

Body mass index associated with severity and mortality of patients with coronavirus disease 2019: A systematic review and meta-analysis

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Research

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Abstract

Background

As an important indicator to measure obesity or underweight, body mass index (BMI) can be used to assess the potential risk for various diseases. The present study systematically examined the relationship between BMI and severity and mortality of patients with coronavirus disease 2019 (COVID-19).

Methods

We systematically searched PubMed, Embase, Cochrane, and China National Knowledge Infrastructure (CNKI) for studies published as of September 3, 2020 and extracted the relevant data of research endpoints in each study.

Results

This study included 16 studies with 6087 patients. This study observed a significant increase in BMI on admission in patients with severe COVID-19 compared with those with non-severe COVID-19 (Mean difference [MD] = 1.95, 95% confidence interval [CI], 1.52 – 2.37, $I^2 = 33%$, $P < 0.00001$). A significant increase in BMI on admission was observed in patients who died from COVID-19 compared with (MD = 3.01, 95% CI: 1.83 to 4.19, $I^2 = 0%$, $P < 0.00001$). In the intensive care unit (ICU) or geriatric ward, the study observed a significant decrease in BMI in the non-survivor group compared with the survivor group (MD = -1.61, 95% CI: -3.07 to -0.16, $I^2 = 72%$, $P = 0.03$).

Conclusions

Higher BMI on admission is associated with severity and mortality of patients with COVID-19, but lower BMI is associated with mortality of patients with COVID-19 in the ICU or geriatric ward. Thus, we strongly recommend that clinicians should closely monitor the BMI of patients with COVID-19, especially those from the ICU or geriatric ward.

Introduction

In late December 2019, a group of patients with pneumonia of unknown cause was reported by several local health facilities in Wuhan, China(1). This pneumonia of unknown cause was later shown to be caused by a highly infectious novel coronavirus infection (2). According to research, the novel coronavirus is a single positive-stranded RNA virus from the *Coronaviridae* family and have enveloped virions that appear as round or oval, with a diameter of 60–140 nm, often polymorphous (3) (4). Subsequently, this novel coronavirus was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)(5). The WHO has named this infectious disease as coronavirus disease 2019 (COVID-19), which has spread worldwide and caused many deaths(6, 7).

The clinical features of COVID-19 mainly included fever, cough, sputum, dyspnea, myalgia, malaise, fatigue, diarrhea, etc(8–13). Although the mortality rate of COVID-19 is approximately 4%, COVID-19 has a higher rate of spread and become a global pandemic in a very short time compared with Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) (14). As a result, the death toll from COVID-19 is high in absolute terms. Comparing the clinical and epidemiological features between severe/non-survivors and non-severe/survivors, a large number of literature reports have found some risk factors for exacerbation prediction of patients with COVID-19, such as hypertension, diabetes, cerebrovascular disease, chronic obstructive pulmonary disease, etc (15–19). As a statistical index to estimate body fat, body mass index (BMI) seems to be related to exacerbation prediction of patients with COVID-

19(20). According to some recent and published studies, higher BMI (obesity) seems to be a risk for exacerbation prediction of patients with COVID-19(21–23). However, some problems cannot be avoided, for example: (1) when race, sex, region, and age are different, BMI threshold for obesity is different. As a result, multiple data combinations cannot be measured with the same BMI threshold. (2) Is lower BMI associated with exacerbation prediction of patients with COVID-19 under special circumstances? To this end, we systematically and comprehensively evaluated the relationship between BMI and the severity and mortality of patients with COVID-19.

