November 29, 2020, and June 8, 2021, data were captured on 2008 patients diagnosed with COVID-19 from the beginning of the pandemic. Median age was 56 years (16–98), 56.4% were females, and 26% were current or ex-smokers. Breast cancer (28.5%) was the leading diagnosis and 50.5% had metastatic disease. Delays of planned treatment (>14 days) occurred in 80.3% for surgery, 48.8% for

radiation therapy, and 32.9% for systemic therapy. Significant reduction in the delays of all three treatment modalities occurred after June 1, 2020. All-cause mortality rates at 30 and 90 days were 17.1% and 23.4%, respectively. All-cause mortality rates at 30 days did not change significantly after June 1, 2020; however, 90-day mortality increased from 33.4% to 42.9% before and after that date ($p = 0.015$). Multivariable regression analysis showed the following predictors of higher 30- and 90-day mortality: age older than 70 years, having metastatic disease, disease progression, and being off chemotherapy. **Conclusion:** Patients with cancer in the MENA region experienced similar risks and outcome of COVID-19 as reported in other populations. Although there were fewer treatment delays after June 1, 2020, 90-day mortality increased, which may be attributed to other risk factors such as disease progression or new patients who presented with more advanced disease.

Keywords: COVID-19, cancer, mortality, MENA Region, cancer care

INTRODUCTION

COVID-19 (caused by SARS-CoV-2) spread rapidly from China in 2019 and was quickly identified as a significant cause of mortality and morbidity throughout the world.[1] Aside from morbidity and mortality from the SARS-CoV-2 virus directly, there was a significant impact of the global pandemic on healthcare systems that were already, in many cases, stretched to their limits. The impact of COVID-19 on oncology patients and oncology healthcare providers has been studied from the point of view of lack of available hospital beds, staff, and facilities to maintain regularly scheduled chemotherapy visits and surgeries.[2–5] Some of these studies were initiated in a short period of time with many participating sites across the globe. The various studies included real-time world registries, cross-sectional studies, and interventional studies.[6–9]

Although analyses of many global regions including Europe,[10,11] North America,[12] South America,[13,14] Asia,[15] and Australia[16] are available, there is limited information from the Middle East and North Africa (MENA) region. In the MENA region, the prevalence of SARS-CoV-2 infection, as well as associated mortality, appears to be unequal across the region.[17] For instance, the MENA region overall case fatality has been estimated at 2.46%, but this ranged from 22.75% (Yemen) to 0.7% (Qatar)[17] compared with 1.1% in the United States and 2.2% in India.[17]

The first reported case of COVID-19 in the MENA region was from the United Arab Emirates (UAE) on Jan 29, 2020, corresponding with a Chinese family coming from Wuhan.[18] By May 31, 2020, COVID-19 had caused 290,428 confirmed cases, 3696 deaths, and 157,886 cured cases in the region. Saudi Arabia, followed by Qatar, UAE, Kuwait, and Egypt, has the highest reported confirmed cases. The highest rate of reported death was in Egypt, followed by Algeria, Saudi Arabia, Sudan, and UAE. Arab countries came fourth after the United States, Brazil, and Russia in reported cases at that time. However, In terms of death, Arab countries were not reported in the top 10 countries.[19] The health care systems encountered the same challenges as the rest of the world; however, multiple countries in the MENA region are affected with poverty, armed conflicts, political instability, and fragile healthcare system. Therefore, there is variation of the official responses to the pandemic.[20,21]

Patients with cancer are particularly susceptible to disruption of healthcare provision, already having an inherent risk of more serious adverse outcome due to their immunocompromised status (either from their disease or the treatment regimen) in this patient population.[22] In this article, we plan to fill this crucial gap in knowledge with our presentation of pertinent MENA COVID-19 and Cancer Registry (MCCR) findings and their impact on patient management and outcomes, especially 30-day and 90-day mortality rates.

METHODS

Study Design

The MCCR was adapted from an American Society of Clinical Oncology (ASCO) Survey "COVID-19 in Oncology Registry" to collect data on patients with cancer and SARS-CoV-2 infection from participating centers. The tool was described by previous publications from the ASCO Registry team.[7,23] Study data were collected and managed using a system based on REDCap electronic data capture tools hosted at Alfaisal University, Riyadh, Saudi Arabia.[24,25] Each site was assigned a unique number and portal access to enter the data. Data on any eligible patients were entered retrospectively for existing information and then prospectively for ongoing updates. To avoid selection bias, all patients diagnosed at the participating centers were included.

