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RESEARCH

Effects of SARS-CoV-2 infections in patients with cancer on mortality, ICU admission and incidence: a systematic review with meta-analysis involving 709,908 participants and 31,732 cancer patients

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Abstract

Background Cancer patients constitute one of the highest-risk patient groups during the COVID-19 pandemic. In this study, it was aimed to perform a systematic review and meta-analysis to determine both the incidence and ICU (Intensive Care Unit) admission rates and mortality in SARS-CoV-2 infected cancer patients.

Methods The PRISMA guidelines were closely followed during the design, analysis, and reporting of this systematic review and meta-analysis. A comprehensive literature search was performed for the published papers in PubMed/Medline, Scopus, medRxiv, Embase, and Web of Science (WoS) databases. SARS-CoV-2 infection pooled incidence in the cancer populations and the risk ratio (RR) of ICU admission rates/mortality in cancer and non-cancer groups, with 95% confidence intervals (CIs), were calculated using the random-effects model.

Results A total of 58 studies, involving 709,908 participants and 31,732 cancer patients, were included in this study. The incidence in cancer patients was calculated as 8% (95% CI: 8–9%). Analysis results showed that mortality and ICU admission rate was significantly higher in patients with cancer (RR = 2.26, 95% CI: 1.94–2.62, $P < 0.001$; RR = 1.45, 95% CI: 1.28–1.64, $p < 0.001$, respectively).

Conclusion As a result, cancer was an important comorbidity and risk factor for all SARS-CoV-2 infected patients. This infection could result in severe and even fatal events in cancer patients. Cancer is associated with a poor prognosis in the COVID-19 pandemic. Cancer patients should be assessed more sensitively in the COVID-19 outbreak.

Keywords SARS-CoV-2 · Cancer · ICU admission · Mortality

Introduction

The COVID-19 outbreak caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which started with a case detected in China on 12 December 2019, was declared as a pandemic by the World Health Organization (WHO) on 11 March 2020 (WHO 2022, 2021; Rothe et al. 2020; Lu et al. 2020; Ge et al. 2020; Sung et al. 2021; Zhang et al. 2020). Currently (May 1, 2020), WHO reported there are 500 million confirmed cases worldwide, with over 6 million deaths documented (WHO 2022). One of the most important problems caused by pandemics is the difficulty in the management of chronic diseases, the frequency of which is increasing with the prolongation of life expectancy in today's world. Today, cancer constitutes a very important subset of chronic diseases. According to the GLOBOCAN (Global Cancer Observatory), in 2040, there will be 9.5 million new cancer cases globally and approximately 6.2 million new cancer-related deaths (GLOBOCAN 2022). It is obvious that the fight against this disease, which is currently very difficult to manage, requires the participation of many branches, and is quite deadly, has become even more difficult during the COVID-19 outbreak. But cancer and cancer-related deaths are just as important as the COVID-19 pandemic (Sung et al. 2021). This reveals the

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need to continue follow-up and treatment of patients even throughout the pandemic. Studies on COVID-19 revealed that advanced age and the presence of several comorbidities in patients result in a more severe COVID-19 clinical tableau and increased mortality (Zhang et al. 2020).

Cancer patients constitute the highest risk patient group during the pandemic due to both underlying diseases, most cancers occur at advanced age, and many chronic diseases increase with age (Rothe et al. 2020; Lu et al. 2020; Ge et al. 2020; Sung et al. 2021; Zhang et al. 2020). The majority of SARS-CoV-2 infected patients experience mild to moderate respiratory symptoms; however, 13.8 percent of COVID-19 patients have severe symptoms, which can lead to multiple organ failure or death (Tian et al. 2020; Pascarella et al. 2020; Li et al. 2020a, b; Jin et al. 2020). According to recent research, SARS-CoV-2 infected individuals with comorbidities, such as endocrinopathies, chronic respiratory, renal, or chronic neurological disease, heart illness and cancer, had a worse prognosis (Jin et al. 2020; Espinosa et al. 2020; Chow et al. 2020; Liang et al. 2020; Wu and McGoogan, 2020).

Current studies have highlighted that cancer enhances sensitivity to SARS-CoV-2 infection and is a risk factor for worse clinical outcomes in SARS-CoV-2 infected patients (Gao et al. 2020; Giannakoulis et al. 2020; Dai et al. 2020; Ma et al. 2020). In a meta-analysis conducted by Giannakoulis et al. (2020), which included a total of 32 studies, on 46,499 SARS-CoV-2 infected patients with malignancy, it was reported that all-cause mortality increased in patients with cancer (RR = 1.66, 95% CI: 1.33–2.07, $p < 0.001$). Similarly, in another meta-analysis that included a total of 63,019 participants, it was concluded that mortality was higher in populations with cancer (RR = 1.80, 95% CI: 1.38–2.35, $p < 0.001$) (Yang et al. 2021). However, current studies had a relatively small sample size for COVID-19. New studies are emerging on this subject day by day. Therefore, the incidence, mortality and ICU admission rate in SARS-CoV-2 infected cancer patients should be calculated in larger samples and wide geographies. The purpose of this study was to perform a systematic review and meta-analysis involving a total of 709,908 participants from 4 continents and 16 countries (Brazil, USA, Sweden, Iran, Spain, Portugal, Switzerland, Turkey, Korea, Ireland, Nigeria, UK, Japan, Italy, People's Republic of China, and India) to determine both the incidence, ICU admission rate and mortality in SARS-CoV-2 infected cancer patients.

Material and methods

Literature search and search strategy

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) reporting guidelines were closely followed during the reporting, design, and analysis of this systematic review and meta-analysis (Liberati et al. 2009). Between March and April 11 (2022), a comprehensive literature searches were conducted for the published papers in PubMed/Medline, Scopus, medRxiv, Embase, and Web of Science (WoS) databases, and an update was performed on April 29 for this search. Related major factors were considered for the search query lines when choosing the keywords: "COVID-19", "clinical characteristics", "coronavirus", "2019-nCoV", "tumour", "SARS-CoV-2", "cancer", "malignancy", "outcomes", and "neoplasm". The related keywords were combined using Medical Subject Headings (MeSH) and text terms, and the Boolean operators AND/OR were used to integrate the keywords. The search strategy was developed in the PubMed, Scopus and WoS databases and applied to other databases (medRxiv, Embase). Search strategies in the related literature are available in Supplemental Table S1. Relevant studies that could be included in the meta-analysis were downloaded from related databases. Afterward, these studies were transferred to Mendeley data management program for data evaluation and analysis.