Methods

Search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline was used for this systematic review and meta-analysis and the PROSPERO registration ID is CRD42020205688(24). We selected relevant studies published as of September 3, 2020, by searching PubMed, Embase, Cochrane, and China National Knowledge Infrastructure (CNKI). Language restrictions were not applied. The following combined text was used in this systematic review and meta-analysis and MeSH terms: “Body Mass Index” and “COVID-19”. The complete search used for PubMed was: (((((((((((“COVID-19” [Supplementary Concept]) OR (2019 novel coronavirus disease)) OR (COVID19)) OR (COVID-19 pandemic)) OR (SARS-CoV-2 infection)) OR (COVID-19 virus disease)) OR (2019 novel coronavirus infection)) OR (2019-nCoV infection)) OR (coronavirus disease 2019)) OR (coronavirus disease-19)) OR (2019-nCoV disease)) OR (COVID-19 virus infection)) AND (((((((“Body Mass Index”[Mesh]) OR (Index, Body Mass)) OR (Quetelet Index)) OR (Index, Quetelet)) OR (Quetelet’s Index)) OR (Quetelets Index))

Selection criteria

Inclusion criteria were (1) patients diagnosed with COVID-19; (2) continuous variable (BMI) expressed as mean \pm SD/median and interquartile range (IQR); (3) comparison between patients with severe and non-severe COVID-19, or between COVID-19 survivors and non-survivors. Exclusion criteria were (1) basic researches, guidelines, case reports, review, editorials, or other unrelated topics; (2) those without continuous variable data for BMI; (3) studies with a sample size of < 10 .

Data extraction and quality assessment

Two investigators independently extracted data from the included studies. Pairs of reviewers (Zheng Zhou; Mingming Zhou) independently extracted data from the included studies, and disagreements were resolved by a third reviewer (Chao Fang).

The following data were extracted from each selected study: details of authors, mean age, total sample size, continuous variable (BMI), and clinical condition (non-severe/severe; non-survivors/survivors). Because most of the included studies were retrospective cohort studies, the Newcastle–Ottawa scale was used for quality evaluation (25).

Statistical analysis

All analyses and plots were performed and made using the Review Manager software (RevMan5.4; Cochrane Collaboration). Statistical significance was determined for $P < 0.05$. By attaining the mean \pm SD and sample size (n) of severe and non-severe groups (or survivor and non-survivor groups), the standardized mean differences were used as the summary statistic for continuous data.. The mean was estimated by $(Q_a + M + Q_c)/3$, and the standard deviation was estimated by $(Q_c - Q_a)/1.35$, when the included studies did not provide the mean and standard deviation but provided median (M) and upper (Q_c) and lower quartiles (Q_a) instead (26).

The Q statistic was used to estimate the heterogeneity in this study, and $P \leq 0.10$ was considered statistically significant for the Q-statistic test. I^2 statistic was used to quantify heterogeneity. When the value of I^2 is 0, heterogeneity is not observed, the heterogeneity increased with larger value of I^2 . To obtain the expected heterogeneity, random-effects model was used in advance. Fixed-effects models are applied if the Q statistic $P > 0.10$.

Results

Study selection

We identified 553 citations, and 88 duplicate citations were removed.

After screening the title and abstract, 426 records were excluded, and 39 potentially relevant publications were retrieved for eligibility. After screening the full-text articles, 23 more records were excluded because of failure to extract valid continuous variables (BMI, expressed as mean \pm SD) or no proper grouping. Ultimately, 16 studies published as of September 3, 2020, including 6087 patients, met our inclusion criteria(27–42). The outline of the search strategy is presented in Fig. 1.

Study characteristics

The baseline characteristics of each included study are summarized in Table 1. The 16 included research papers were mainly observational cohort studies and published/available online until September 3, 2020. Seven studies were from China, six were from the USA, and the remaining three were from Spain, Mexico, and Italy. Most of the studies were published in English, but two studies were published in Chinese. The number of patients with COVID-19 enrolled in each study ranged from 30 to 2215, and no study had a sample size < 10 . The median or mean age of patients with COVID-19 approximately varied from 35 to 90 years. Ten studies were grouped by COVID-19 severe vs. non-severe, six studies were grouped by COVID-19 non-survivors vs. survivors. No obvious difference was found for the sex distribution of patients with COVID-19 for each study and not shown in Table 1.

Table 1
Baseline characteristics of each included study.

