pooled prevalence of AP and other clinical outcomes. The overall pooled prevalence and mortality were assessed for group I with a random-effects model and Freeman– Tukey double arcsine transformation using R statistical software (V.4.1.0). Heterogeneity was assessed using the I² statistic and Cochran Q test. Publication bias was assessed using the funnel plots and Egger's test. Other analyses were performed using Review Manager (V.5.4).

Eleven studies were included (online supplemental file 1),¹⁻¹¹ of which six were multicentre and eight were retrospective. The pooled prevalence of AP in patients with COVID-19 was 3.1% (95% CI 1.6% to 5.1%, $I^2 = 98.3\%$; figure 1A) comprising 183 with AP among 88635 patients with COVID-19 in seven studies. The pooled mortality was 18.5% (95% CI 12.6% to 25.1%, I²=40%; figure 1B) comprising 74 patients out of 384 who had both AP and COVID-19 in 11 studies. The visual inspection of the funnel plot indicated relative symmetry (online supplemental file 1), and Egger's test showed no evidence of significant publication bias for mortality (p=0.087).

Compared with AP patients without COVID-19 (group II), patients with AP and COVID-19 (group I) had a higher proportion of males (five studies), unknown/ idiopathic aetiology (five studies), greater severity of AP (Bedside Index of Severity in Acute Pancreatitis (BISAP) in four studies), increased risk of pancreatic necrosis (four studies), ICU admission (three studies), persistent organ failure (two studies) and need for mechanical ventilation (two studies). The mortality of group I was increased compared with group II (five studies) and group III (four studies; table 1).

Prevalence and outcomes of acute pancreatitis in COVID-19: a meta-analysis

The study by Pandanaboyana *et al*¹ showed that acute pancreatitis (AP) patients with COVID-19 had a significantly higher mortality than those without COVID-19. Nevertheless, a similar trend of mortality was found by another observational cohort study.² The true prevalence and outcomes of AP in patients with COVID-19 are not known. The aim of this study was to conduct a meta-analysis to determine the pooled prevalence and clinical outcomes of AP in patients with COVID-19.

PubMed, Embase, Scopus and Cochrane library were searched for outcome studies of adult patients with AP and COVID-19 published before 15 September 2021 (online supplemental file 1). Excluded were studies that either did not use the revised Atlanta criteria for AP diagnosis or reported patients with COVID-19 with a prior history of pancreatitis. Patients were divided into three groups: group I—AP with COVID-19, group II—AP without COVID-19 and group III—COVID-19 without AP. The primary endpoint was mortality (both in-hospital or 30-day). Secondary endpoints were





Gut: first published as 10.1136/gutjnl-2021-325941 on 20 October 2021. Downloaded from http://gut.bmj.com/ on January 12, 2023 by guest. Protected by copyright

Table 1 Associations between acute pancreatitis and COVID-19 by random-effects model						
Subgroup	No of studies	OR	95% CI	P value	I ² %	P _H
Group I vs group II						
Demographics						
Male	5	1.51	1.18 to 1.94	0.001	0	0.80
BISAP≥3	4	2.71	1.04 to 7.06	0.04	80	0.002
Comorbidities						
Hypertension	2	0.99	0.36 to 2.74	0.98	76	0.04
Diabetes	2	1.23	0.72 to 2.09	0.45	0	0.80
Aetiology						
Alcohol	4	0.28	0.11 to 0.72	0.009	65	0.04
Gallstone	5	0.74	0.54 to 1.02	0.06	20	0.29
Unknown/idiopathic	5	3.36	1.43 to 7.90	0.006	82	0.0002
Drug-induced	3	1.57	0.49 to 5.03	0.45	0	0.93
Hyperlipidaemia	4	0.92	0.31 to 2.76	0.88	46	0.14
Morbidities						
Pancreatic necrosis	4	1.79	1.21 to 2.64	0.004	0	0.85
Thromboembolic complications	2	1.30	0.48 to 3.53	0.60	0	0.43
Persistent organ failure	2	7.37	3.48 to 15.60	< 0.00001	33	0.22
ICU admission	3	3.91	2.53 to 6.05	< 0.00001	0	0.52
Mechanical ventilation	2	7.52	3.23 to 17.49	< 0.00001	0	0.33
Mortality	5	5.75	3.62 to 9.14	< 0.00001	0	0.66
Group I vs group III						
Male	3	1.74	1.09 to 2.80	0.02	0	0.45
ICU admission	2	3.80	0.95 to 15.18	0.06	77	0.04
Mortality	4	2.76	1.17 to 6.54	0.02	61	0.05

BISAP, Bedside Index of Severity in Acute Pancreatitis; ICU, intensive care unit.

This meta-analysis is the first systematic evaluation of the prevalence and outcome of AP in patients with COVID-19. Comparing AP patients with or without COVID-19 is striking. The increased prevalence of unknown/idiopathic aetiology in patients with concomitant disease suggests that SARS-CoV-2 might itself cause AP in some patients (possibly via a higher density of ACE2 receptors). The overall pooled prevalence was low at 3.1%, but this might be an underestimate as two studies²⁷ excluded patients that developed AP during hospitalisation. Sensitivity analysis with these two studies excluded showed that the pooled prevalence of AP was 6.7%. Patients with AP and COVID-19 had a high pooled mortality (18.5%) and significantly worse clinical outcomes. There was no significant difference in ICU admission rate between groups I and III who both had COVID-19 even though AP and COVID-19 both cause systemic inflammatory response and multiple organ dysfunction.

