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ASSOCIATION BETWEEN PRE-EXISTING COMORBIDITIES AND COVID-19 RELATED MORTALITY: A META-ANALYSIS STUDY

EK HASTALIKLAR İLE COVID-19 KAYNAKLI MORTALİTE ARASINDAKİ İLİŞKİ: META ANALİZ ÇALIŞMASI

Sibel Balcı[1], Emrah Gökay Özgür[1*], Canan Baydemir[1]

[1]Kocaeli University, Faculty of Medicine, Department of Biostatistics and Medical Informatics, Kocaeli, Turkey

ORCID iD: Sibel Balcı: 0000-0002-5875-7546; Emrah Gökay Özgür: 0000-0002-3966-4184; Canan Baydemir: 0000-0002-1521-7793

***Sorumlu Yazar / Corresponding Author:** Emrah Gökay Özgür **e-posta / e-mail:** emrahgokayozgur@gmail.com

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Abstract

Objective: In our study, we aimed to examine the proportion of comorbidities in survivors and non-survivors and investigate the association between the comorbidities and COVID-19 related mortality.
Methods: We searched Scopus, PubMed and Web of Science for articles up to January, 2021. Patients' outcomes were selected as survived and non-survived. Comorbidities were selected as kidney disease, hypertension, diabetes mellitus, cardiovascular disease, liver disease, autoimmune disease and malignancy. Odds ratios (ORs) were reported using fixed-effect and random-effect meta-analysis. The heterogeneity was assessed by the *Chi-square test* and *Higgins' I^2 test*. The publication bias was examined via *funnel plot* and *Hegger's test*.
Results Our meta-analysis was conducted based on 11467 COVID-19 cases from 16 studies. Compared to the survivors, the odds of kidney disease (OR=2.30; 95% CI: 1.96-2.70; p<0.001), odds of hypertension (OR=2.14; 95% CI: 1.67-2.76; p<0.001), odds of diabetes mellitus (OR=1.85; 95% CI: 1.63-2.10; p<0.001), odds of cardiovascular disease (OR=2.85; 95% CI: 2.00-4.06; p<0.001) were higher in non-survivors. There was no significant difference for the odds of liver disease, malignancy and autoimmune disease (p>0.05).
Conclusion: Our meta-analysis suggests that the major comorbidities such kidney disease, hypertension, diabetes mellitus and cardiovascular disease increase the risk of death from COVID-19 disease. Our study also highlights the importance of appropriate treatment for the patients with these specific comorbidities to meet their need.

Keywords: *Comorbidities, COVID-19, mortality, meta-analysis*

Öz

Amaç: Bu çalışmada, hayatta kalan ve ölen hastalardaki ek hastalık oranları incelenerek ek hastalık varlığı ile COVID-19 kaynaklı mortalite arasındaki ilişkinin ortaya konması amaçlandı.
Yöntem: Bu meta-analiz çalışması için Scopus, PubMed ve Web of Science veri tabanları üzerinde, Ocak 2021'e kadar makale taraması yapıldı. Hastalara ilişkin sonuç değişkeni olarak ölüm seçildi. Ek hastalıklar; böbrek hastalığı, hipertansiyon, diyabet, kardiyovasküler hastalık, karaciğer hastalığı, otoimmün hastalık ve malignite olarak seçildi. Odds oranlarını (OR) belirlemek için sabit etkili ve rastgele etkili meta-analiz kullanıldı. Heterojenlik varlığı *Ki-kare* ve *Higgins I^2* testleri ile değerlendirildi. Yayın yanlılığı ise *huni grafiği* ve *Hegger testi* ile incelendi.
Bulgular: Bu meta-analizde 16 çalışmadan elde edilen 11467 COVID-19 hastasına ilişkin sonuçlar kullanıldı. Böbrek hastalığı varlığı (OR=2,30; %95 GA: 1,96-2,70; p<0,001), hipertansiyon varlığı (OR=2,14; %95 GA: 1,67-2,76; p<0,001), diyabet varlığı (OR=1,85; %95 GA: 1,63-2,10; p<0,001), kardiyovasküler hastalık varlığı (OR=2,85; %95 GA: 2,00-4,06; p<0,001) ölen hastalarda daha yüksekti. Karaciğer hastalığı, malignite ve otoimmün hastalık bakımından ise anlamlı bir fark bulunamadı (p>0,05).
Sonuç: Bu meta-analiz çalışması; böbrek hastalığı, hipertansiyon, diyabet ve kardiyovasküler hastalık gibi majör ek hastalıkların COVID-19 kaynaklı ölüm riskini artırdığını göstermektedir. Bu nedenle çalışmamızda, spesifik ek hastalığı olan hastaların ihtiyaçlarını karşılamak için uygun tedavi seçiminin ne kadar önemli olduğu vurgulanmaktadır.

Anahtar Kelimeler: *Ek hastalıklar, COVID-19, mortalite, meta-analiz*

Introduction

Coronavirus disease 2019 (COVID-19) which first appeared in Wuhan, China in December 2019, spread to the whole world in a short time and was declared a pandemic by World Health Organization (WHO) on March, 2020. The number of COVID-19 cases continues to rise quickly threatening people having chronic diseases, especially. Currently, approximately 272 million people worldwide have caught COVID-19, while approximately 5 million of them died according to WHO. Despite international efforts to prevent spread and vaccination efforts, the number of cases has not yet been controlled.