Study	Year	Country	Language	Age(mean \pm SD or median, range)	Groups	simple size	BMI,mean (SD)	
							Severe/non-survived	Non-severe/survived
Auld, S.et al.	2020	USA	English	64.00 (54.00–73.00)	Non-survivors vs survivors	181	29.00(4.44)	31.33(6.67)
Alkhatib, A. L.et al.	2020	USA	English	Severe: 62 \pm 14.60; Non-Severe:55.00 \pm 14.70	Severe vs non-severe	158	36.50(7.80)	31.90(8.50)
Cai, Q.et al.	2020	China	English	47.00 (33.00–61.00)	Severe vs non-severe	298	24.5(4.3)	22.90(3.41)
Cai, S. H.et al.	2020	China	English	BMI < 24:35.41 \pm 18.45;BMI \geq 24:44.00 \pm 17.23	Severe vs non-severe	96	24.89(3.17)	22.35(3.56)
Chen, Q.et al.	2020	China	English	47.50 \pm 14.60	Severe vs non-severe	145	24.94(2.88)	23.52(3.00)
Gayam, V.et al.	2020	USA	English	67.00 (56.00–76.00)	Non-survivors vs survivors	408	31.77(7.78)	28.97(6.37)
Gupta, S.et al.	2020	USA	English	60.50 \pm 14.50	Non-survivors vs survivors	2215	30.67(7.16)	31.23(7.11)
Hundt, M. A.et al.	2020	USA	English	65.00 (1.00-103.00)	Severe vs non-severe	1827	30.70(8.50)	29.20(7.30)
Liu, M.et al.	2020	China	Chinese	35.00 \pm 8.00	Severe vs non-severe	30	27.00(2.50)	22.00(1.30)
Mani, V. R.et al.	2020	USA	English	64.72 (28.00–97.00)	Severe vs non-severe	184	31.47(8.65)	28.45(7.02)
Muñoz, Pet al.	2020	Spain	English	61.50(39.50–82.00)	Non-survivors vs survivors	100	30.33(5.04)	27.60(4.52)
Ortiz-Brizuela, E. et al.	2020	Mexico	English	43.00 (11.00–92.00)	Severe vs non-severe	140	30.47(5.06)	28.42(4.22)
Recinella, G. et al.	2020	Italy	English	Survivor:80.50 (73.70–92.20) Non-survivor:90 (82.00–95.00)	Non-survivors vs survivors	37	22.77(1.48)	25.30(4.15)

Study	Year	Country	Language	Age(mean \pm SD or median, range)	Groups	simple size	BMI,mean (SD)	
							Severe/non-survived	Non-severe/survived
Xu, J.et al.	2020	China	Chinese	41.99 \pm 15.42	Severe vs non-severe	155	25.69(3.22)	23.75(3.17)
Yu, T.et al.	2020	China	English	Severe:49.58 \pm 22.16; Non-Severe:38.37 \pm 15.80	Severe vs non-severe	70	25.38(2.49)	22.95(3.61)
Zhang, F.et al.	2020	China	English	14.00–45.00(median unknown)	Non-survivors vs survivors	43	27.79(5.18)	23.38(3.02)

Quality assessment

The quality assessment of the included studies, using the Newcastle–Ottawa scale, is shown in Table 2. The risk of bias assessment of these studies was based on three main categories of selection, comparability, and exposure. All eligible studies received five or more stars.

Table 2
Newcastle–Ottawa quality assessment scale of cohort studies for included studies.