Study selection and inclusion/exclusion criteria

Original research (case–control or cohort) published about the effect of SARS-CoV-2 infection on cancer from the beginning of the pandemic to April 29th were included in this study. Original studies that were published in the English language were researched, and no other types of paper were examined. In addition, studies covering the following criteria listed below were included in this research: (i) determination of patients in the study as SARS-CoV-2 through clinical/laboratory diagnosis; (ii) the research includes information on the number of cases or deaths or ICU (Intensive Care Unit) admission of participants with and without cancer in populations infected with SARS-CoV-2. Exclusion criteria: (i) reviews, guidelines, opinions, or other non-original data publications; (ii) projects and clinical trials that were incomplete; and (iii) no clinical evidence from animal and laboratory studies.

PICOS:

1. Population: "SARS-CoV-2 infected cancer and non-cancer patients".
2. Intervention: "Cancer".
3. Comparison: "Non-cancer".
4. Outcomes: (i) "SARS-CoV-2 infection risk in patients with cancer"; (ii) "COVID-19 severity risk, including: ICU admission/mortality risk".
5. Study: "Cohort or case-control studies".

Data extraction, acquisition, and quality assessment

Papers were initially scanned based on the title and abstract in related database, and the full text of the appropriate papers were examined. The article titles and abstracts, and any differences amongst co-authors regarding which papers were eligible and which were not were handled using Delphi consensus criteria were examined by two independent authors (MEA and HE) (Verhagen et al. 1998), and the data was extracted into a pre-defined spreadsheet created using Microsoft Excel®. COVID-19 infection incidence, ICU admission, and mortality in cancer patients were separated into three groups and their risks were evaluated. Location, population, type of study, sex, number of patients with cancer and without cancer, ICU admission and mortality in patients with cancer and without cancer, with median age (if given) were also extracted into the same Excel file, in addition to the three key outcomes indicated above. To overcome data limitations-in case of missing data or doubt-the corresponding author(s) of the articles were contacted via email to obtain more details. Prepared data were cross-checked by two investigators via a standard spreadsheet to reach consensus. The Newcastle-Ottawa quality rating scale (NOS) was applied to all studies to evaluate the quality of the articles (Stang 2010).

Statistical analysis

Forest plots were utilized to compute and graphically illustrate the risk ratio (RR) with 95% confidence interval (CI) of COVID-19 infection incidence, ICU admission and mortality rates in the cancer and non-cancer groups, and to summarize them. All research that reported SARS-CoV-2 infection incidence, mortality and/or ICU admission rates in cancer patients as an outcome were evaluated in primary and secondary meta-analyses. Sensitivity analysis -all studies were excluded from analysis separately- was performed to test the reliability of the study results. Mortality and ICU admission rate results in Europe, America and Asia were included in the subgroup analyses. I^2 statistics and Cochran's Q test were used to quantified between-study heterogeneity in all meta-analyses. A ratio of more than 50% in I^2 statistics and a $p \leq 0.05$ in Cochran's Q test revealed that significant heterogeneity (Higgins et al. 2003). If the findings were heterogeneous, the analysis was carried out using random-effect models. Non-heterogeneous findings were calculated using fixed-effects models. For each significant outcome in our research, Egger's linear regression test and funnel plots were utilized to examine the possibility of publication bias. Furthermore, NOS risk assessment method was used to evaluate the risk of bias in the included studies (Stang 2010). For each study, this instrument assigns a maximum score of nine in three categories: "selection", "comparability", and "outcome". The statistical significance level was determined as a 2-sided $p < 0.05$. The Review Manager (v.5.4) (RevMan, 2020), ProMeta3® (Prometa-3, 2015) and Jamovi (version 2.3.3) (Jamovi, 2021) software were used for all the analyses.

Results

In the initial search, a total of 8806 articles were found, with 1357 in Web of Science, 2346 in PubMed, 1689 in Embase, 2956 in Scopus, and 458 in medRxiv databases. After a preliminary review and the elimination of duplicates, 5328 papers were screened and chosen for further evaluation. A total of 58 studies (Adejumo et al. 2021; Akhtar et al. 2021; Alpert et al. 2021; Arslan et al. 2021; Azarkar et al. 2021; Baker et al. 2021; Benelli et al. 2020; Bennett et al. 2021; Bergman et al. 2021; Bernard et al. 2021; Bhargava et al. 2021; Borobia et al. 2020; Pinto et al. 2020; Chai et al. 2021; Fu et al. 2021; Chudasama et al. 2021; Costa et al. 2021; Duanmu et al. 2020; Gold et al. 2020; Görgülü et al. 2020; Goyal et al. 2020; Gude-Sampedro et al. 2021; Guo et al. 2021; Joharatnam-Hogan et al. 2020; Katkat et al. 2021; Kim et al. 2021; Kokturk et al. 2021; Liang et al. 2021; Sun et al. 2021; Cavanna et al. 2020; Lunski et al. 2021; Martinot et al. 2021; Mirgh et al. 2021; Miyashita et al. 2020; Nakamura et al. 2021; Nikpouraghdam et al. 2020; Panda et al. 2022; Péron et al. 2021; Poli et al. 2022; Li et al. 2020a, b; Reddy et al. 2021; Regina et al. 2020; Ricoca-Peixoto et al. 2020; Giorgi-Rossi et al. 2020; Rugge et al. 2020; Erdal et al. 2021; Sami et al. 2020; Santorelli et al. 2021; Pérez-Segura et al. 2021; Serraino et al. 2021; Shahidsales et al. 2021; Sorouri et al. 2020; Stroppa et al. 2020; Tehrani et al. 2021; Vergara et al. 2021; Vila-Corcoles et al. 2021; Zhang et al. 2021; Zhou et al. 2021) (30 in Europe, 16 in Asia, 11 in America, and 1 in Africa) and 709,908 participants (31,732 cancer patients) were included in this systematic review and meta-analysis after applying the inclusion/exclusion criteria. A flow diagram demonstrating the selection process is available in Fig. 1, and the major parameters of the included studies are presented in Table 1. The quality scores of the included studies ranged from 6 to 9. The quality risk assessment of the relevant articles is shown in Supplementary Table S2. Furthermore, a bubble chart showing the distribution of studies by years is visually presented in Fig. S7.