All sites obtained the appropriate ethical committee's approval from their institutions.

Participating Sites and Eligibility

Oncology centers in the MENA region were eligible to participate in the study. A total of 12 centers in eight countries joined the study, including Saudi Arabia, Jordan, Lebanon, Turkey, Egypt, Algeria, UAE, and Morocco.

Eligible patients with confirmed SARS-CoV-2 infection from the onset of the pandemic were eligible for the study if they had active cancer that was undergoing initial workup, or on systemic therapy or on adjuvant therapy within a year.

Data Collection

The Registry included data on patient demographics and comorbidities and disease characteristics, cancer treatment, infection diagnosis, symptoms, treatment, and complications of the infection. Patient outcomes, including date of death and cause of death were captured. Data were entered manually into REDCap.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS version 28) was used for data cleaning, management, and analysis. Descriptive analysis was carried out, in which number and percent were calculated for categorical variables, and median and IQR were calculated for continuous ones. Associations were assessed using the chi-square test. Moreover, multivariable logistic regression analysis assesses the predictors of 30- and 90-day mortality and adjusts for confounders. To be included in analysis, patients must have had a death even before the landmark time (30 or 90 days) or survive beyond the landmark time. Results were presented as odds ratio (OR) and 95% CI. A p-value of < 0.05 was used to indicate statistical significance. Multivariable regression analysis included all significant variables on univariate analysis with p-value of < 0.05. A Kaplan-Meier curve was used to display overall survival, defined as time from confirmed SARS-CoV-2 infection until death.

RESULTS

Between November 29, 2020, and June 8, 2021, data on 2008 patients from the onset of the pandemic were captured. Median age was 57 years (18–98), 56.1% were women, and 27.1% were current or ex-smokers. Most patients (87.8%) had solid tumors; breast cancer (29%) was the leading diagnosis. Most of the patients had metastatic disease (59.6%). Most patients were at 25 or greater body mass index (63.09%). Table 1 contains the patient and disease characteristics.

Table 1. Patient characteristics ($N = 2008$)

Characteristics	*n* (%)
Age, median (range)	56 (16–98)
< 70 y	1619 (80.8)
≥ 70 y	384 (19.2)
Sex	
Female	1132 (56.4)
Male	876 (43.6)
ECOG performance status	
0	490 (32.4)
1	674 (44.6)
2	223 (14.8)
3	56 (3.7)
4	18 (1.2)
Unknown	50 (3.3)
Smoking	
Current or former	522 (26.0)
Never	1486 (74.0)
Body mass index ($n = 1695$)	
≤ 20	169 (10.0)
20.1–24.9	457 (27.0)
25–34.9	862 (50.89)
≥ 35	207 (12.2)
Comorbidities	
Coronary artery disease	101 (5.0)
Diabetes mellitus	480 (23.9)
Hypertension	615 (30.6)
Pulmonary disease	98 (4.9)
Renal disease	65 (3.2)
Other	113 (6.4)
No comorbidity	1103(54.9)
Country	
Saudi Arabia	253 (12.6)
Jordan	384 (19.1)
Lebanon	128 (6.4)
Egypt	117 (5.8)
Algeria	397 (19.8)
Morocco	22 (1.1)
Turkey	367 (18.3)
United Arab Emirates	340 (16.9)
Disease type	
Breast cancer	572 (28.5)
Gastrointestinal malignancies	373 (18.6)
Genitourinary cancer (bladder/prostate/kidney)	185 (9.2)
Lung cancer	139 (6.9)
Head and neck	175 (8.7)
Gynecologic oncology	98 (4.9)
Hematologic malignancies	245 (12.2)
Others	221 (11.0)
Cancer extent	
Cancer free	262 (15.2)
Locoregional cancer	590 (40.4)
Metastatic cancer	869 (59.6)
Cancer treatment when diagnosed with COVID-19	
Surgery within 6 weeks	107 (5.3)
Radiation therapy	82 (4.1)
Chemotherapy	1090 (54.3)
Stem cell transplant	7 (0.3)
Not receiving any therapy	774 (38.5)
Disease status at COVID-19 diagnosis	
Stable	694 (48.5)
Progressing	634 (44.34)
Unknown	102 (7.1)

ECOG performance status, Eastern Cooperative Oncology Group Performance Status.