This study does not necessarily represent the global situation, drawing data only from the USA, China and European countries. However, it clearly shows that patients with concomitant AP and COVID-19 have a high risk of adverse outcomes and almost a 20% chance of dying. This study is limited by the small number of included studies, the low event rate and high heterogeneity due to differences in study design and methodology. However, this is the best available data and the meta-analysis can be updated after publication of more prospective studies.

Feng Yang ⁽²⁾, ¹ Yuting Huang,² Tian Li,³ Yunting Fu,⁴ Chenyu Sun ⁽²⁾, ⁵ Yecheng Xu,¹ John Windsor ⁽²⁾, ⁶ Deliang Fu ⁽²⁾

¹Department of Pancreatic Surgery, Huashan Hospital Fudan University, Shanghai, Shanghai, China ²Department of Medicine, University of Maryland Medical Center Midtown Campus, Baltimore, Maryland, USA ³Department of Medicine, SUNY Downstate Health and Science University, New York City, New York, USA ⁴Health Sciences and Human Services Library, University of Maryland, Baltimore, Baltimore, Maryland, USA ⁵Internal Medicine, AMITA Health Saint Joseph Hospital Chicago, Chicago, Illinois, USA ⁶Surgical and Translational Research Centre, The

University of Auckland, Auckland, New Zealand

Correspondence to Dr Feng Yang, Department of Pancreatic Surgery, Huashan Hospital Fudan University, Shanghai, Shanghai, China; yffudan98@126.com

Twitter John Windsor @jwindsor3

Collaborators None.

Contributors Concept and design: FY, JW and DF; acquisition, analysis and interpretation of data: FY, YH, TL, YF, CS, YX, JW and DF; drafting of the manuscript: FY; critical revision of the manuscript: JW and DF. All authors finally approved the manuscript.

Funding The research was supported by the National Key R&D Program of China No.2017YFC1308604 (Dr Yang).

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; internally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peerreviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

This article is made freely available for use in accordance with BMJ's website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.

© Author(s) (or their employer(s)) 2022. No commercial re-use. See rights and permissions. Published by BMJ.

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/gutjnl-2021-325941).



To cite Yang F, Huang Y, Li T, *et al. Gut* 2022;**71**:1451–1453.

Received 22 August 2021 Accepted 9 October 2021 Published Online First 20 October 2021

Gut 2022;**71**:1451–1453. doi:10.1136/ gutjnl-2021-325941

ORCID iDs

Feng Yang http://orcid.org/0000-0001-8790-6072 Chenyu Sun http://orcid.org/0000-0003-3812-3164 John Windsor http://orcid.org/0000-0001-5995-5432 Deliang Fu http://orcid.org/0000-0003-1832-2000

REFERENCES

- Pandanaboyana S, Moir J, Leeds JS, *et al*. SARS-CoV-2 infection in acute pancreatitis increases disease severity and 30-day mortality: COVID pan collaborative study. *Gut* 2021;70:1061–9.
- 2 Inamdar S, Benias PC, Liu Y, et al. Prevalence, risk factors, and outcomes of hospitalized patients with coronavirus disease 2019 presenting as acute pancreatitis. Gastroenterology 2020;159:2226–8.
- 3 Akarsu C, Karabulut M, Aydin H, et al. Association between acute pancreatitis and COVID-19: could pancreatitis be the missing piece of the puzzle about increased mortality rates? J Invest Surg 2020:1–7.
- 4 Dirweesh A, Li Y, Trikudanathan G, et al. Clinical outcomes of acute pancreatitis in patients with coronavirus disease 2019. Gastroenterology 2020;159:1972–4.
- 5 Bulthuis MC, Boxhoorn L, Beudel M, et al. Acute pancreatitis in COVID-19 patients: true risk? Scand J Gastroenterol 2021;56:585–7.
- 6 Kumar V, Barkoudah E, Souza DAT, et al. Clinical course and outcome among patients with acute pancreatitis and COVID-19. Eur J Gastroenterol Hepatol 2021;33:695–700.

- 7 Miró Òscar, Llorens P, Jiménez S, *et al*. A case-control emergency department-based analysis of acute pancreatitis in Covid-19: results of the UMC-19-S₆. *J Hepatobiliary Pancreat Sci* 2020. doi:10.1002/ jhbp.873. [Epub ahead of print: 01 Dec 2020].
- Szatmary P, Arora A, Thomas Raraty MG, et al. Emerging phenotype of severe acute respiratory syndrome-coronavirus 2-associated pancreatitis. *Gastroenterology* 2020;159:1551–4.
- 9 Vatansev H, Yildirim MA, Kuccukturk S, et al. Clinical evaluation of acute pancreatitis caused by SARS-CoV-2 virus infection. *Gastroenterol Res Pract* 2021;2021:1–5.
- 10 Ding P, Song B, Liu X, *et al*. Elevated pancreatic enzymes in ICU patients with COVID-19 in Wuhan, China: a retrospective study. *Front Med* 2021;8:663646.
- 11 Karaali R, Topal F. Evaluating the effect of SARS-Cov-2 infection on prognosis and mortality in patients with acute pancreatitis. *Am J Emerg Med* 2021;49:378–84.