Table 1
Patients' characteristics and outcomes

Variable	All patients who underwent MV surgery* (n = 107,936)			Patients who underwent MV surgery and had TVD† (n = 19,434)		
	No TVD† (n = 88,502)	TVD† (n = 19,434)	P-value§	No TV Surgery‡ (n = 13,213)	TV Surgery‡ (n = 6,221)	P-value§
Age (years), median (IQR)	62 (46-80)	65 (51-79)	<0.001	65 (61-69)	66 (62-70)	<0.001
Women	48941 (55.3%)	12107 (62.3%)	<0.001	7711 (58.4%)	3876 (62.3%)	<0.001
White	57956 (65.5%)	11904 (61.3%)	<0.001	8324 (63%)	3580 (57.5%)	0.006
Admission type			<0.001			<0.001
Elective admissions	55581 (62.8%)	12636 (65%)		8531 (64.6%)	4099 (65.9%)	
Urgent admissions	32696 (36.9%)	6761 (34.8%)		4649 (35.2%)	2112 (33.9%)	
Comorbidities						
Hypertension	44893 (50.7%)	10198 (52.5%)	<0.001	6899 (52.2%)	3299 (53%)	<0.001
Diabetes mellitus	16325 (18.4%)	3784 (19.2%)	<0.001	2491 (18.9%)	1293 (20.8%)	<0.001
Smoker	21100 (23.8%)	3965 (20.4%)	<0.001	2791 (21.1%)	1174 (18.9%)	0.077
Obesity¶	8533 (9.6%)	1901 (9.8%)	0.593	1316 (10%)	585 (9.4%)	0.025
Dyslipidemia#	31844 (36%)	6606 (34%)	<0.001	4607 (34.9%)	1999 (32.1%)	<0.001
Atrial fibrillation	44196 (49.9%)	12797 (65.8%)	<0.001	8530 (64.6%)	4267 (68.6%)	<0.001
Liver disease	1450 (1.6%)	446 (2.3%)	<0.001	270 (2%)	176 (2.8%)	<0.001
Coagulopathy	21057 (23.8%)	5517 (28.4%)	<0.001	3713 (28.1%)	1804 (29%)	0.149
Renal failure	11278 (12.7%)	3128 (16.1%)	<0.001	2058 (15.6%)	1070 (17.2%)	0.008
Chronic lung disease	17416 (19.7%)	4168 (21.4%)	<0.001	2950 (22.3%)	1248 (20.1%)	<0.001
Peripheral vascular Disorder	7534 (8.5%)	1653 (8.5%)	0.931	1201 (9.1%)	452 (7.3%)	0.068
Outcomes						
Length of stay (days), mean ± SD	13.2 ± 13.3	13.8 ± 12.4	<0.001	13.4 ± 11.8	14.7 ± 13.7	<0.001
Total charges ($), mean ± SD	208,292 ± 204,165	218,589 ± 198,124	<0.001	210,296 ± 185,424	236,224 ± 221,724	<0.001
Discharge needing care$	54055 (61.1%)	12998 (66.9%)	<0.001	8794 (66.6%)	4204 (67.6%)	0.141
Acute kidney injury	16905 (19.1%)	3944 (20.3%)	<0.001	2535 (19.2%)	1409 (22.6%)	<0.001
Stroke	3727 (4.2%)	502 (2.6%)	<0.001	348 (2.6%)	154 (2.5%)	<0.001
Bleeding	11813 (13.3%)	2035 (10.5%)	<0.001	1423 (10.8%)	612 (9.8%)	<0.001
Mortality	5150 (5.8%)	1225 (6.3%)	0.010	814 (6.2%)	411 (6.6%)	<0.001

* Mitral valve surgery. Defined using the following procedure codes: ICD9; 35.24, 35.23, 35.12, ICD10; 02RG0JZ, 02RG4JZ, 02RG07Z, 02RG08Z, 02RG47Z, 02RG48Z, 02RG4KZ, 027G04Z, 027G0DZ, 027G0ZZ, 02NG0ZZ, 02QG0ZZ, 02VG0ZZ, 02QG4ZZ.
† Tricuspid valve disease. Defined using the following diagnosis codes: ICD9; 397.0, 424.2, 746.1, ICD10; I070, I071, I072, I360, I361, I362, Q224.

TV surgery in our sample were not clear and require further evaluation. However, this study is the largest and most recent in the medical literature to assess patients who underwent MV surgery while having concomitant TVD.

In conclusion, this nationwide study showed that although about one-fifth of patients who undergo MV surgery also have TVD, only a portion of them undergo concomitant TV surgery.

Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Meta-Analysis of Atrial Fibrillation in Patients With COVID-19

A number of published papers have investigated the relation between atrial fibrillation (AF) and clinical outcomes of patients with coronavirus disease 2019 (COVID-19). However, the conclusions

drawn from previous studies are not consistent. For instance, some studies observed that AF was significantly associated with an increased risk of mortality among COVID-19 patients,[1-3] while several other studies reported opposite results that there was no significant relation between AF and unfavorable outcomes of COVID-19 patients.[4-6] Several confounding factors such as gender, age and pre-existing medical disorders (diabetes, hypertension, autoimmune diseases, chronic kidney disease, and chronic obstructive pulmonary disease, etc.) have been reported to significantly influence the clinical outcomes of COVID-19 patients,[7-13] suggesting that these factors might have significant impacts on the relation between AF and unfavorable outcomes of COVID-19 patients. In this meta-analysis, the pooled effect size was estimated on the basis of adjusted effect estimates reported in published papers.

We systematically searched PubMed, Web of Science, and EMBASE databases to identify all potential documents published between January 1, 2020 and December 24, 2020, using the following keywords and terms: "severe acute respiratory syndrome coronavirus-2" or "SARS-CoV-2" or "coronavirus disease 2019" or "COVID-19" or "2019 novel coronavirus" or "2019-nCoV" and "atrial fibrillation" and "severity" or "severe" or "critical" or "mortality" or "death" or "fatality" or "intensive care unit" or "mechanical ventilation". Studies were eligibly included if they met the following criteria: (1) studies reporting laboratory-confirmed COVID-19 patients; (2) articles should be peer-reviewed; (3) articles should be published in English; (4) the adjusted effect estimate on the relation between AF and unfavorable outcomes of COVID-19 patients are available. Accordingly, studies were excluded if they were: (1) repeated studies, review papers, comments, errata, protocols and case reports; (2) articles reporting crude effect size; (3) articles with insufficient data; (4) in vitro studies or animal studies.

Two investigators independently extracted the basic characteristics including name of authors, country and/or region, number of cases, percentage of male, age (mean ± standard deviation or median (interquartile range), study design, adjusted effect size and outcomes. In case of disagreement, a third investigator was consulted and made a final decision. Statistical analysis was carried out using Stata 12.1 software. I^2 statistic and Cochran's Q test were adopted in the assessment of heterogeneity among the included studies. The pooled effect size and 95% confidence interval (CI) were calculated to estimate the relation between AF and unfavorable outcomes of COVID-19 patients. A fixed-effects analysis was conducted if there was no heterogeneity ($I^2 < 50\%$ or $p > 0.1$), otherwise, a random-effects analysis was carried out ($I^2 > 50\%$ or $p < 0.1$). Leave-one-out sensitivity analysis was performed to assess the stability of our results. Publication bias was evaluated by Begg's rank correlation test and Egger's linear regression test. Subgroup analysis and meta-regression analysis were also performed to probe the source of heterogeneity. A p-value < 0.05 was deemed statistically significant.

Nine hundred and sixteen potentially relevant studies were screened according to the inclusion and exclusion criteria. Finally, 23 studies with 108,745 COVID-19 patients[1-6,14-30] were eligibly included in the present quantitative meta-analysis. The study characteristics are summarized in Table 1. Ten studies came from United States of America (USA) and 13 studies were from Europe (5 from United Kingdom, 4 from Italy, 2 from Spain and 1 each from Denmark and France). Results of our meta-analysis