Study ID	Selection (max 4 stars)				Comparability (max 2 stars)	Exposure (max 3 stars)			Total stars
	(1)	(2)	(3)	(4)		(1)	(2)	(3)	
Auld, S.et al.	0	*	0	0	*	*	*	*	5
Alkhatib, A. L.et al.	0	*	0	0	*	*	*	*	5
Cai, Q.et al.	0	*	0	0	*	*	*	*	5
Cai, S. H.et al.	*	*	0	0	*	*	*	*	6
Chen, Q.et al.	0	*	0	0	*	*	*	*	5
Gayam, V.et al.	*	*	0	0	*	*	*	*	6
Gupta, S.et al.	0	*	0	0	*	*	*	*	5
Hundt, M. A.et al.	0	*	0	0	*	*	*	*	5
Liu, M.et al.	0	*	0	0	*	*	*	*	5
Mani, V. R.et al.	0	*	0	0	*	*	*	*	5
Muñoz, P.et al.	0	*	0	0	*	*	*	*	5
Ortiz-Brizuela, E. et al.	*	*	0	0	*	*	*	*	6
Recinella, G. et al.	0	*	0	0	**	*	*	*	6
Xu, J.et al.	0	*	0	0	*	*	*	*	5
Yu, T.et al.	0	*	0	0	*	*	*	*	5
Zhang, F.et al.	0	*	0	0	*	*	*	*	5
Selection									
(1) Is the case definition adequate? (a) yes, with independent validation*, (b) yes, e.g. record linkage or based on self-reports, (c) no description.									
(2) Representativeness of the cases: (a) consecutive or obviously representative series of cases*, (b) potential for selection biases or not stated.									
(3) Selection of controls: (a) community controls*, (b) hospital controls, (c) no description.									
(4) Definition of controls: (a) no history of disease (end-point)*, (b) no description of source									
Comparability									
(1) Comparability of cases and controls on basis of design or analysis: (a) study controls for ___ (most important factor)*, (b) study controls for any additional factor* (could be modified to indicate specific control for a second factor).									
Exposure									
(1) Ascertainment of exposure: (a) secure record (e.g. surgical records)*, (b) structured interview where blind to case/control status*, (c) interview not blinded to case/control status, (d) written self-report or medical record only, (e) no description.									
(2) Same method of ascertainment for cases and controls: (a) yes*, (b) no.									

Study ID	Selection (max 4 stars)				Comparability (max 2 stars)	Exposure (max 3 stars)			Total stars
	(1)	(2)	(3)	(4)		(1)	(2)	(3)	
(3) Non-response rate: (a) same rate for both groups*, (b) non-respondents described, (c) rate different and no designation.									

Publication bias

Ten studies were included in the analysis regarding the association between BMI and severity of patients with COVID-19. The remaining six studies were used to analyze the correlation of BMI and the mortality of patients with COVID-19. Due to the limited power among studies, and the outcome was no more than 10 for the funnel plot, publication bias was not calculated(43).

Correlation of BMI and severity of patients with COVID-19

The severe and non-severe groups included 941 and 2162 patients with COVID-19, respectively. Based on the ten included studies, a significant increase in BMI on admission was observed in severe patients with COVID-19 compared with non-severe patients with COVID-19 for the fixed-effects model (Mean difference [MD] = 1.95, 95% confidence interval [CI], 1.52 - 2.37, $I^2 = 33%$, $P < 0.00001$). The result of the correlation of BMI and severity of patients with COVID-19 is shown in Fig. 2.

Correlation of BMI and mortality of patients with COVID-19

The non-survivor and survivor groups included 1014 and 1970 patients with COVID-19, respectively. Based on the six included studies, no obvious change in BMI was found in COVID-19 non-survivors compared with survivors for the random-effects model (MD = 0.55, 95% CI: -1.33 to 2.43, $I^2 = 88%$, $P = 0.57$). The result is shown in Fig. 3A. For the subgroup analysis, a significant increase in BMI on admission was observed in COVID-19 non-survivors compared with survivors for the fixed-effects model (MD = 3.01, 95% CI: 1.83 to 4.19, $I^2 = 0%$, $P < 0.00001$). The result is shown in Fig. 3B. In the intensive care unit (ICU) or geriatric ward, the BMI significantly decreased in COVID-19 non-survivors compared with survivors for the random-effects model in the subgroup analysis (MD = -1.61, 95% CI: -3.07 to -0.16, $I^2 = 72%$, $P = 0.03$). The result is shown in Fig. 3C.

Discussion

Higher BMI tends to indicate overweight or obesity, which is associated with increased morbidity and mortality from various diseases(44, 45). Similarly, higher BMI is associated with increased risk of acquiring infections with worse outcomes(46). With more in depth research, obesity seems to be a risk factor for exacerbation prediction of patients with COVID-19. In the systematic review or meta-analysis published to date, BMI is usually analyzed as a dichotomous variable. Multiple data sets from different races, sexes, regions, and ages were measured using the same BMI threshold, which may not be appropriate. Therefore, this study summarized currently available research regarding the correlation between BMI and the severity and mortality of patients with COVID-19 in the form of continuous variables.