Most common symptoms of COVID-19 are fever, cough, arthralgia and shortness of breath. Less common symptoms are headache, sore throat and diarrhea. Although the most cases show mild symptoms or remain asymptomatic, some cases develop severe pneumonia, multi-organ failure or death. When the potential risk factors of COVID-19 related mortality are examined, it is seen that the presence of comorbidities may increase the risk of death from COVID-19. Bai et al. revealed in their study that 41.7% of people who died from COVID-19 had hypertension.[1] Chen et al. stated that 48% of the deceased had hypertension, 12% had diabetes and 14% had cardiovascular disease.[2] Fu et al. found that 21.8% of people who died from coronavirus had hypertension, 19% had diabetes, and 12.5% had cardiovascular disease.[3] Graselli et al. reported that 50% of the deceased had hypertension, 17% had diabetes and 17% had cardiovascular disease in their study on 3988 people.[4] Gupta et al. stated in their study that 41% of the people who died had autoimmune disease, 52% diabetes and 49% hypertension.[5] On the other hand, some studies report no association between underling disease and mortality. Therefore, we performed a meta-analysis study to obtain convincing results. In our study, we aimed to examine the proportion of comorbidities in survivors and non-survivors and investigate the association between the comorbidities and COVID-19 related mortality. Our hypothesis was that the presence of any comorbidity, such as kidney disease, hypertension, diabetes mellitus, cardiovascular disease, liver disease, autoimmune disease and malignancy were increasing the risk of mortality. To the best of the authors' knowledge, this is the most comprehensive meta-analysis conducted on this subject with regard to the number of studies and comorbidities included.

Methods

Study Selection and Eligibility Criteria

Meta-analysis was performed by strictly following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We searched Scopus, PubMed and Web of Science for articles up to February, 2021. Literature searches conducted based on title, abstract, and keywords. The following search terms were used: "COVID-19" and "Comorbidity" and "Mortality" and "Risk Factors". No language and country restrictions were applied. Study titles and abstracts were screened by authors independently for inclusion eligibility.

The following criteria were applied to select studies:

- The studies involving patients diagnosed with COVID-19 were included.
- Patients' outcomes were selected as survived and non-survived.
- Comorbidities were selected as kidney disease, hypertension, diabetes mellitus, cardiovascular disease, liver disease, autoimmune disease and malignancy.
- Studies examining the associations between comorbidities and mortality were included.
- Studies reporting count and percentage for binary variables were included.

Statistical Analysis

STATA version 15 and SPSS version 20 (SPSS, Chicago, IL, USA) were used in the statistical analyses. Kidney disease, diabetes mellitus, hypertension, cardiovascular disease, autoimmune disease, liver disease and malignancy were summarized as counts (percentages). For each study, the comparisons of comorbidities between COVID-19 survivors and non-survivors were carried out using Chi-square test.

Odds ratios (OR) with 95% confidence intervals (CI) were reported using fixed-effect and random-effect meta-analysis with "*metan*" command. The *Chi-square test* and *Higgins' I^2 test* were used to test the heterogeneity between the studies. In the presence of heterogeneity, random-effect meta-analysis was performed. The publication bias was examined via *funnel plot* and *Hegger's test*. A p-value<0.05 was considered as statistically significant.

Results

Identified Studies

Database searching identified totally 970 studies (802 studies in Scopus, 109 studies in PubMed and 59 studies in Web of Science). The 99 duplicate studies were removed. The 846 studies were excluded after title and abstract reviews. The remaining 25 studies were applied exclusion criteria such as not reporting outcome of interest, not meeting selection criteria and lack of sufficient data and 9 of them were removed. Therefore, 16 studies were retained, which fulfilled inclusion criteria (Figure 1). Study characteristics were given in Table 1.

Meta-Analysis Results

The comparisons of comorbidities between COVID-19 survivors and non-survivors per study were given in Table 2. Three studies from 7 studies for kidney disease, 9 studies from 14 studies for hypertension, 5 studies from 15 studies for diabetes mellitus and 7 studies from 9 studies for cardiovascular disease reported statistically significant difference between survivors and non-survivors. Of 4 studies included for autoimmune disease, just one study reported significant difference. For the liver disease (5 studies) and malignancy (6 studies), none of the included studies reported significant difference between survivors and non-survivors.

Meta-analysis results such as OR with 95% confidence interval were also given via forest graphs in Figure 2. According to this figure, compared to the survivors, the odds of kidney disease (OR=2.30; 95% CI: 1.96-2.70; p<0.001), the odds of hypertension (OR=2.14; 95% CI: 1.67-2.76; p<0.001), the odds of diabetes mellitus (OR=1.85; 95% CI: 1.63-2.10; p<0.001), the odds of cardiovascular disease (OR=2.85; 95% CI: 2.00-4.06; p<0.001) were statistically greater in non-survivors. There was no significant difference for the odds of liver disease (OR=1.12; 95% CI: 0.77-1.63; p=0.555), malignancy (OR=1.90; 95% CI: 0.91-3.97;

p=0.088) and autoimmune disease (OR=1.99; 95% CI: 0.65-6.13; *p*=0.162).

