

## LETTERS

## Duration of organ failure impacts mortality in acute pancreatitis

We read with great interest the recent *Gut* publication by Schepers *et al*<sup>1</sup> reporting no association between the time of onset or duration of persistent organ failure (POF, >48 hours, distinguished from transient organ failure <48 hours) and mortality in a subset of patients (240/639) with acute pancreatitis (AP). Previously it has been proposed that there are two peaks of POF and mortality in patients with AP, namely the early phase (first week) accompanied by persistent systemic inflammatory response syndrome and late phase (>second week) caused by infected pancreatic necrosis (IPN).<sup>2</sup> Patients with early fulminant POF have been considered to have a higher mortality than those developing POF later,<sup>3–6</sup> and those with POF in combination with IPN to have a higher mortality than those with POF alone.<sup>7</sup> The findings from Schepers *et al*<sup>1</sup> have challenged these views but require confirmation. We have determined whether their findings are applicable to our AP patient populations.

We analysed 2145 and 939 patients with AP from retrospective (single centre) and prospective cohorts (multicentre), respectively, who were admitted ≤48 hours of symptoms onset (online supplementary table 1). There were 469 (21.9%) and 132 (14.1%) patients who had POF in these

**Table 1** Unadjusted and adjusted OR and 95% CI in multivariate analysis of risk for mortality

Covariate	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI) *	P value
POF alone versus POF with IPN	1.522 (0.883 to 2.623)	0.131	1.721 (0.909 to 3.257)	0.095
Onset of POF	0.779 (0.603 to 1.005)	0.054	0.85 (0.668 to 1.082)	0.188
Duration of all organ failure	1.041 (1.026 to 1.057)	<0.001	1.034 (1.018 to 1.051)	<0.001



\*Adjustment for age, sex, Charlson and modified CT severity index.  
 IPN, infected pancreatic necrosis.; POF, persistent organ failure.

two cohorts, respectively. Our data demonstrate that the prevalence of different types of POF (including respiratory, cardiovascular and renal failure) all peaked during the first week; the patterns were similar in the retrospective and prospective cohorts (online supplementary figure 1). Of 601 patients with POF, 370 (61.6%) had an onset ≤24 hours of admission, followed by 159 (26.5%) on day 2 and 40 (6.7%) on day 3 (online supplementary figure 2). Mortality was related to the number of organs that failed: 5.5% (25/453) for one, 44.9% (35/78) for two and 88.6% (62/70) for three (online supplementary table 2). Our data were in accord with Schepers *et al*<sup>1</sup> showing no biphasic pattern of mortality in the total 3084 patients, with a single peak ≤2 weeks followed by a steady decrease >2 weeks (figure 1). There was no significant increase in mortality among patients with POF and IPN compared with those with POF and no IPN (median 26.3% vs 19.4%, p=0.16) (online supplementary table 3).

In contrast with the Dutch data, however, we found a significant association between the duration of POF and mortality (table 1). The mortality of those

with POF for >2 weeks was significantly higher than those ≤2 weeks (online supplementary table 4). This was confirmed by multivariate logistic regression analyses with an adjusted OR 1.034 (95% CI 1.018 to 1.051, p<0.001) for duration of POF and mortality. There was no significant impact of POF onset or IPN in those that also had POF on mortality, consistent with the findings from Guo *et al*<sup>8</sup> and Schepers *et al*.<sup>1</sup>

Our large multicentre series confirms that there is a single peak in incidence of POF and mortality in AP but in contrast to the Dutch data, we found a relationship between the duration of POF and mortality. Recent improvements in the treatment of IPN have erased the second mortality peak and demotes IPN as a determinant of mortality.<sup>7</sup> We maintain that shortening the duration of all organ failure is an important treatment target and should be routinely reported. This is illustrated by recent findings that early initiation of aggressive fluid therapy may be helpful, but if delayed 6–8 hours after admission the risk of POF and mortality may be increased.<sup>9</sup> The frequent early onset of POF and impact of its duration underline the importance of door-to-needle time<sup>10</sup> and the duration of POF as an outcome in clinical trials of new treatments for AP.