In this study, BMI on admission significantly increased in patients with severe COVID-19 compared with non-severe patients. This suggests that patients admitted with higher BMI are more likely to develop severe COVID-19 infection. However, we did not observe a significant change in BMI in COVID-19 non-survivors compared with survivors. The statistical results showed very high heterogeneity, up to 88%. Further analysis of the six included studies were showed that the patients of the three studies were mainly from the ICU or geriatric ward and tend to have a long history of

hospitalization. Thus, a subgroup analysis was performed. A significant increase in BMI on admission was observed in COVID-19 non-survivors compared with survivors. This suggests that the risk of mortality of patients with COVID-19 with higher BMI on admission increases. Nevertheless, a significant decrease in BMI was observed in the non-survivor group compared with the survivor group in the ICU or geriatric ward. It may be related to a worsened nutritional status of patients with COVID-19 from the ICU or geriatric ward. A similar phenomenon was also observed by other previous studies; for example, patients with BMI < 20 had greater 60-day mortality in the ICU setting (47); lower BMI was associated with a higher risk of death for patients with sepsis (48); patients who are underweight have a higher mortality rate in the pediatric ICU (49). Hence, patients with COVID-19 from the ICU or geriatric ward may need to maintain BMI within the normal range.

Finally, this study has several limitations: (1) Due to the lack of prospective study or randomized controlled trial, studies included in our analysis are mainly retrospective cohort studies. (2) Although we observed a significant decrease in BMI in the non-survivor group compared with the survivor group in the ICU or geriatric ward, more research is needed for further analysis. (3) Most studies included in this study were conducted in China or USA, and studies from other countries or regions need to be included in future studies.

Conclusion

In summary, higher BMI on admission is associated with severity and mortality of patients with COVID-19, but lower BMI is associated with mortality of patients with COVID-19 in the ICU or geriatric ward. BMI should be used properly based on the different situation of patients with COVID-19 during treatment.

Declarations

Ethics approval and consent to participate:

Not applicable.

Consent for publication:

Not applicable.

Availability of data and materials:

Data sharing is not applicable to this article.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

CF takes responsibility for the conception and design of the study and drafting the article. ZZ and MZ contributed to acquisition and analysis and interpretation of data. JL contributed to manuscript review and editing. All authors read and

approved the final manuscript.