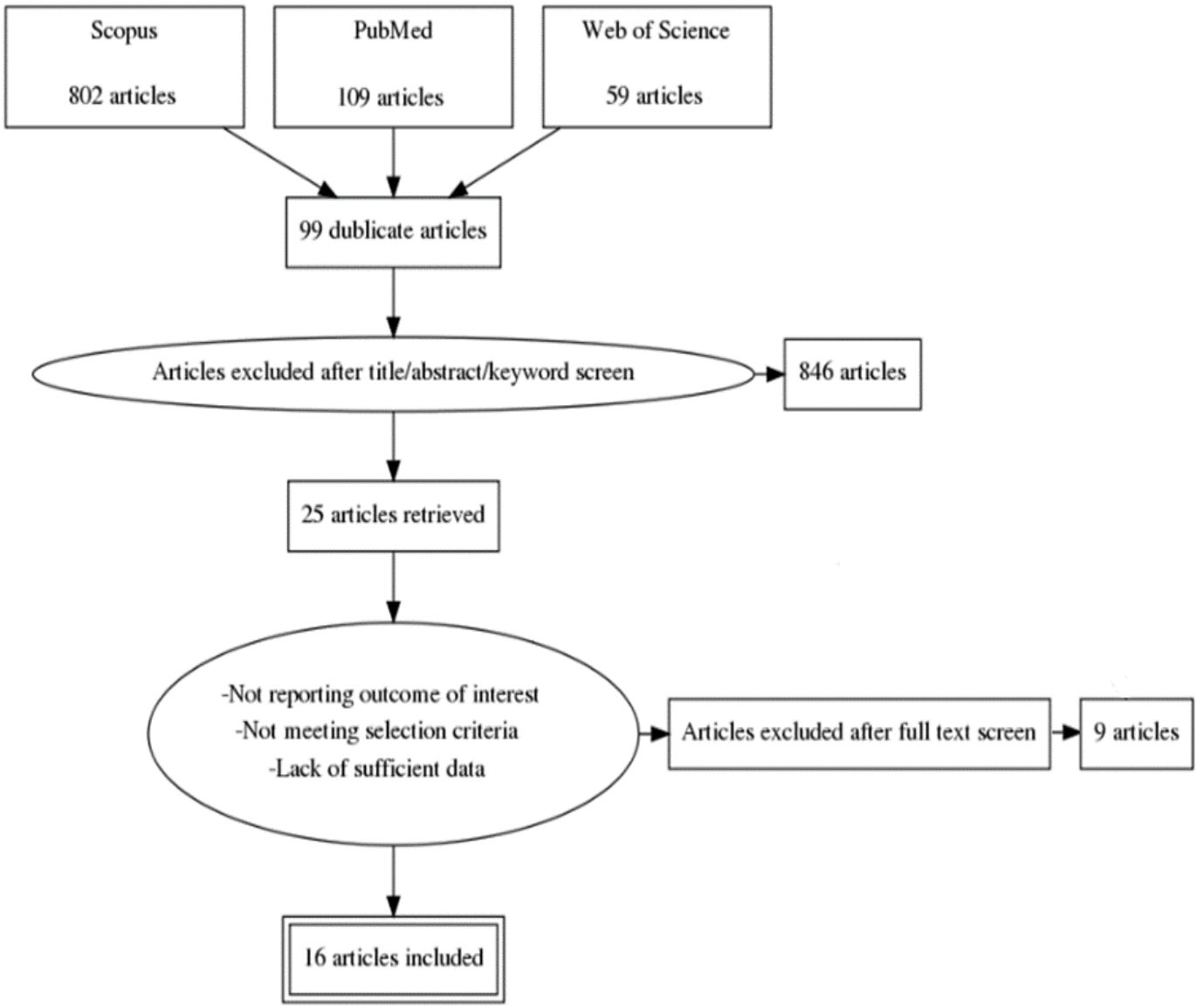

Figure 1. PRISMA flow diagram for selection of studies

Table 1. Study characteristics

Studies	Countries	Study type	Sample sizes (Survivor-Non-survivor)	Age, year (Mean±SD/ Median [IQR])	Male (%)	Comorbidities
Bai[1] (03, 2020)	Jinyintan Hospital in Wuhan, China	Retrospective	60-56	55 [44-67]	63	1. Hypertension 2. Diabetes Mellitus 3. Cardiovascular Disease
Chen[2] (03, 2020)	Tongji Hospital in Wuhan, China	Retrospective	161-113	62.0 [44.0-70.0]	62	1. Kidney Disease 2. Hypertension 3. Diabetes Mellitus 4. Cardiovascular Disease 5. Autoimmune Disease 6. Malignancy
Luo[6] (03, 2020)	Renmin Hospital of Wuhan University in Wuhan, China	Retrospective	303-100	56 [39-68]	47.9	1. Kidney Disease 2. Hypertension 3. Diabetes Mellitus 4. Cardiovascular Disease
Zhou[7] (03, 2020)	Jinyintan Hospital and Wuhan Pulmonary Hospital in Wuhan, China	Retrospective	137-54	56.0 [46.0–67.0]	62	1. Hypertension 2. Diabetes Mellitus 3. Cardiovascular Disease
Wang[8] (03, 2020)	Renmin Hospital of Wuhan University in Wuhan, China	Retrospective	274-65	69 [65-76]	49	1. Kidney Disease 2. Hypertension 3. Diabetes Mellitus 4. Cardiovascular Disease 5. Liver Disease 6. Malignancy
Fu[3] (03, 2020)	Union Hospital of Huazhong University of Science and Technology, China	Hospital based case-cohort	166-34	-	49.3	1. Hypertension 2. Diabetes Mellitus 3. Cardiovascular Disease
Du[9] (03, 2020)	Wuhan Pulmonary Hospital, China	Prospective	158-21	57.6±13.7	54.2	1. Hypertension 2. Diabetes Mellitus 3. Malignancy
Cao[10] (04, 2020)	Wuhan University Zhongnan Hospital in Wuhan, China	-	85-17	54 [37-67]	52	1. Kidney Disease 2. Hypertension 3. Diabetes Mellitus 4. Cardiovascular Disease 5. Liver Disease 6. Autoimmune Disease 7. Malignancy
Gu[11] (04, 2020)	All areas in mainland China outside of Hubei Province	Nested case-control	181-94	66.4±14.5	62.9	1. Hypertension 2. Diabetes Mellitus
Yang[12] (05, 2020)	Wuhan Jin Yin-tan hospital in Wuhan, China	Retrospective	20-32	59.7±13.3	67	1. Kidney Disease 2. Diabetes Mellitus 3. Liver Disease 4. Malignancy
Deng[13] (06, 2020)	Hankou and Caidian Branch of Tongji Hospital and Hankou Branch of the Central Hospital of Wuhan, China	Retrospective	116-109	-	-	1. Hypertension 2. Diabetes Mellitus
Lee[14] (06, 2020)	UK Cancer Center, UK	Prospective	574-226	69 [59-76]	56	1. Hypertension 2. Diabetes Mellitus 3. Cardiovascular Disease
Graselli[4] (07, 2020)	Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy	Retrospective	2062-1926	63 [56-69]	79.9	1. Kidney Disease 2. Hypertension 3. Diabetes Mellitus 4. Cardiovascular Disease 5. Liver Disease
Klang[15] (09, 2020)	Mount Sinai Hospital, Mount Sinai Brooklyn, Mount Sinai Queens, Mount Sinai Morningside and Mount Sinai West, New York City, USA	Retrospective	2270-1136	-	-	1. Kidney Disease 2. Hypertension
Abbattista[16] (12, 2020)	Milan, Italy	-	294-83	62 [51-72]	66	1. Diabetes Mellitus 2. Liver Disease 3. Autoimmune Disease