Cancer incidence in SARS-CoV-2 infected patients

Data were analyzed from a total of 55 studies (Adejumo et al. 2021; Akhtar et al. 2021; Alpert et al. 2021; Arslan et al. 2021; Azarkar et al. 2021; Baker et al. 2021; Benelli et al. 2020; Bennett et al. 2021; Bergman et al. 2021; Bernard et al. 2021;

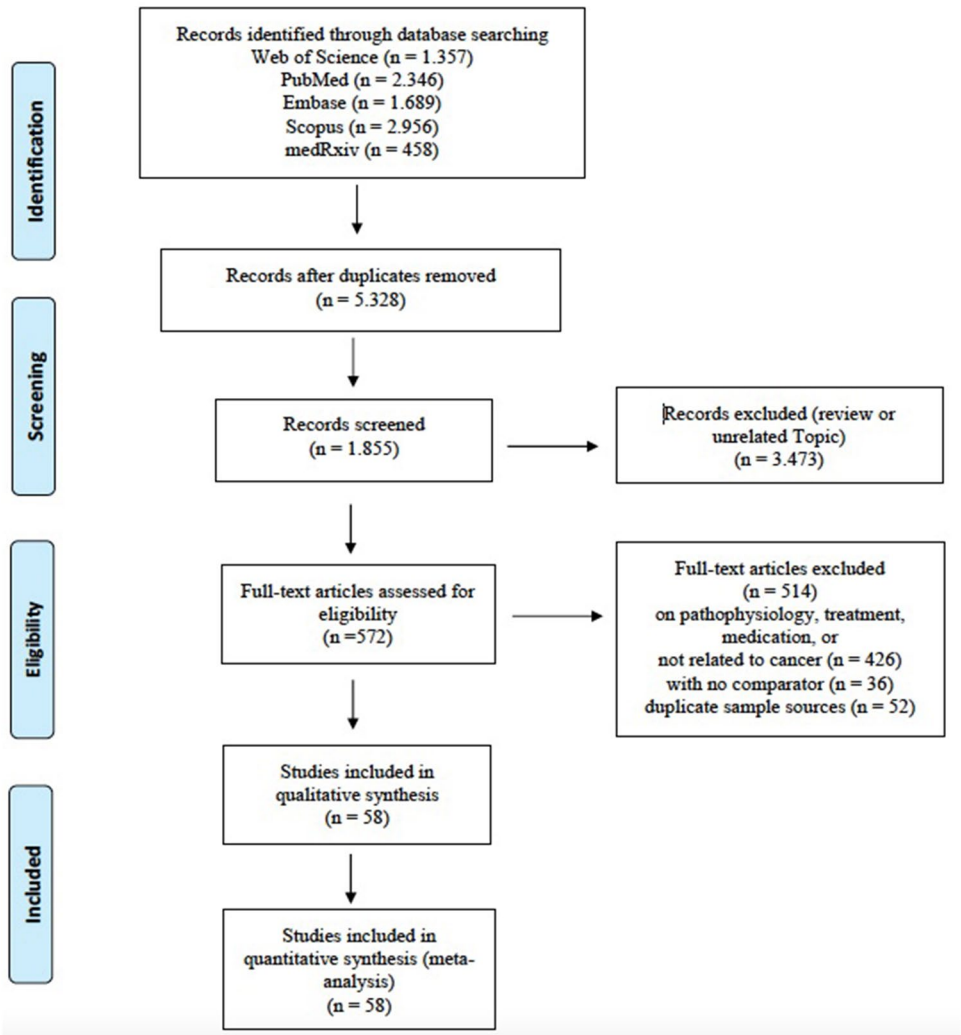

Fig. 1 PRISMA flow diagram of the study collection process

Bhargava et al. 2021; Borobia et al. 2020; Pinto et al. 2020; Chai et al. 2021; Fu et al. 2021; Chudasama et al. 2021; Costa et al. 2021; Duanmu et al. 2020; Gold et al. 2020; Görgülü and Duyan, 2020; Goyal et al. 2020; Gude-Sampedro et al. 2021; Guo et al. 2021; Katkat et al. 2021; Kim et al. 2021; Kokturk et al. 2021; Liang et al. 2021; Sun et al. 2021; Cavanna et al. 2020; Lunski et al. 2021; Martinot et al. 2021; Mirgh et al. 2021; Miyashita et al. 2020; Nakamura et al. 2021; Nikpouraghdam et al. 2020; Panda et al. 2022; Péron et al. 2021; Poli et al. 2022; Li et al. 2020a, b; Reddy et al. 2021; Regina et al. 2020; Giorgi Rossi et al., 2020; Rugge et al. 2020; Erdal et al. 2021; Sami et al. 2020; Santorelli et al. 2021; Pérez-Segura et al. 2021; Serraino et al. 2021; Shahidsales et al. 2021; Sorouri et al. 2020; Tehrani et al. 2021; Vergara et al. 2021; Vila-Corcoles et al. 2021; Zhang et al. 2021; Zhou et al. 2021) on the incidence of cancer in SARS-CoV-2 infected participants (689,462 total participants, 31,066 with cancer). The pooled incidence of cancer in SARS-CoV-2 infected patients is presented in Fig. 2. The pooled ES of incidence in cancer patients was calculated as 8% (95% CI: 8–9%). The cancer incidence in SARS-CoV-2 infected patients was higher than the global cancer incidence (approximately 0.2%) (Bray et al. 2018). The incidence differences between countries were also examined. Among the included studies, the highest incidence was in France (16.912%, 5939/89,952); the lowest incidence was found in Nigeria and Brazil (0.024%, 7406/322,816; 0.004%, 14/2848) (Supplementary Table S3). There was no significant publication bias in the analysis results ($P > 0.05$) (Supplementary Fig. S2). In our analysis, a significant level of heterogeneity was determined among the studies (df = 54, $I^2 = 99\%$, $p < 0.001$). Sensitivity analyzes were performed by extracting each study separately. No significant change was observed in the analysis results. Thus, the robustness of the analysis results was confirmed by sensitivity analysis.