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Figures

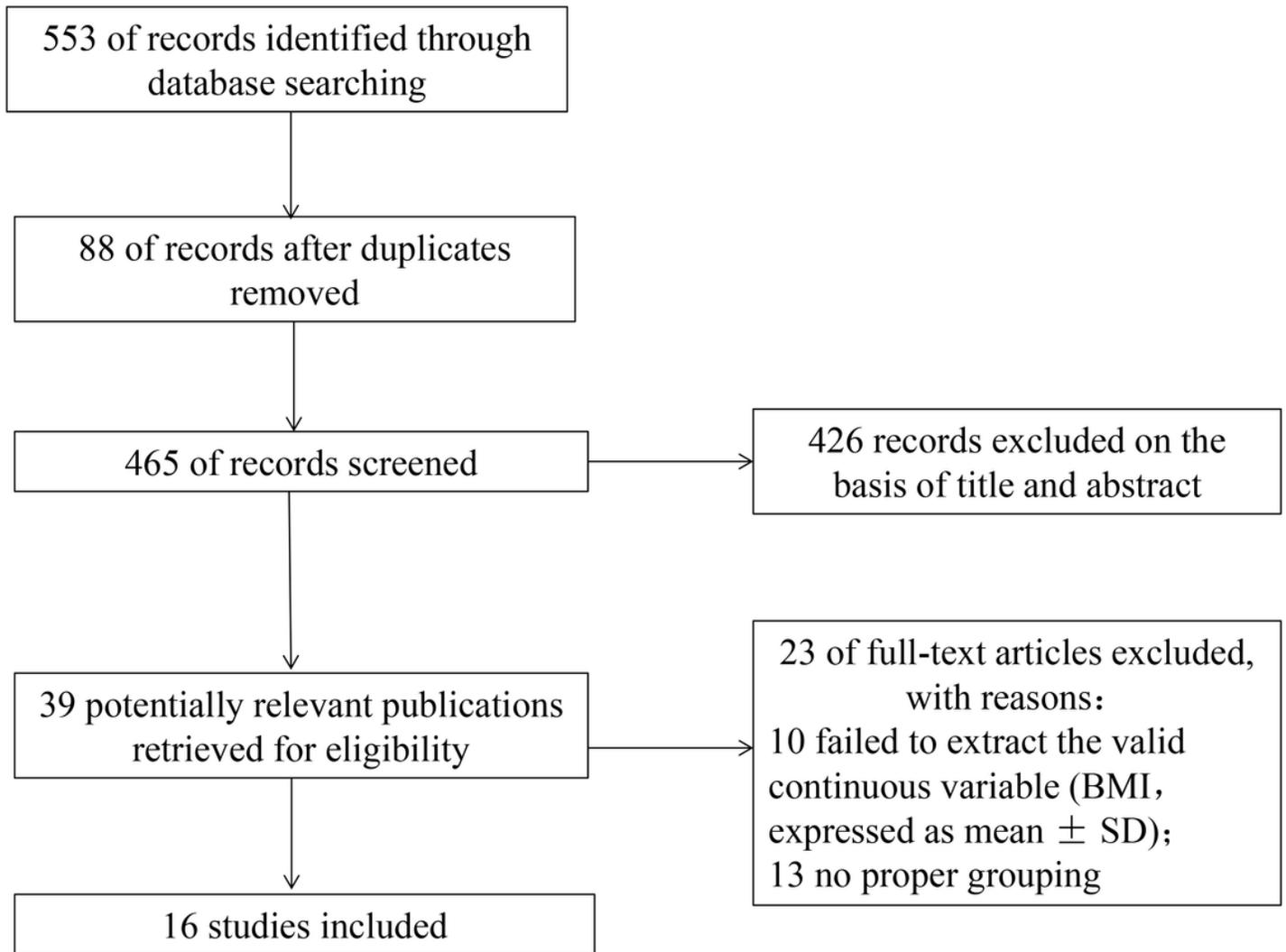


Figure 1

Flow chart of included studies.

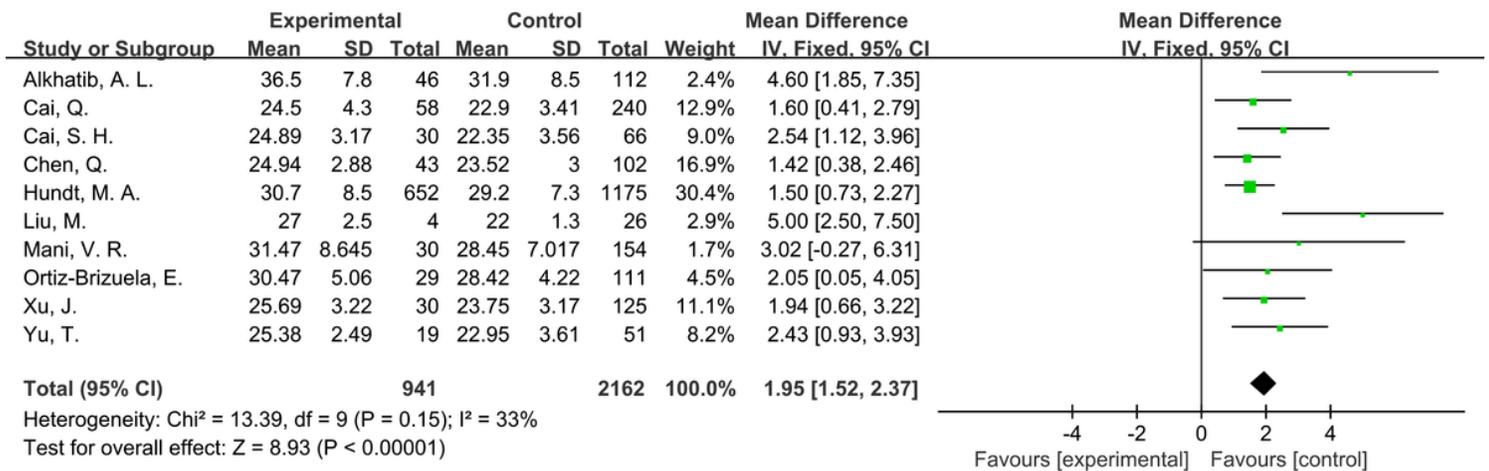


Figure 2

Forest plot: correlation of BMI and severity of patients with COVID-19.