Gupta[5] (01, 2021)	State University of New York and Downstate Medical Center, USA	Retrospective	274-254	Median=70	54	1. Hypertension 2. Diabetes Mellitus 3. Autoimmune Disease

SD: Standard Deviation, IQR: Interquartile range

Table 2. Comparisons of survivors and non-survivors given by each study

Comorbidities	Studies	Sample sizes (Survivor-Non-survivor)	Comorbidity Proportions in Survivor, n (%)	Comorbidity Proportions in Non-Survivor, n (%)	*p*
Kidney Disease	Chen	161 - 113	1 (0.6)	4 (3.5)	0.163
	Luo	303 - 100	4 (1.3)	3 (3.0)	0.372
	Wang	274 - 65	9 (3.3)	4 (6.2)	0.284
	Cao	85 - 17	1 (1.2)	3 (17.6)	**0.014**
	Yang	20 - 32	3 (15.0)	12 (37.5)	0.153
	Graselli	2062 - 1926	18 (0.9)	71 (3.7)	**<0.001**
	Klang	2270 - 1136	351 (15.4)	316 (27.8)	**<0.001**
Hypertension	Bai	91 - 36	21 (23.1)	15 (41.7)	0.061
	Wang	274 - 65	106 (38.7)	32 (49.2)	0.125
	Fu	166 - 34	79 (47.6)	22 (64.7)	0.103
	Du	158 - 21	45 (28.5)	13 (61.9)	**0.005**
	Chen	161 - 113	39 (24.2)	54 (47.8)	**<0.001**
	Luo	303 - 100	53(17.5)	60 (60.0)	**<0.001**
	Zhou	137 - 54	32 (23.4)	26 (48.1)	**0.001**
	Gu	181 - 94	67 (37.0)	42 (44.7)	0.243
	Cao	85 - 17	17 (20.0)	11 (64.7)	**<0.001**
	Deng	116 - 109	18 (15.5)	40 (36.7)	**<0.001**
	Lee	574 - 226	155 (27.0)	92 (40.7)	**<0.001**
	Graselli	2062 - 1926	681 (33.0)	962 (49.9)	**<0.001**
	Klang	2270 - 1136	1411 (62.2)	888 (78.2)	**<0.001**
	Gupta	274 - 254	212 (77.4)	204 (80.3)	0.456
Diabetes Mellitus	Bai	91 - 36	10 (11.0)	5 (13.9)	0.761
	Wang	274 - 65	43 (15.7)	11 (16.9)	0.956
	Fu	166 - 34	111 (66.9)	26 (76.5)	0.370
	Du	158 - 21	27 (17.1)	6 (28.6)	0.231
	Chen	161 - 113	23 (14.3)	24 (21.2)	0.180
	Luo	303 - 100	32 (10.6)	25 (25.0)	**0.001**
	Zhou	137 - 54	19 (13.9)	17 (31.5)	**0.009**
	Gu	181 - 94	46 (25.4)	26 (27.7)	0.797
	Cao	85 - 17	5 (5.9)	6 (35.3)	**0.003**
	Yang	20 - 32	2 (10.0)	7 (21.9)	0.454
	Deng	116 - 109	9 (7.8)	17 (15.6)	0.103
	Lee	574 - 226	85 (14.8)	46 (20.4)	0.071
	Graselli	2062 - 1926	186 (9.0)	328 (17.0)	**<0.001**
	Abbattista	295 - 83	46 (15.6)	26 (31.3)	**0.002**
	Gupta	274 - 254	139 (50.7)	150 (59.1)	0.066
Cardiovascular Disease	Bai	91 - 36	1 (1.1)	2 (5.6)	0.163
	Wang	274 - 65	32 (11.7)	21 (32.3)	**<0.001**
	Chen	161 - 113	7 (4.3)	16 (14.2)	**0.004**
	Fu	166 - 34	14(8.4)	2 (5.9)	1.000
	Luo	303 - 100	20(6.6)	16 (16.0)	**0.004**
	Zhou	137 - 54	2(1.5)	13(24.1)	**<0.001**
	Cao	85 - 17	2 (2.3)	3 (17.6)	**0.030**
	Lee	574 - 226	61(10.6)	48(21.2)	**<0.001**
	Graselli	2062 - 1926	191 (9.3)	342 (17.8)	**<0.001**
Liver Disease	Wang	274 - 65	1 (0.4)	1 (1.5)	0.347
	Cao	85 - 17	2 (2.4)	1 (5.9)	0.425
	Yang	20 - 32	6 (30.0)	9 (28.0)	0.885
	Graselli	2062 - 1926	44 (2.1)	42(2.2)	0.915
	Abbattista	295 - 83	8 (2.7)	4 (4.8)	0.306
Autoimmune Disease	Chen	161 - 113	1 (0.6)	1 (0.9)	1.000
	Wang	274 - 65	4 (1.5)	1 (1.5)	1.000
	Abbattista	295 - 83	8(2.7)	8(9.6)	**0.011**
	Gupta	274 - 254	22 (8.0)	15 (5.9)	0.340
Malignancy	Wang	274 - 65	12 (4.4)	3 (4.6)	1.000
	Du	158 - 21	3 (1.9)	1 (4.8)	0.396
	Chen	161 - 113	2 (1.2)	5 (4.4)	0.129
	Cao	85 - 17	3 (3.5)	1 (5.9)	0.524
	Yang	20 - 32	1 (5.0)	1 (3.1)	1.000
	Deng	116 - 109	2 (1.7)	6 (5.5)	0.161