Mortality in SARS-CoV-2 infected cancer and non-cancer patients

A total of 42 studies (Akhtar et al. 2021; Alpert et al. 2021; Arslan et al. 2021; Azarkar et al. 2021; Baker et al.

Table 1 Patient characteristics of included studies in qualitative and quantitative synthesis

Author	Country	Type of study	Sex (Male)	Median age	Cancer patients	Total patients
Adejumo et al. (2021)	Nigeria	R. cohort	1872	60	14	2848
Akhtar et al. (2021)	UK	R. cohort	169	NA	51	293
Alpert et al. (2020)	USA	R. cohort	2907	66.5	421	5556
Arslan et al. (2021)	Turkey	R. cohort	374	52	41	713
Azarkar et al. (2021)	Iran	R. cohort	207	45	11	364
Baker et al. (2021)	UK	R. cohort	173	75	33	316
Benelli et al. (2020)	Italy	R. cohort	359	70.5	33	411
Bennett et al. (2021)	Ireland	R. cohort	8636	NA	747	19,789
Bergman et al. (2021)	Sweden	R. case-control	26,808	NA	5515	68,575
Bernard et al. (2021)	France	R. cohort	NA	NA	5722	89,051
Bhargava et al. (2021)	USA	R. cohort	294	64.4	46	565
Borobia et al. (2020)	Spain	R. cohort	1074	61	385	2226
Pinto et al. (2020)	Italy	R. cohort	733	71.7	138	1226
Chai et al. (2021)	China	R. cohort	246	65	166	498
Fu et al. (2021)	USA	R. Case-control	2438	71	233	4186
Chudasama et al. (2021)	UK	R. cohort	981	NA	179	1706
Costa et al. (2021)	Brazil	R. cohort	181,419	NA	7406	322,816
Duanmu et al. (2020)	USA	R. cohort	56	45	3	100
Gold et al. (2020)	USA	R. cohort	151	60	12	305
Gorgulu et al. (2020)	Turkey	R. cohort	278	74.4	75	483
Goyal et al. (2020)	USA	R. cohort	238	62.2	23	393
Gude-Sampedro et al. (2021)	Spain	R. cohort	4172	58	238	10,454
Guo et al. (2021)	China	R. cohort	3827	55	277	7926
Joharatnam-Hogan et al. (2020)	UK	R. case-control	80	NA	30	120
Katkat et al. (2021)	Turkey	R. cohort	270	NA	34	508
Kim et al. (2021)	Korea	R. cohort	3095	47	569	7590
Kokturk et al. (2021)	Turkey	R. cohort	850	NA	76	1500
Liang et al. (2021)	China	R. cohort	NA	65	109	3060
Sun et al. (2021)	USA	R. cohort	137	56	67	323
Cavanna et al. (2020)	Italy	R. cohort	NA	71	51	973
Lunski et al. (2021)	USA	R. cohort	2013	NA	312	5145
Martinot et al. (2021)	France	R. cohort	346	71.09	109	600
Mirgh et al. (2021)	India	R. cohort	126	43	109	200
Miyashita et al. (2020)	USA	R. cohort	NA	NA	334	5688
Nakamura et al. (2020)	Japan	R. cohort	22	74.5	32	235
Nikpouraghdam et al. (2020)	Iran	R. cohort	1955	56	17	2964
Panda et al. (2022)	India/China	R. cohort	279	37	10	420
Péron et al. (2021)	France	R. case-control	143	76.5	108	301
Poli et al. (2021)	Italy	R. cohort	653	71	141	1091
Li et al. (2020a, b)	China	R. cohort	934	59	65	1859
Reddy et al. (2021)	India	R. cohort	NA	40	23	4494
Regina et al. (2020)	Swiss	R. cohort	120	70.0	26	200
Ricoca Peixoto et al. (2020)	Portugal	R. cohort	8370	NA	611	20,270
Rossi et al. (2021)	Italy	R. cohort	1328	63.2	301	2653
Rugge et al. (2020)	Italy	R. cohort	4529	NA	723	9275
Erdal et al. (2021)	Turkey	R. cohort	NA	62	71	4489
Sami et al. (2020)	Iran	R. cohort	299	56.6	15	490
Santorelli et al. (2021)	UK	R. cohort	329	NA	47	582
Segura et al. (2021)	Spain	R. cohort	NA	75	770	5838
Serraino et al. (2021)	Italy	R. cohort	19,328	NA	3098	41,366

Table 1 (continued)

Author	Country	Type of study	Sex (Male)	Median age	Cancer patients	Total patients
Shahidsales et al. (2021)	Iran	R. case-control	111	59.6	92	185
Sorouri et al. (2020)	Iran	R. case-control	91	NA	53	159
Stroppa et al. (2020)	Italy	R. case-control	NA	NA	25	56
Tehrani et al. (2021)	USA	R. cohort	4991	60.4	892	8222
Vergara et al. (2021)	Italy	R. cohort	710	71.1	49	1049
Vila-Corcoles et al. (2021)	Spain	R. cohort	235	NA	67	536
Zhang et al. (2022)	China	R. cohort	17,662	59	824	36,358
Zhou et al. (2021)	China	R. case-control	171	66	103	309
Total					31,732	709,908