Table 2. Rates of treatment interruption

Treatment Administration Time	Surgery *n* = 107	Radiation Therapy *n* = 82	Systemic Therapy *n* =1090	Stem Cell Transplant *n* = 7
Patient received on schedule or within 14 days	10 (9.3)	28 (34.1)	614 (56.3)	3 (42.9)
Patient receipt of therapy or surgery was delayed at least 14 days from initial treatment date	86 (80.3)	40 (48.8)	359 (32.9)	3 (42.9)
Patient receipt of therapy or surgery was discontinued or cancelled with no plans of restart	11 (10.2)	14 (17.1)	123 (11.3)	1 (14.3)

Values are *n* (%).

Treatment Interruption

Delays of planned treatment of more than 14 days occurred in 80.3% for surgery, 48.8% for radiation therapy, and 32.9% for drug therapy (Table 2). The delay or cancellation of all three treatment modalities was reduced significantly after Jun 1, 2020 (Table 3). The most common cause for delaying treatment was the diagnosis of COVID-19 in the patients and to a much lesser extent cancer progression. Lack of resources was a rare reason to delay treatment (Table 4).

Patient Outcomes

All-cause mortality rates at 30 and 90 days were 17.1% and 34.5%, respectively. These rates increased after June 1, 2020. The increase was significant for 90-day mortality (Table 5).

Cause of death was determined to be related to COVID-19 in 204 patients (41.12%), cancer in 224 patients (45.16%), and other causes in 68 patients (13.70%). Most of the deaths occurred at home; 41.65% died in the hospital and 19.65% died in the intensive care unit (Table 6).

The median overall survival of all patients was 533 days ± 10 (513–553) (Fig. 1).

The results of univariate analysis showed age older than 70 years, male gender, lung cancer versus other solid tumors, diagnosis of COVID-19 before Jun 2020, ever smokers, not being on chemotherapy, having progressing cancer versus stable disease, metastatic cancer, or having comorbidities were significant adverse prognostic factors (Table 7).

In a multivariable logistic regression analysis, male sex, diagnosis before Jun 1, 2020, having progressive disease or metastatic cancer, and others were significant variables as depicted in Table 8.

Table 3. Treatment delay or cancellation before and after Jun 1, 2020

Treatment Delivery Delay > 14 d or Cancellation	Eligible Patients (*n*)	Before June 1, 2020	After June 1, 2020	
Surgery delay	86	82 (5.4)	4 (0.8)	< 0.0001
Surgery cancellation	9	8 (0.5)	1 (0.2)	0.352
Radiation therapy delay	39	35 (2.3)	4 (0.8)	0.038
Radiation therapy cancellation	14	10 (0.7)	4 (0.8)	0.72
Drug therapy delay	359	296 (19.6)	63 (12.9)	0.001
Drug therapy cancellation	122	87 (5.7)	35 (7.2)	0.26

Values are *n* (%).

DISCUSSION

Our study provided real-world data on the risks and outcome of patients with cancer affected by COVID-19 in the MENA region and allowed us to compare this and other population's experiences. The fact that the tool used was identical to the ASCO Registry tool enabled us to benefit from ASCO experience and created an opportunity to compare some of the findings in the U.S. population studies by the ASCO Registry. For example, we used the cutoff of June 1, 2020, to enable us to benchmark our findings to published data from the ASCO Registry.[23]

All-cause mortality rates of our patient population were 17.1% and 34.5% at 30 and 90 days, which are somewhat comparable with reports in different populations.

Table 4. Reasons for delaying, altering, or discontinuing treatment

	Surgery *n* = 89	Radiation *n* = 51	Drug Therapy *n* = 474	Transplant *n* = 4
Progressive or recurrent disease	3 (3.4)	2 (3.9)	32 (6.8)	0
Patient's COVID-19 disease	79 (88.8)	44 (86.3)	412 (86.9)	4 (100)
Lack of clinical resources (i.e., restrictions or shortages due to COVID-19 pandemic)	0 (0.0)	1 (2.0)	5 (1.1)	0
Patient's choice	4 (4.5)	0 (0.0)	9 (1.9)	0
Other or unknown	3 (3.4)	4 (7.8)	16 (3.4)	0

Values are *n* (%).