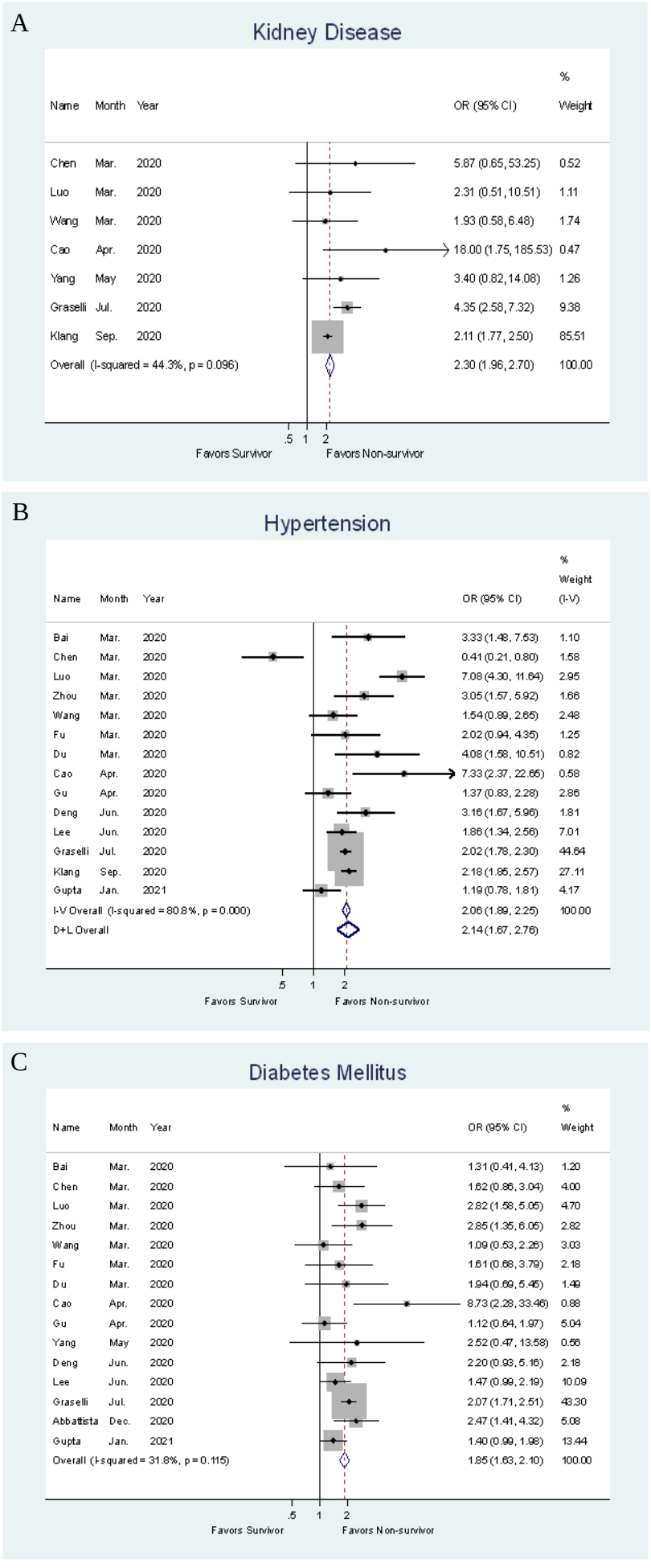

Figure 2. Forest plots for the kidney disease (A), hypertension (B), diabetes mellitus (C)