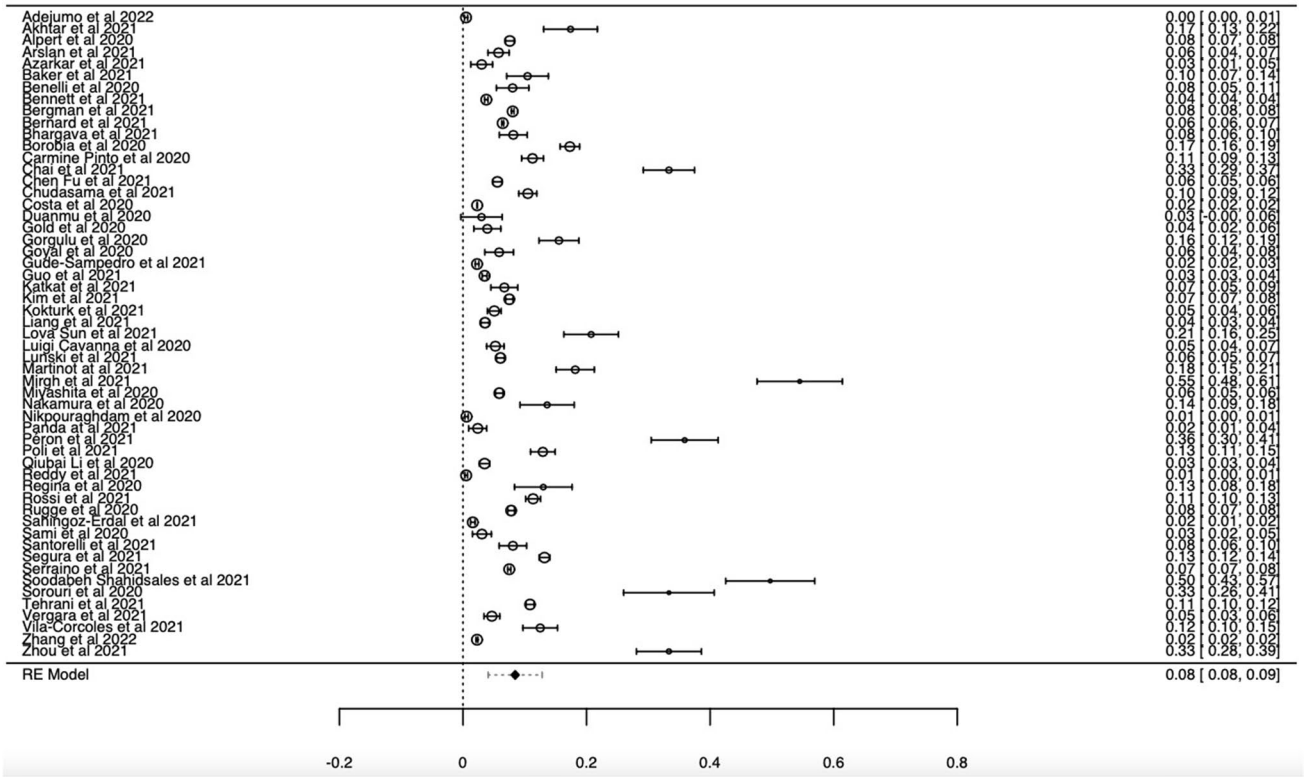

Fig. 2 Forest plot illustrating the incidence of patients with cancer in all SARS-CoV-2 infected participants

2021; Benelli et al. 2020; Bennett et al. 2021; Bernard et al. 2021; Bhargava et al. 2021; Borobia et al. 2020; Pinto et al. 2020; Chai et al. 2021; Fu et al. 2021; Gude-Sampedro et al. 2021; Guo et al. 2021; Joharatnam-Hogan et al. 2020; Katkat et al. 2021; Kim et al. 2021; Kokturk et al. 2021; Liang et al. 2021; Sun et al. 2021; Lunski et al. 2021; Martinot et al. 2021; Mirgh et al. 2021; Miyashita et al. 2020; Péron et al. 2021; Poli et al. 2022; Li et al. 2020a, b; Reddy et al. 2021; Ricoca Peixoto et al. 2020; Giorgi-Rossi et al. 2020; Rugge et al. 2020; Erdal et al. 2021; Pérez-Segura et al. 2021; Serraino et al. 2021; Shahidsales et al. 2021; Sorouri et al. 2020; Stroppa et al. 2020; Vergara et al. 2021; Vila-Corcoles et al. 2021; Zhang et al. 2021; Zhou et al. 2021) were included in the analysis to compare the mortality rates of cancer and non-cancer patients infected with SARS-CoV-2. There were a total of 557,053 participants, of whom 21,599 were cancer patients. According to the analysis results, cancer is a serious risk factor for mortality among patients infected with SARS-CoV-2 (RR = 2.26, 95% CI: 1.94–2.62, $P < 0.001$, Fig. 3). Mortality rates between continents were also evaluated as subgroup analysis and presented in Fig. 4. Mortality in cancer patients infected with SARS-CoV-2 varies between continents, with the highest mortality rate