Table 5. All-cause mortality at 30 days and 90 days and change after June 1, 2020

Outcome	Eligible Population (*n*)	Total Deaths	Deaths Among Patients With COVID-19, Feb 1–May 31, 2020	Deaths Among Patients With COVID-19, June 1, 2020–June 8, 2021	*P*
30-day mortality	1655	283 (17.1)	238 (16.6)	45 (19.8)	0.233
90-day mortality	1432	494 (34.5)	422 (33.4)	72 (42.9)	0.015

Values are *n* (%).

In a systematic review of 15 studies with 3019 patients, Europe, the United States, and China revealed an overall case fatality rate of COVID-19 patients with cancer that measured 22.4% (95% CI, 17.3%–28.0%).[26]

The 30- and 90-day mortality in our study was lower in patients who were receiving cancer therapy, as was reported in other studies. It was reported by other investigators that patients receiving recent cancer therapy may have better outcome to COVID-19,[27] but larger studies and other registry data showed recent cancer treatment was associated with adverse outcomes.[22,28] This discrepancy may be explained by the heterogeneity the diseases itself, the treatment regimens used, and their effects on the immune system and other organs. Metastatic disease status was associated with increased risk compared with localized disease in cancer patients with COVID-19. This is likely to reflect delay or interruption in treatments designed to halt cancer spread and progression of localized tumors to metastatic tumors. Interruption of chemotherapy or radiotherapy has been shown to negatively affect outcome in several studies.[9,28] In a large U.S. study of more than 500,000 patients with cancer or no cancer, patients with cancer had worse outcomes. Patients with metastatic disease or receiving recent cancer treatment had worse outcomes.[22]

In a systemic review of 15 studies including 3019 patients from Europe, North America, and Asia, the case fatality rate was 22% and male gender and age older than 65 were associated with poor prognosis.[26]

Contrary to our findings, a reduction in mortality rate after June 2020 reflects what was reported in the ASCO Registry study (a drop in 90-day mortality from 28% to 21%). The reasons may include improved patient management and diagnosis, inclusion of milder cases, or asymptomatic patients.[23] Other investigators reported similar observations of improving outcome after the initial few months of the pandemic.[29]

The reason for increasing mortality after Jun 1 in our population may be the results of the effects of delaying or holding treatment on a large number of patients before that date led to increased risk of dying from advanced cancer after that date. Early strict restriction may have contributed to the reduction in hospital admissions in certain areas and led to increase in the rates of more advanced disease.[30] Many patients cancelled their appointments with their cancer doctors in the early phase of the pandemic. In one study from the region, 16% of the patients cancelled an appointment and 12% cancelled treatment sessions.[31]

Other reasons for increased mortality may include the capture of more severe cases of COVID-19 in participating centers, whereas mild cases were treated in the periphery without referral to the cancer centers or were not even tested. Slow recovery of healthcare systems in the region and continuation of

Table 6. Patient outcome at the time of last encounter ($N = 2008$)

Outcome	*n* (%)
Disposition	
Expired	496 (24.7)
Alive	1512 (75.3)
Place of death	
Home	290 (58.5)
Hospital	109 (22.0)
Intensive care unit	97 (19.65)
Current COVID-19 status/symptoms	$N = 2007$
Symptomatic	459 (22.9)
COVID-19 test positive but asymptomatic	45 (2.2)
Fully recovered with no current symptoms	1007 (50.2)
Deceased due to COVID-19 or COVID-19-related complication	204 (10.2)
Deceased due to other or unknown cause	68 (3.4)
Deceased due to cancer	224 (11.2)

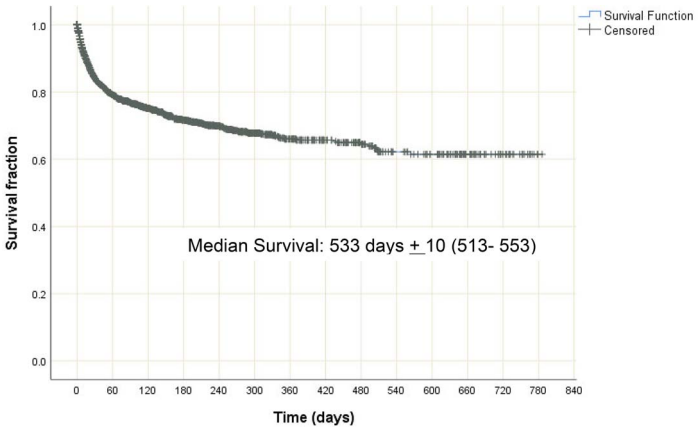

Figure 1. Survival of patients with cancer and COVID-19 ($N = 2008$).