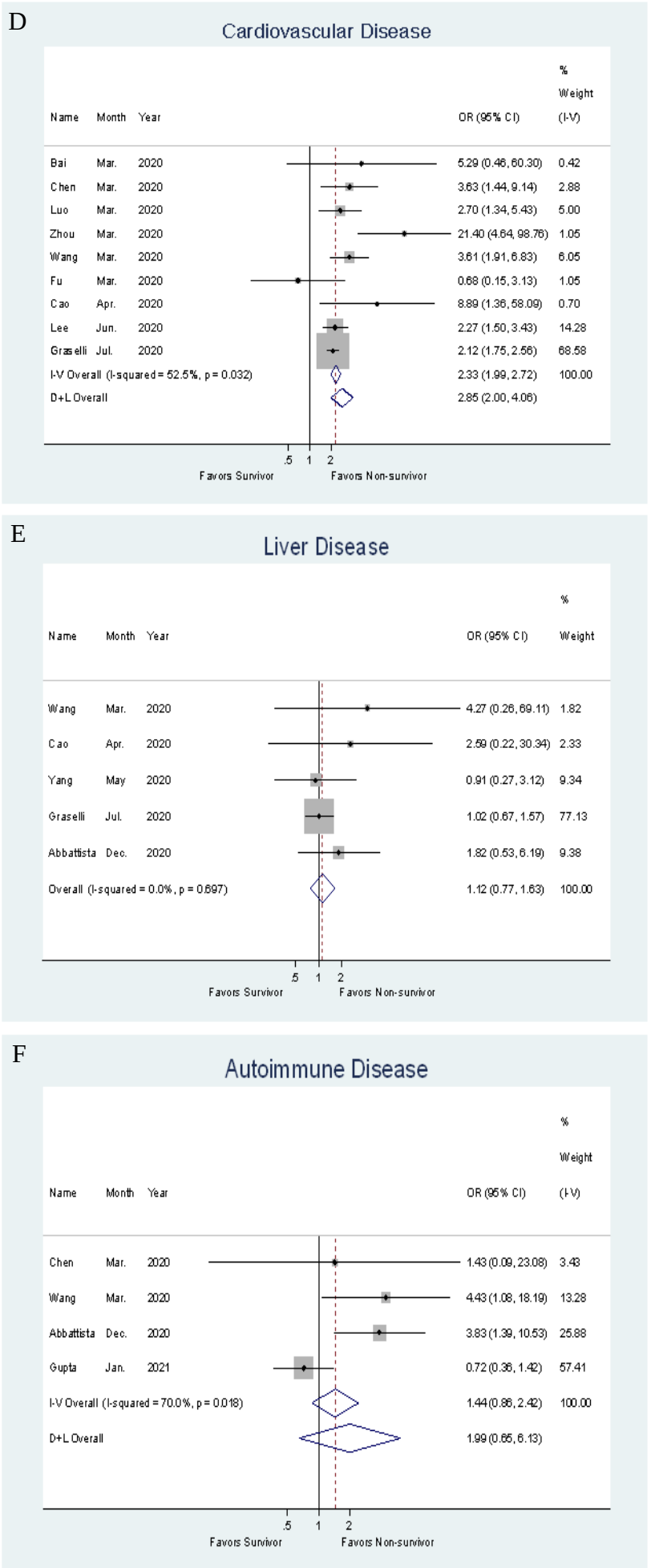

Figure 2. Cardiovascular disease (D), liver disease (E), autoimmune disease (F) (Continuation)

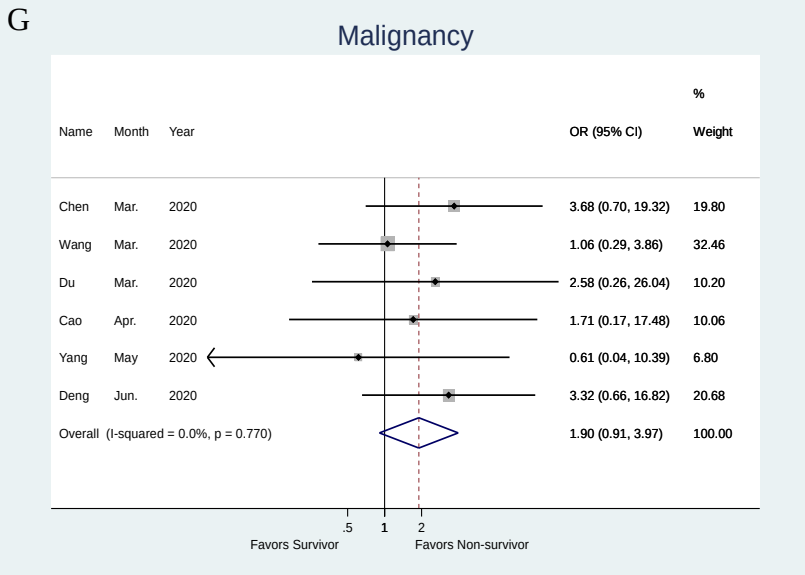

Figure 2. Malignancy (G) (Continuation)