Table 1
Main characteristics of the studies included in this meta-analysis

Author	Country	Cases	Male (%)	Age§	Study design	Adjusted-effect size (95% CI)
Lala A	USA	2736	59.6%	66.4	Retrospective study	OR: 1.08 (0.81-1.44)
Atkins JL	UK	507	61.3%	74.3±4.5	UK biobank cohort	OR: 1.63 (0.98-2.71)
van Gerwen M	USA	3703	55.3%	56.8±18.2	Retrospective study	OR: 1.19 (0.87-1.62)
Hippisley-Cox J	UK	19486	48.1%	62.18±20.84	Prospective study	HR: 0.87 (0.55-1.39)
Peterson E	USA	355	51%	66.21±14.21	Retrospective study	OR: 0.475 (0.190-1.188)
Perez-Guzman PN	UK	614	62.2%	69 (25)	Retrospective study	OR: 1.25 (0.73-2.13)
Reilev M	Denmark	11122	42.2%	48 (33-62)	Population-based study	OR: 1.6 (1.2-2.0)
Rodilla E	Spain	12226	57.4%	67.5±16.1	Retrospective study	OR: 1.2 (1.01-1.33)
Elias P	USA	1258	54%	61.6±18.4	Retrospective study	OR: 2.54 (1.05-6.2)
Peltzer B	USA	1053	62.3%	62±17	Retrospective study	OR: 2.16 (1.33-3.52)
Rodriguez-Molinero A	Spain	418	56.9%	65.4±16.6	Observational cohort study	OR: 1.86 (0.86-4.02)
Clift AK	UK	10776	55.3%	69.63±17.91	Observational cohort study	HR: 1.18 (1.04-1.34) HR: 1.11 (1.00-1.24)
Alvarez-Garcia J	USA	6349	55.1%	63.5±18	Retrospective study	HR: 0.91 (0.63-1.31)
Tang O	USA	752	39.9%	71.16±51.68	Retrospective study	HR: 0.86 (0.57-1.30)
Shah C	USA	487	56.1%	68.42±16.70	Retrospective study	OR: 0.91 (0.50-1.65)
Tomasoni D	Italy	692	69.5%	67.4±13.2	Retrospective study	HR: 1.27 (0.73-2.23)
Polverino F	USA	3179	68.3%	69.0 (57-78)	Retrospective study	OR: 0.97 (0.69-1.36)
Loffi M	Italy	1252	63.7%	64.7±15.5	Retrospective study	HR: 1.09 (0.75-1.58)
Canevelli M	Italy	2621	67.6%	78.16±10.51	Retrospective study	OR: 0.99 (0.72-1.37)
Rossi L	Italy	590	66.1%	76.2 (68.2-82.6)	Retrospective study	HR: 1.390 (0.925-1.885)
Gue YX	UK	486	38.7%	73.42±15.97	Retrospective study	OR: 0.49 (0.35-1.58)
Izurieta HS	USA	27961	48.8%	79.07±10.15	Retrospective study	OR: 0.97 (0.92-1.01)
Lano G	France	122	65%	73.5 (64.2-81.2)	Observational cohort study	OR: 1.838 (0.751-4.481)

Note: § indicates the values are presented as mean ± standard deviation (SD) or median (interquartile range, IQR); CI, confidence interval; HR, hazard ratio; OR, odds ratio; UK, the United Kingdom; USA, the United States of America.