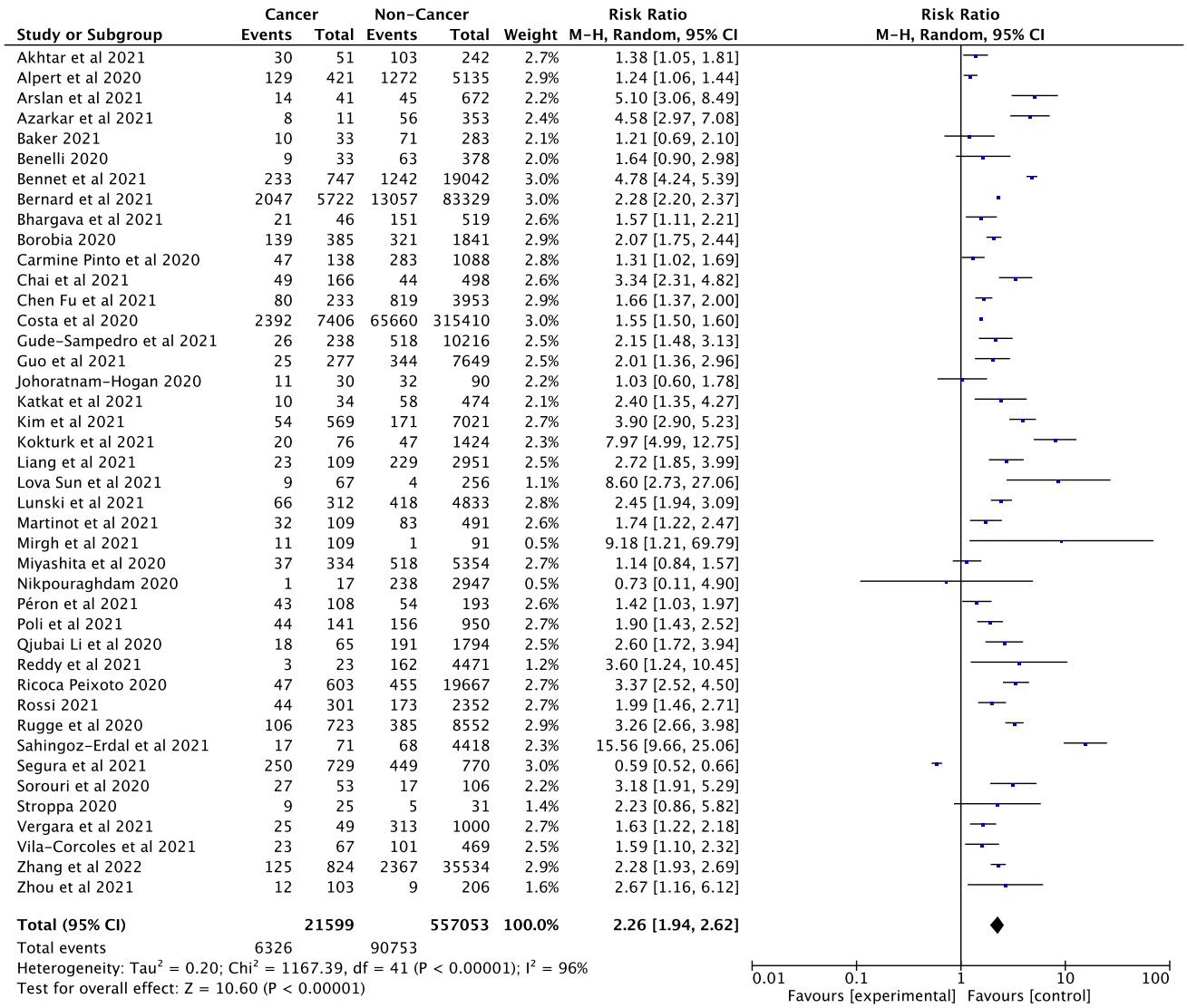

Fig. 3 Forest plot illustrating the mortality of patients with cancer/non-cancer and SARS-CoV-2 infection

in the Asian continent (RR = 2.92, CI: 2.42—3.53) and with the lowest in the European Continent (RR = 2.21, 95% CI: 1.69–2.89, $p < 0.001$). No noticeable publication bias and obvious asymmetry was observed among the included studies (Supplementary Fig. S3 and S5). We found significant heterogeneity in this study results as seen in Fig. 3 (df = 41, $I^2 = 96\%$, $p < 0.001$). Sensitivity analyses were conducted by subtracting each of the studies. No significant change was observed in the analysis results.

ICU admission rates in SARS-CoV-2 infected cancer and non-cancer patients

ICU admission rates of a total of 22,671 SARS-CoV-2 infected cancer patients and 532,161 non-cancer patients were analyzed from 22 eligible studies (Alpert et al. 2021; Benelli et al. 2020; Bergman et al. 2021; Bernard et al. 2021; Pinto et al. 2020; Fu et al. 2021; Costa et al. 2021; Görgülü et al. 2020; Gude-Sampedro et al. 2021; Guo et al. 2021; Joharatnam-Hogan et al. 2020; Sun et al. 2021; Lunski et al. 2021; Martinot et al. 2021; Mirgh et al. 2021; Miyashita et al. 2020; Péron et al. 2021; Li et al. 2020a, b; Ricoca Peixoto et al. 2020; Rugge et al. 2020; Shahidsales et al. 2021; Sorouri et al. 2020). The rate of ICU admission in patients with cancer was significantly higher than in individuals without cancer (RR = 1.45, 95% CI: 1.28–1.64, $p < 0.001$; heterogeneity: df = 21, $I^2 = 87\%$, $p < 0.001$) (Fig. 5). It was determined that there was no publication bias according to the symmetry of the funnel plot and Egger's linear regression test (Supplementary Fig. S4). ICU admission in cancer patients infected with SARS-CoV-2 varies between continents, with the highest ICU admission rate in the Asian