Publication Bias

One of the important problems in conducting a meta-analysis is the publication bias. It may occur frequently when the studies showing statistically significant differences are more likely to be published or studies are preferentially published in English language journals and higher impact journals. Since the publication bias can lead to inflated estimates of efficacy, the presence of publication bias should be explored. There are graphical and statistical methods to identify the publication bias. The main graphical method is the funnel plot. In our study, funnel plots were used firstly to examine the publication bias. The funnel plot gives a visual representation of the potential bias and its interpretation is subjective. Therefore, we also used Egger's test which is one of the most commonly used tests to assess the publication bias.

For each comorbidity, the funnel plots were provided in Figure 3. Since they were qualitatively symmetrical and inverted funnel, it could be considered that there was no publication bias. In addition, the results of Egger's tests were given in Table 3. As shown in the table, Egger's tests showed no publication bias (p>0.05 for all).

Study Heterogeneity

In a meta-analysis study, the covered studies should be homogeneous since the meta-analysis combines these studies to get a summary result. Therefore, we used *Chi-square test* to test the heterogeneity between included studies in meta-analysis and quantified it by I^2 *statistic* (Table 3). As shown in table, significant heterogeneities were observed for hypertension (p<0.001), cardiovascular disease (p=0.032) and autoimmune disease (p=0.018), but there were no heterogeneities for kidney disease (p=0.096), diabetes mellitus (p=0.115), liver disease (p=0.679) and malignancy (p=0.770). The I^2 values were ranging from 0.0% to 80.8%. In the case of heterogeneity between studies, the random-effect meta-analysis was used.

Table 3. Egger's test results for publication bias and heterogeneity of studies

	Egger's test		**Heterogeneity of studies**		
Comorbidities	***t***	***p***	χ^2	***p***	I^2 **(%)**
Kidney Disease	1.84	0.124	10.78	0.096	44.3
Hypertension	0.34	0.739	67.69	**<0.001**	80.8
Diabetes Mellitus	0.21	0.836	20.52	0.115	31.8
Cardiovascular Disease	1.91	0.098	16.85	**0.032**	52.5
Liver Disease	2.42	0.094	2.21	0.697	0.0
Autoimmune Disease	0.90	0.465	10.02	**0.018**	70.0
Malignancy	-0.08	0.937	2.54	0.770	0.0