Na Shi,<sup>1</sup> Tingting Liu,<sup>1,2</sup>  
 Daniel de la Iglesia-Garcia,<sup>3</sup> Lihui Deng,<sup>1</sup>  
 Tao Jin,<sup>1</sup> Lan Lan,<sup>4</sup> Ping Zhu,<sup>1</sup> Weiming Hu,<sup>5</sup>  
 Zongguang Zhou,<sup>6</sup> Vikesh Singh,<sup>7</sup>  
 J Enrique Dominguez-Munoz,<sup>3</sup> John Windsor,<sup>8</sup>  
 Wei Huang ,<sup>1,2</sup> Qing Xia,<sup>1</sup> Robert Sutton <sup>2</sup>

<sup>1</sup>Department and Laboratory of Integrated Traditional Chinese and Western Medicine, Sichuan Provincial Pancreatitis Centre and West China-Liverpool Biomedical Research Centre, West China Hospital, Sichuan University, Chengdu, China

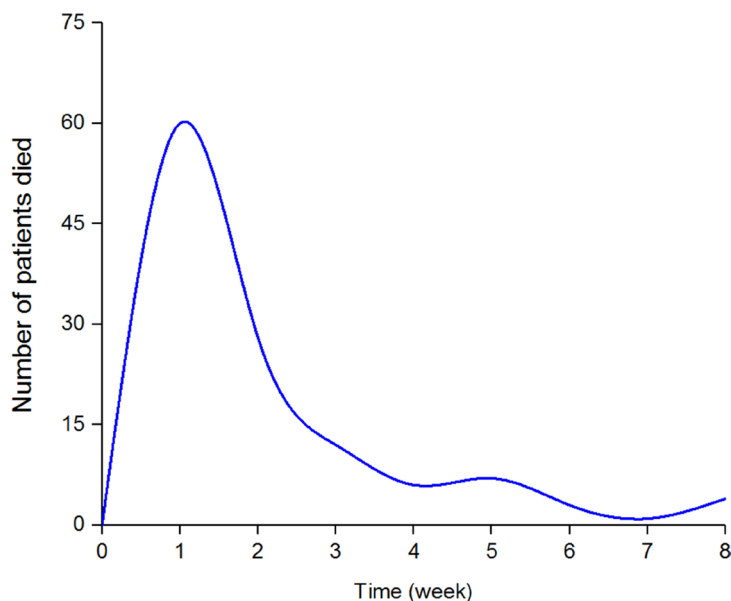
<sup>2</sup>Liverpool Pancreatitis Study Group, Royal Liverpool University Hospital and Institute of Translational Medicine, University of Liverpool, Liverpool, UK

<sup>3</sup>Department of Gastroenterology and Hepatology, University Hospital of Santiago de Compostela, Spain

<sup>4</sup>West China Biomedical Big Data Centre, West China Hospital, Sichuan University, Chengdu, China

<sup>5</sup>Department of Pancreatic Surgery, West China Hospital, Sichuan University, Chengdu, China

<sup>6</sup>Institute of Digestive Surgery, West China Hospital, Sichuan University, Chengdu, China



**Figure 1** Pattern of mortality over time in patients with acute pancreatitis, showing the number of patients who died on a weekly basis for a total of 123 deceased out of 3084 patients.

<sup>7</sup>Pancreatitis Centre, Division of Gastroenterology, Johns Hopkins Medical Institutions, Baltimore, USA  
<sup>8</sup>Surgical and Translational Research Centre, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand

**Correspondence to** Dr Wei Huang, Department of Integrated Traditional Chinese and Western Medicine, Sichuan Provincial Pancreatitis Centre and West China-Liverpool Biomedical Research Centre, West China Hospital, Sichuan University, 5B Floor 2nd Building, Tianfu Life Science Park of Hi-Tech Industrial Development Zone, No 88 Keyuan South Road, Chengdu 610041, China; dr\_wei\_huang@scu.edu.cn and Dr Qing Xia, Department of Integrated Traditional Chinese and Western Medicine, West China Hospital, Sichuan University, No 37 Wannan Guoxue Alley, Chengdu 610041, China; xiaqing@medmail.com.cn

**Acknowledgements** The authors thank all the members of the pancreas multidisciplinary teams in West China Hospital, Royal Liverpool University Hospital and University Hospital of Santiago de Compostela.