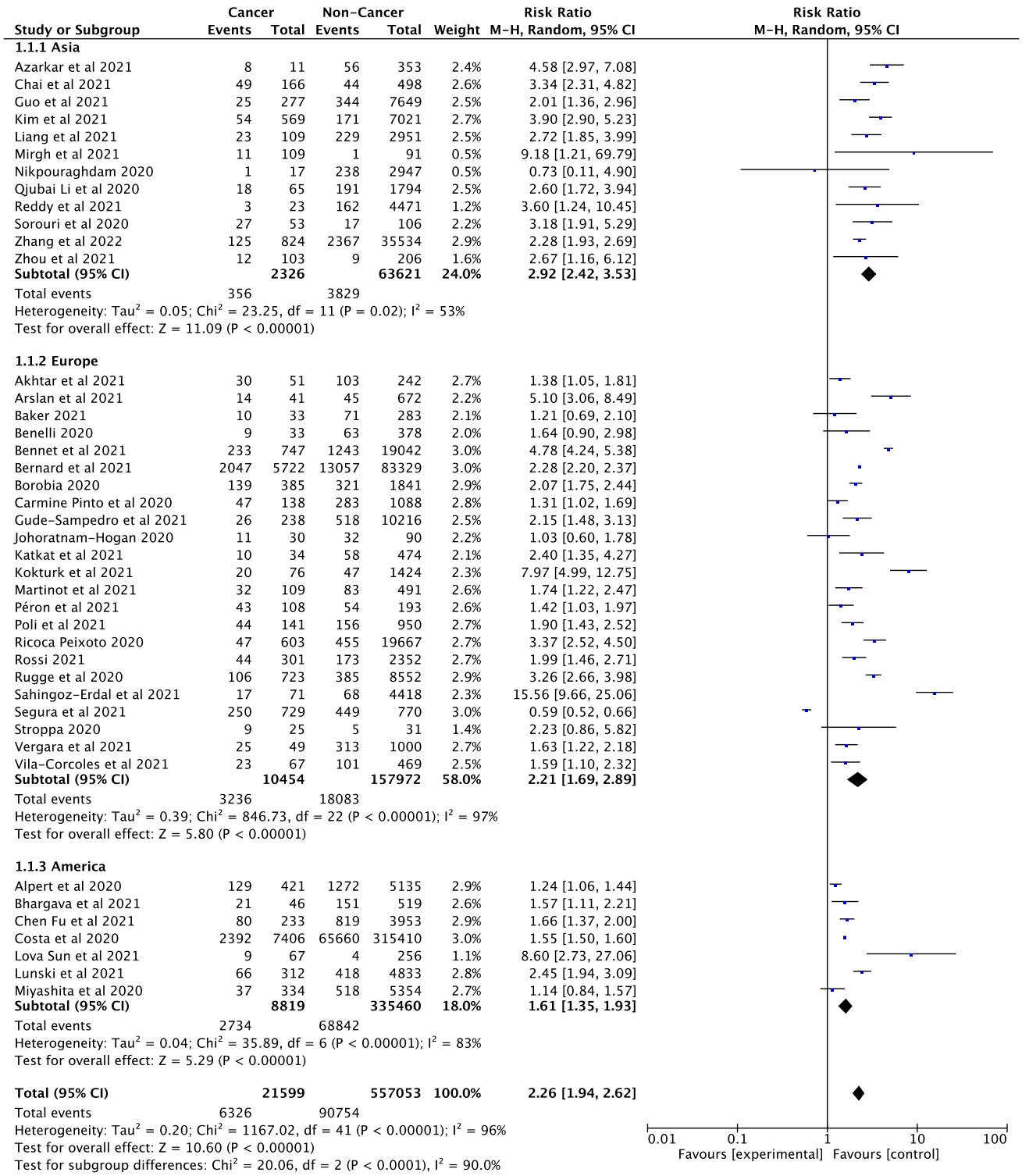

Fig. 4 Forest plot for region subgroup analysis of the cancer mortality of patients with cancer/non cancer in all SARS-CoV-2 infected participants

continent (RR = 2.26, CI: 1.80–2.83) and with the lowest in the European Continent (RR = 1.13, 95% CI: 0.86–1.48, $p < 0.001$) with no publication bias (Supplementary Fig. S1 and S6). Although there is a significant heterogeneity in Europe and America (df = 8, $I^2 = 78\%$, $p < 0.001$; df = 5, $I^2 = 86\%$, $p < 0.001$, respectively), no significant

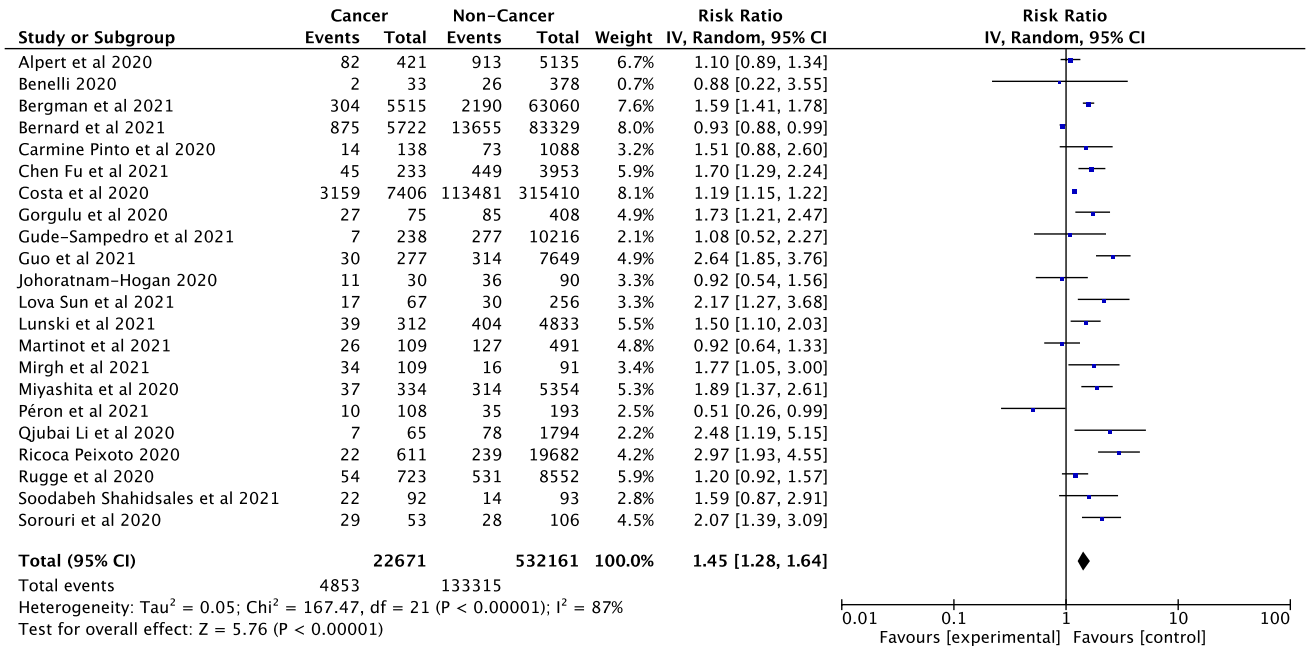

Fig. 5 Forest plot illustrating the ICU admission of patients with cancer/non-cancer in all SARS-CoV-2 infected participants

heterogeneity was observed in the Asian continent (df = 3, $I^2 = 0\%$, $p = 0.61$).