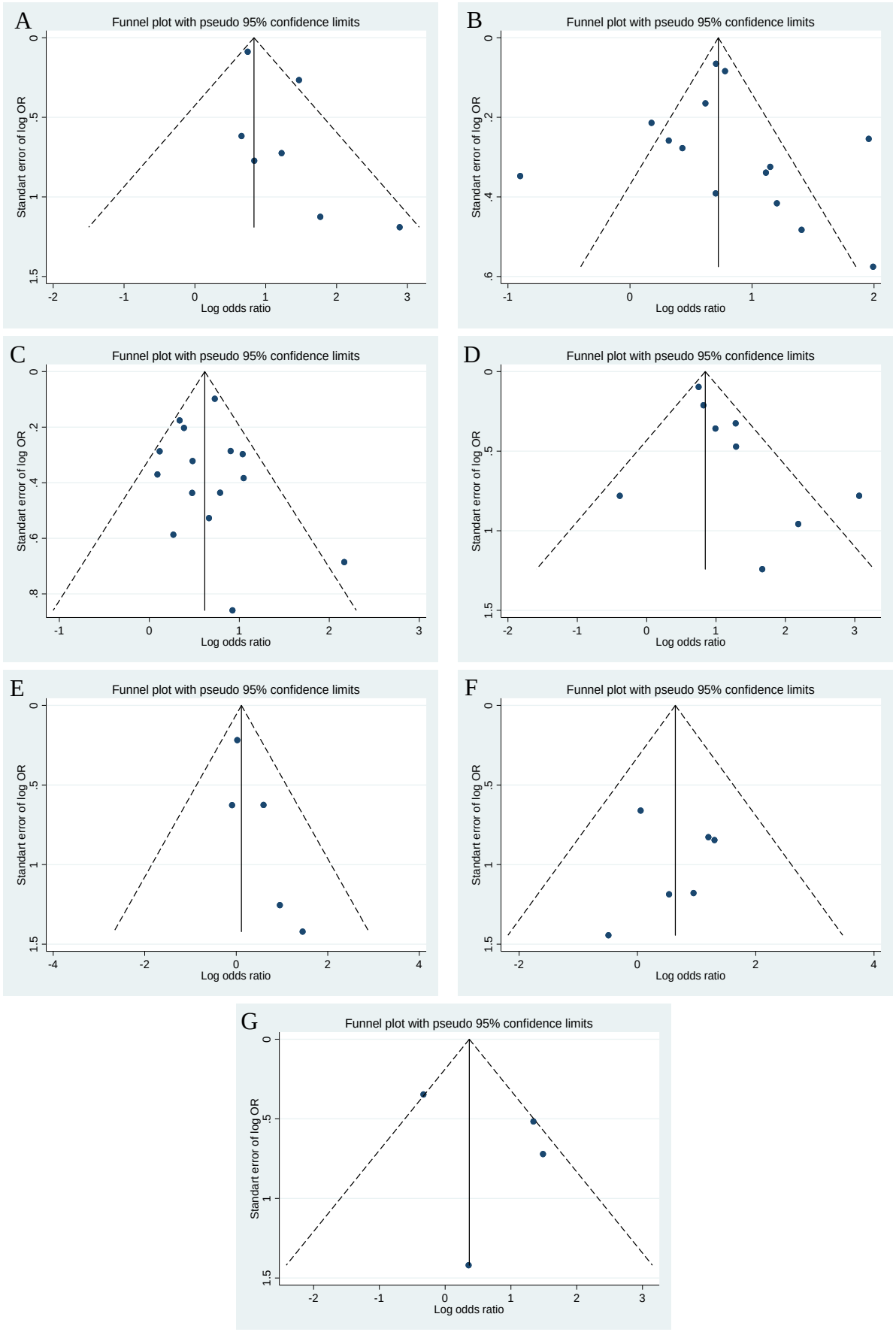

Figure 3. Funnel plots; kidney disease (A), hypertension (B), diabetes mellitus (C), cardiovascular disease (D), liver disease (E), autoimmune disease (F) and malignancy (G)

Discussion

Since the first day of its emergence, the COVID-19 pandemic has affected millions of people worldwide, indirectly affecting billions of people for different reasons. In people directly affected by this pandemic, the existing comorbidity of the people negatively affected the extent of the disease. Therefore, we aimed to provide an in-depth analysis of comorbidities and COVID-19 mortality from the published literature using a meta-analysis study.

Our meta-analysis was conducted based on data from 16 studies with the COVID-19 diagnosed cases. A total of 11467 cases were examined in these studies. Most of the cases were from the hospitals in China. Many of the included studies were retrospective cohort study in which the outcome variable was mortality and the odds ratios for comorbidities were reported. In the meta-analysis, we handle the survivor and non-survivor groups in terms of the 7 comorbidities: kidney disease, hypertension, diabetes mellitus, cardiovascular disease, liver disease, autoimmune disease and malignancy. The results of our study showed that the patients with pre-existing kidney disease (OR=2.30; 95% CI: 1.96-2.70; p<0.001), hypertension (OR=2.14; 95% CI: 1.67-2.76; p<0.001), diabetes mellitus (OR=1.85; 95% CI: 1.63-2.10; p<0.001) and cardiovascular disease (OR=2.85; 95% CI: 2.00-4.06; p<0.001) have a greater risk of death from COVID-19. Although, many of the included studies[2,6,8,12] did not report any relationship between the presence of kidney disease and living status, the meta-analysis results showed that the COVID-19 patients with kidney disease had approximately 2 times higher risk of mortality. Similar result was obtained for the diabetes mellitus. From the examined 15 studies for this comorbidity, just 5 of them[4,6,7,12,16] showed the diabetes mellitus as a risk factor for the COVID-19 related mortality. The current meta-analysis gave the risk of mortality approximately 2 times higher in patients with diabetes mellitus. For hypertension and cardiovascular disease, many of the included studies reported these comorbidities as a risk factor of mortality which was similar to our result. This study showed that the risk of mortality was approximately 2 times higher in COVID-19 patients with hypertension and 3 times higher in COVID-19 patients with cardiovascular disease. On the other hand, there were no significant differences between survivor and non-survivor groups for the liver disease (OR=1.12; 95% CI: 0.77-1.63; p=0.555), malignancy (OR=1.90; 95% CI: 0.91-3.97; p=0.088) and autoimmune disease (OR=1.99; 95% CI: 0.65-6.13; p=0.162). From the included studies, only Abbatista et al.[16] found a statistically significant relationship between the presence of autoimmune disease and life status. In other studies, similar results were found with our results. Lastly, in this meta-analysis, there was no publication bias for all comorbidities and there were moderate heterogeneities between the studies overall.

Our study findings were also similar to results from previously published systematic reviews.

Ssentongo reported that COVID-19 patients with pre-existing cardiovascular disease, hypertension, diabetes, kidney disease and malignancy had a greater risk of death from COVID-19.[17] Pranata et al. included a total of 4448 patients from 16 studies and showed that the cardiovascular disease was associated with the mortality.[18] In their study, the risk of mortality was approximately 2 times higher in the patients with cardiovascular disease. Qiu et al. studied with 2401 patients in 15 articles. Hypertension, cardiovascular disease and diabetes mellitus were found common comorbidities among COVID-19 deceased in their study.[19]

The strength of this meta-analysis can be summarized as follows:

- The number of included patients is very large.
- Numerous comorbidities were examined.
- Low heterogeneity of most of the studies was retained.
- No publication bias among the studies was obtained.

The quality of the study can be considered as another strength of our meta-analysis. Three reviewers searched the database Scopus, PubMed and Web of Science independently and selected the studies according to the predetermined eligibility criteria.

In conclusion, our meta-analysis shows the major comorbidities such kidney disease, hypertension, diabetes mellitus and cardiovascular disease increase the risk of death from COVID-19. Our study also highlights the importance appropriate treatment for the patients with these specific comorbidities to meet their need.

Conflict of Interest

Authors declare that there is no conflict of interest.

Ethical approval

Since this study is a meta-analysis, no human or animal participants were recruited to this study.

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