**Contributors** NS and TL are co-first authors. RS, QX, WH and JAW conceived, designed and supervised the study, and obtained funding. NS, TL, DdII-G, TJ, LD, LL, PZ, WH, ZZ and JED-M acquired, analysed and interpreted the data. NS, TL and WH wrote the paper. RS, QX, JAW and VKS undertook critical revision of the manuscript for important intellectual content.

**Funding** This work was supported by the NZ-China Strategic Research Alliance 2016 Award (China: 2016YFE0101800, QX, TJ, WH and LD; New Zealand: JAW); Key Technology R&D Programme of Sichuan Provincial Department of Science and Technology (2015SZ0229, LD and XQ); National Science Foundation of China (No. 81703911, TJ; No. 81774120, QX, WH, TL and TJ); Biomedical Research Centre and Biomedical Research Unit Funding Scheme of the National Institute for Health Research (TL, WH and RS); and National Institute for Health Research Senior Investigator Award (RS).

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Ethics approval** Liverpool Acute Pancreatitis Research Biobank was approved by the UK Health Research Authority (reference: 15/YH/0193).

**Provenance and peer review** Not commissioned; internally peer reviewed.

**Data sharing statement** Upon publication raw data from individual studies may be requested from the corresponding author to interested researchers requesting data for bona fide scientific purposes.



## OPEN ACCESS

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

© Author(s) (or their employer(s)) 2020. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/gutjnl-2019-318241>).

NS and TL contributed equally.



**To cite** Shi N, Liu T, de la Iglesia-Garcia D, *et al.* *Gut* 2020;**69**:604–605.

Received 8 January 2019

Revised 18 January 2019

Accepted 22 January 2019

Published Online First 11 February 2019

*Gut* 2020;**69**:604–605. doi:10.1136/gutjnl-2019-318241

### ORCID iDs

Wei Huang <http://orcid.org/0000-0001-8659-322X>

Robert Sutton <http://orcid.org/0000-0001-6600-562X>

## REFERENCES

- 1 Schepers NJ, Bakker OJ, Besselink MG, *et al.* Dutch Pancreatitis Study Group. Impact of characteristics of organ failure and infected necrosis on mortality in necrotising pancreatitis. *Gut* 2019;**68**:1044–51.
- 2 Banks PA, Bollen TL, Dervenis C, *et al.* Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013;**62**:102–11.
- 3 Johnson CD, Abu-Hilal M. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. *Gut* 2004;**53**:1340–4.
- 4 Sharma M, Banerjee D, Garg PK. Characterization of newer subgroups of fulminant and subfulminant pancreatitis associated with a high early mortality. *Am J Gastroenterol* 2007;**102**:2688–95.
- 5 Lytras D, Manes K, Triantopoulou C, *et al.* Persistent early organ failure: defining the high-risk group of patients with severe acute pancreatitis? *Pancreas* 2008;**36**:249–54.
- 6 Thandassery RB, Yadav TD, Dutta U, *et al.* Dynamic nature of organ failure in severe acute pancreatitis: the impact of persistent and deteriorating organ failure. *HPB* 2013;**15**:523–8.
- 7 Petrov MS, Shanbhag S, Chakraborty M, *et al.* Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. *Gastroenterology* 2010;**139**:813–20.
- 8 Guo Q, Li A, Xia Q, *et al.* The role of organ failure and infection in necrotizing pancreatitis: a prospective study. *Ann Surg* 2014;**259**:1201–7.
- 9 Jin T, Jiang K, Deng L, *et al.* Response and outcome from fluid resuscitation in acute pancreatitis: a prospective cohort study. *HPB* 2018;**20**:1082–91.
- 10 Wen L, Voronina S, Javed MA, *et al.* Inhibitors of ORAI1 Prevent Cytosolic Calcium-Associated Injury of Human Pancreatic Acinar Cells and Acute Pancreatitis in 3 Mouse Models. *Gastroenterology* 2015;**149**:481–92.