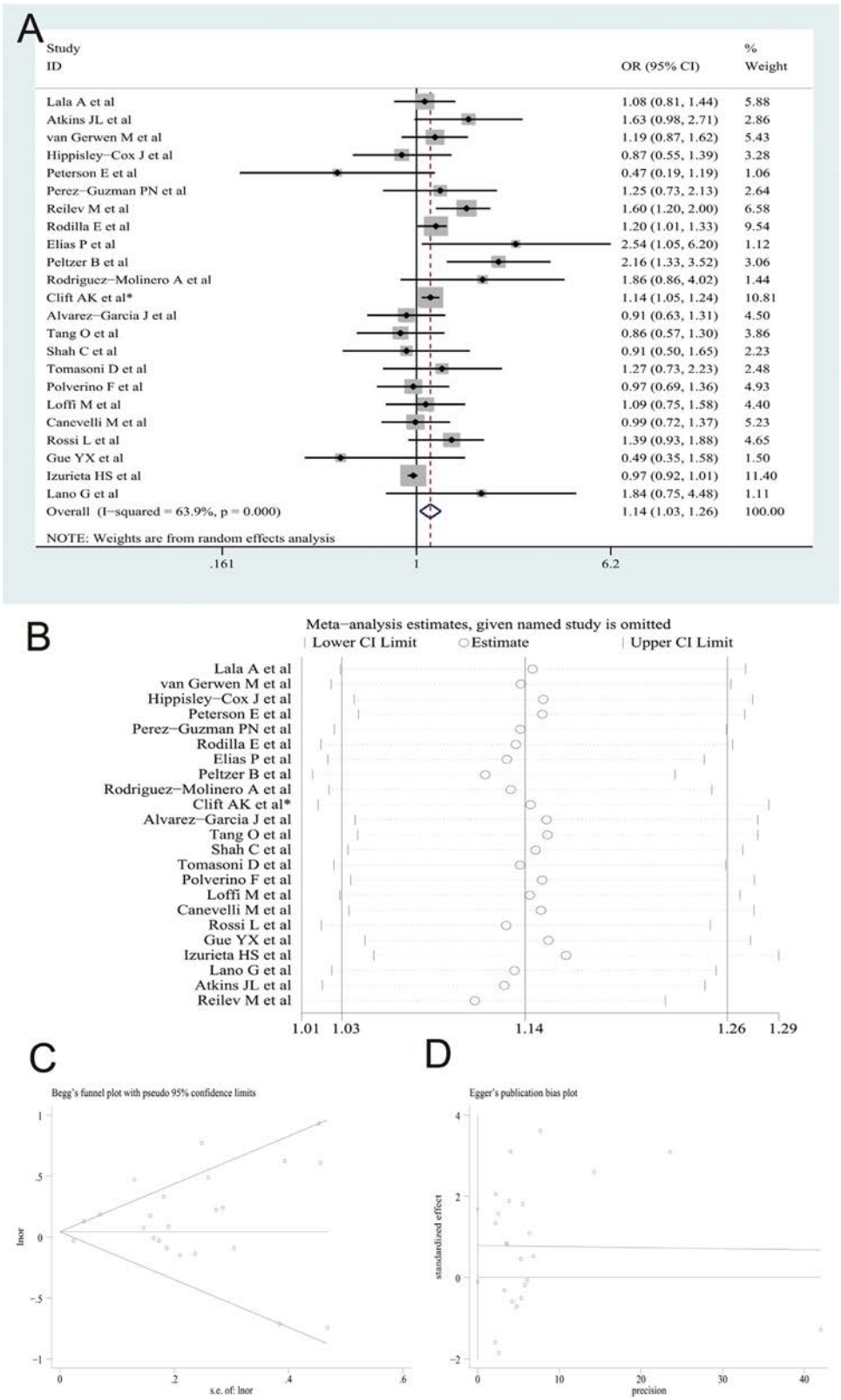

Figure 1. The forest plot indicating the relation between atrial fibrillation (AF) and unfavorable outcomes among patients with coronavirus disease 2019 (COVID-19) based on 23 studies with 108,745 cases (*A*); Leave-one-out sensitivity analysis showed our results were stable and robust (*B*); Publication bias was assessed by both Begg's rank correlation test (*C*) and Egger's linear regression test (*D*). * indicates the value was combined from subgroups.

indicated that AF was significantly associated with an increased risk of unfavorable outcomes among COVID-19 patients (pooled effect size = 1.14, 95% CI: 1.03 to 1.26, p = 0.01; I^2 = 63.9%, random-effects analysis; Figure 1). When the clinical outcomes were limited to death, there was still a significant relation between AF and COVID-19 mortality (pooled effect size = 1.13, 95% CI: 1.02 to 1.25). Subgroup analysis by effect estimate showed consistent results (pooled effect size = 1.12, 95% CI: 1.04 to 1.21 for hazard ratio (HR)-reported studies and pooled effect size = 1.18, 95% CI: 1.02 to 1.37 for odds ratio (OR)-reported studies). Inconsistent results were observed in the subgroup analyses by sample size (pooled effect size = 1.14, 95% CI: 1.02 to 1.27 for ≥ 1,000 cases and pooled effect size = 1.12, 95% CI: 0.87 to 1.44 for < 1,000 cases), age (pooled effect size = 1.18, 95% CI: 1.06 to 1.31 for < 70 years old and pooled effect size = 1.06, 95% CI: 0.87 to 1.29 for ≥ 70 years old), percentage of male (pooled effect size = 1.26, 95% CI: 1.06 to 1.51 for ≥ 60% and pooled effect size = 1.09, 95% CI: 0.97 to 1.22 for < 60%) and region (pooled effect size = 1.21, 95% CI: 1.08 to 1.35 for Europe and pooled effect size = 1.06, 95% CI: 0.90 to 1.24 for USA). We observed no significant relation between AF and unfavorable outcomes among COVID-19 patients in the subgroup analysis of study design (pooled effect size = 1.08, 95% CI: 0.97 to 1.22 for retrospective study, pooled effect size = 1.27, 95% CI: 0.95 to 1.70 for observational cohort study and pooled effect size = 1.34, 95% CI: 0.92 to 1.96 for the others). Sensitivity analysis showed that our results were stable and reliable since omitting each study one by one had no obvious effects on the overall effect size (Figure 1). There was no obvious publication bias assessed by Begg's test (p = 0.428, Figure 1) and Egger's test (p = 0.081, Figure 1). Meta-regression analysis exhibited that the tested variables such as sample size, age, percentage of male, region, study design, and effect estimate might not be the source of heterogeneity (data not shown).

Limitations: (1) All the included studies came from USA and Europe. (2) Because medications for COVID-19 were not clearly reported in most of the included studies, we did not address the effects of these factors on the relation between AF and unfavorable outcomes of COVID-19 patients. (3) The adjusted risk factors are variable across the included studies. (4) Most of the studies are retrospective, further meta-analyses based on prospective studies with large sample size are warranted to verify our findings when more data are available.

In conclusion, our study demonstrates that AF was significantly associated with an increased risk of unfavorable outcomes among COVID-19 patients, especially for death.

Author Contributions

Yadong Wang and Haiyan Yang designed the study. Xuan Liang and Jie Xu performed literature search. Haiyan Yang and Xuan Liang performed data extraction. Xuan Liang, Haiyan Yang, Jie Xu and Hongjie Hou performed statistical analyses. Haiyan Yang, Xuan Liang and Yadong Wang wrote and reviewed the manuscript. All the authors approved the final version of the manuscript.

Conflicts of Interest Statement

The authors declare that they have no any potential conflict of interest regarding this submitted manuscript.

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