Discussion

It is a well-known fact that the incidence of cancer continues to increase rapidly worldwide, with lifestyle changes and environmental factors such as poor nutrition, polluted air, obesity, and sedentary lifestyle (Sung et al. 2021). Cancer patients have been severely affected by the outbreak of the COVID-19 pandemic caused by the SARS-CoV-2 virus. Studies with COVID-19 and cancer patients have reported that cancer is a risk factor that can lead to adverse clinical outcomes for SARS-CoV-2 infected cancer patients (Desai et al. 2020; Serraino 2020). However, in several studies, it was revealed that there was no significant difference in cancer and non-cancer populations in terms of mortality rates of COVID-19 (Liu et al. 2020; Spezzani et al. 2020; Barlesi et al. 2020). In another study conducted in France, it was reported that serious events in breast cancer patients were proximate to the general population. It has been stated that the reason for this situation is the stricter social distance procedures in terms of the location of cancer patients (Vuagnat et al. 2020). In addition to all these, in meta-analyses conducted on relatively small samples to our studies evaluating mortality, incidence and ICU hospitalization rates in cancer and non-cancer groups, it was reported that both mortality and ICU hospitalization rates of cancer patients were higher than non-cancer patients (Giannakoulis et al. 2020; Yang et al. 2021; Salunke et al. 2020). Therefore, a more comprehensive meta-analysis is required to perform for determine the relationship between cancer and COVID-19 in larger geographies and samples.

A total of 58 papers were included in this systematic review and meta-analysis. 709,908 SARS-CoV-2 infected participants worldwide were systematically analyzed and a meta-analysis was performed. The incidence of cancer was estimated in all SARS-CoV-2 infected patients (8%, 95% CI: 8–9%). We concluded that this result is much higher than the rate of approximately 2% in the general population (Bray et al. 2018). However, cancer appeared to be an important risk factor for mortality in SARS-CoV-2 infected patients (RR = 2.26, 95% CI: 1.94–2.62, $P < 0.001$). In addition, the ICU admission rate was significantly higher in patients with cancer than in patients without cancer (RR = 1.45, 95% CI: 1.28–1.64, $p < 0.001$). The risk of infection in cancer patients differs according to factors such as genetic predisposition, physical condition, ethnicity, nutritional status, age and sex of individuals (Zhang et al. 2020). Thus, virus can more easily enter cells in cancer patients (Zhang et al. 2020; Dai et al. 2020; Ma et al. 2020). Moreover, it can make the immune system weak in cancer patients even more dysfunctional (Zhang et al. 2020; Dai et al. 2020). Besides, patients with cancer must visit the hospital on a routine basis to have their treatment. This may be a factor that directly increases the risk of SARS-CoV-2 infection.

Previous studies (Giannakoulis et al. 2020; Gao et al. 2020; Salunke et al. 2020; Yang et al. 2021) were carried out with relatively smaller samples compared to our study. Studies on COVID-19 are constantly increasing cumulatively. Our study included a substantial sample covering large geographic regions and many countries. There were studies with duplicate samples. To avoid duplication of sample sources, we included only studies with the largest sample size. We evaluated the quality of the included studies using the NOS. Studies with a score of six or more were considered high-quality studies. Sensitivity analysis, a method that excludes each study separately, was performed. There was no noticeable difference in the analysis results. These findings showed that the study was stable and robust.

Limitations

There were some limitations to this research. The most of data in the included studies were from hospital-based studies. In this regard, there may be inherent biases, particularly in patient selection, medical and surgical treatment regimens, and loss of follow-up of patients. In addition, most SARS-CoV-2 infected cancer patients without hospitalization may have been excluded. Because most of the included studies did not have information on the effect of treatment or chemotherapy on ICU admission and / or mortality, their impact could not be evaluated. In addition to all these, the inability to compare cancer patients without COVID-19 with cancer patients suffering from COVID-19, which can be resulting in a potential bias in the study, was another important limitation of the study. A high level of heterogeneity was detected in most of the results, including the incidence analysis. Furthermore, although we performed subgroup analysis and sensitivity analysis, these results were not sufficient to explain the source of heterogeneity. However, our study included large sample sizes in a wide range of countries and populations across several geographies. This may indicate that healthcare, lifestyles, ethnic differences, treatment types and procedures may have increased or decreased susceptibility to cancer or SARS-CoV-2 infection. Importantly, the COVID-19 pandemic was managed diversely in different nations, as were the techniques adopted to control and prevent to SARS-CoV-2 infection. All these reasons could potentially have influenced the high level of heterogeneity. Finally, in all countries, further improvement, and development of community-based registries, where hospital-based information is collected, may also allow meta-analyses to be conducted with larger populations.

Conclusions

To date, the pandemic has caused the loss of many people. But it should be kept in mind that cancer is at least as deadly as COVID-19. As a result, cancer was an important comorbidity and risk factor for all COVID-19 patients, and SARS-CoV-2 infection could result in severe and even fatal events in cancer patients. The results of the current systematic review and meta-analysis show that cancer patients with SARS-CoV-2 infection have higher ICU admission and higher mortality rates. The most important advantage of this study was that the sample size was very large, and it represented and covered a wide range of geographies. This study emphasized the importance of managing patients with comorbidities, especially cancer, during the COVID-19 pandemic. In addition, cancer patients may have more hospital visits due to multi-stage treatment in cancer. Thus, cancer patients may become prone and susceptible to COVID-19. So, the frequency of follow-up of cancer patients could be reduced during periods when the rate of the epidemic was high, and if possible, treatments could be postponed for a while. Also, and importantly, healthcare professionals should be vigilant for cancer patients, especially COVID-19 period, individualized treatment plans should be devised to avoid disease progression.

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Declarations

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