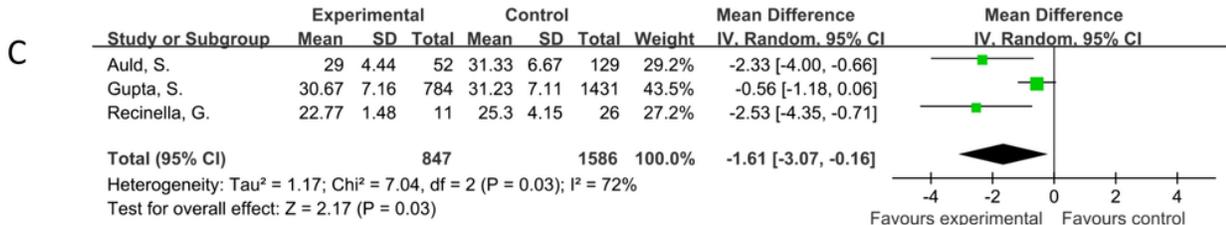
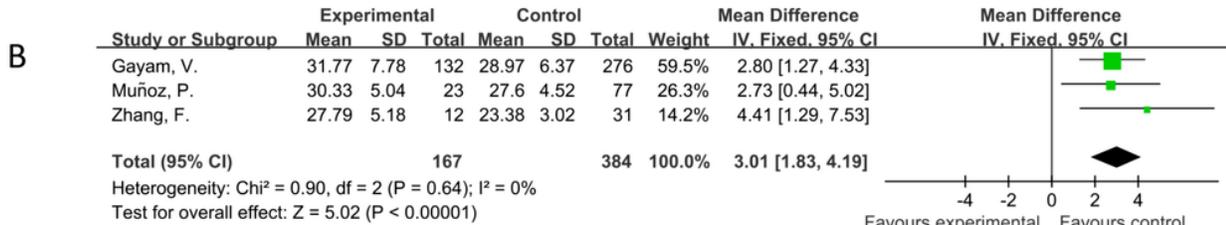
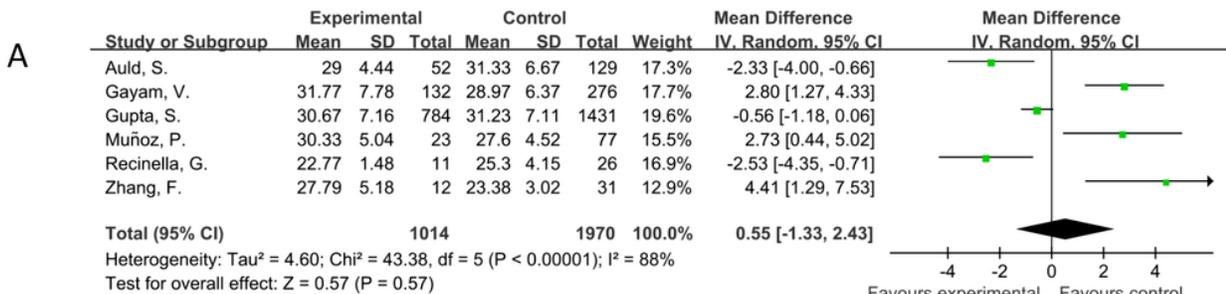


Figure 3

Forest plot: the correlation of BMI and the mortality of COVID-19 patients A: Forest plot: correlation of BMI and mortality of patients with COVID-19 based on the six included studies. B: Forest plot: BMI on admission in COVID-19 non-survivors compared with survivors in the subgroup analysis. C: Forest plot: the BMI of the non-survivor group compared with the survivor group in the ICU or geriatric ward in the subgroup analysis.