Table 7. Univariate analysis for 30-day and 90-day all-cause mortality rate

	30-Day All-Cause Mortality			90-Day All-Cause Mortality		
Variables	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***p***
Age > 70 y vs ≤ 70 y*	2.05	1.54–2.74	< 0.0001	2.39	1.83–3.11	< 0.0001
Female vs male*	0.64	0.48–0.81	< 0.0001	0.58	0.46–0.72	< 0.0001
Solid tumors vs hematology malignancy (lymphoma/leukemia/myeloma)*	0.85	0.60–1.21	0.356	1.03	0.75–1.40	0.869
Lung cancer vs other solid tumors*	1.69	1.12–2.55	0.012	1.90	1.29–2.80	0.001
Current/ex-smokers vs never smokers*	1.60	1.22–2.21	0.0001	1.72	1.35–2.18	< 0.0001
Diagnosed after June 1, 2020 vs before June 1, 2020*	1.24	0.87–1.77	0.233	1.50	1.08–2.08	< 0.015
On chemotherapy when diagnosed vs no therapy*	0.74	0.58–0.96	0.024	1.02	0.82–1.27	0.860
Stable vs progressing*	0.18	0.13–0.26	< 0.0001	0.10	0.08–0.14	< 0.0001
Metastatic disease vs locoregional disease*	4.16	2.88–6.02	< 0.0001	6.45	4.73–8.79	< 0.0001
Obesity vs no obesity*	0.67	0.49–0.90	0.007	0.52	0.40–0.67	< 0.0001
Comorbidities vs no comorbidity*	1.61	1.25–2.09	< 0.0001	1.63	1.31–2.03	< 0.0001

*Reference group. OR: odds ratio.

overwhelming demands on beds and other resources might have contributed to the increase in mortality.[32]

Despite the increase in mortality after June 1, 2020, median survival of the overall population compared favorably with the results of the COVID-19 and Cancer Consortium study in the United States. Of the 398,579 patients with cancer, the 63,413 patients who had COVID-19 had 30-day and 90-day survival probability of 55% and 35%.[33]

Limitations

This study may not represent all patients with cancer in the region, as disruption of care initially may have resulted in that patient staying at home or getting care in a local hospital and not the cancer centers. However, we included multiple tertiary cancer centers that may have the best representation of cancer patients in the countries. Also, we collect information over a period of time that reflected different stages of the pandemic. We tried to benefit from the ASCO earlier experience and the update of the Registry to capture relevant information.

CONCLUSIONS

The MCCR study contained real-world data about the COVID-19 impact on patients with cancer from multiple countries in the MENA region. The study revealed that patients with cancer and COVID-19 from the MENA region had similar outcomes to those in other populations in terms of 30- and 90-day mortality and many previously identified prognostic factors affect the outcome of patients in this population. Further studies about the impact of local policies and the vaccinations and supportive therapy provided may help identify approaches to manage any similar crisis in the future.

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Table 8. Multivariable logistic regression analysis of 30- and 90-day all-cause mortality

	30-Day All-Cause Mortality			90-Day All-Cause Mortality		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***
Female vs male*	1.008	0.64–1.59	0.972	1.04	0.68–1.59	0.856
Age > 70 y vs ≤ 70 y*	1.699	1.06–2.73	0.028	2.03	1.25–3.32	0.004
Current/ex-smokers vs never smokers*	1.152	0.70–1.90	0.579	1.29	0.80–2.10	0.297
Diagnosed after June 1, 2020, vs before June 1, 2020*	1.672	0.60–2.93	0.072	1.62	0.87–3.04	0.128
On chemotherapy when diagnosed vs no therapy*	0.498	0.33–0.75	0.001	0.60	0.40–0.88	0.010
Stable disease vs progressing disease*	0.308	0.19–0.051	< 0.0001	0.16	0.11–0.26	< 0.0001
Metastatic disease vs locoregional disease*	2.463	1.41–4.29	0.001	3.15	1.94–5.11	< 0.0001
Comorbidities vs no comorbidity*	1.249	0.89–1.88	0.289	1.45	0.98–2.15	0.064
Obesity vs no obesity*	0.728	0.49–1.09	0.125	0.61	0.42–0.90	0.013
Cancer type lung vs others	1.205	0.61–2.38	0.590	1.07	0.48–1.61	0.858

*Reference group. OR: odds ratio.

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