Pre-existing Diabetes Elevates Risk of Local and Systemic Complications in Acute Pancreatitis Systematic Review and Meta-analysis

SUPPLEMENTAL DIGITAL CONTENT

SUPPLEMENTARY TABLE 1. Characteristics of Studies Evaluating Outcome Data of Acute Pancreatitis

Study	Mortality	Cardiovascular	Respiratory	Renal	Neurologic	Local	ICU Admission	Length of Hospitalization
Huh et al, 2016	√	—	—	—	—	√	√	√
Kikuta et al, 2015	√	√	√	√	—	—	—	—
Kumar et al. 2015	—	—	—	√	—	—	—	—
Méndez-Bailón et al, 2015	√	—	—	—	—	—	—	√
Mole et al, 2016	—	—	—	—	—	—	√	—
Nawaz et al, 2015	√	√	√	√	—	—	—	√
Shen et al, 2012a	√	√	√	√	√	√	√	√
Shen et al, 2012b	—	—	—	—	—	√	—	—
Zhao et al, 2012	√	—	—	—	—	—	—	√

ICU, indicates intensive care unit.

SUPPLEMENTARY TABLE 2. Modified Newcastle–Ottawa Scale Criteria

	Adapted Newcastle-Ottawa Scale Items	High-quality Items Carrying a Low Risk of Bias (Green)	Low-quality Items Carrying a High (Red) or an Unknown (Yellow) Risk of Bias
Selection	**Item 1:** Representativeness of the initial study population – AP with DM	All patients with acute pancreatitis and concomitant diabetes mellitus were included.	Low: any selection criteria were applied to the study population (e.g., inclusion of adults, those with severe AP). Unknown: no data on selection process.
	Item 2: Representativeness of the initial study population – AP without DM	All patients with acute pancreatitis and without concomitant diabetes mellitus were included.	Low: any selection criteria were applied to the study population (e.g., inclusion of adults, those with severe AP). Unknown: no data on selection process.
	Item 3: Diagnosis of AP and DM	AP patients met minimum two out of three of the following criteria: elevation of pancreatic enzymes (amylase and/or lipase) at least up to three times higher than the upper cut-off of the normal range, suffering from abdominal pain, inflammation detected with abdominal ultrasound scan and/or computed tomography. Standard definition of pre-existing diabetes mellitus was applied while the inclusion of newly diagnosed DM based on elevated HgbA1C is also acceptable.[42]	Low: definitions did not match the criteria listed in the high-quality column. Unknown: no definitions of the conditions mentioned are provided.
	Item 4: Demonstration that outcome of interest was not present at start of study	There were no pre-existing chronic heart failure, chronic renal failure and/or chronic obstructive pulmonary disease in the study population.	Low: patients with pre-existing heart failure, chronic renal failure and/or chronic obstructive pulmonary disease. Unknown: no statement.
Comparability	**Item 5:** Study controls for age	No significant difference was detected between diabetic and non-diabetic AP patients regarding age.	Low: significant difference was detected between diabetic and non-diabetic AP patients regarding age. Unknown: no comparison made by age.
	Item 6: Study control for body mass index	No significant difference was detected between diabetic and non-diabetic AP patients regarding body mass index [43].	Low: significant difference was detected between diabetic and non-diabetic AP patients regarding body mass index. Unknown: no comparison made by body mass index.
Outcome	**Item 7:** Adequacy of follow-up	Complete follow-up or incomplete follow-up with explanations revealing low risk of bias	Low: incomplete follow-up with explanations revealing high risk of bias Unknown: incomplete follow-up without explanation of the loss.

AP indicates acute pancreatitis; DM, diabetes mellitus.

SUPPLEMENTARY TABLE 3. Stars Based on the Modified Newcastle–Ottawa Scale

ARTICLE	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Total
Huh et al, 2016	-	-	*	-	*	-	*	3*
Kikuta et al, 2015	*	*	*	-	*	-	-	4*
Kumar et al, 2015	-	-	*	-	-	-	*	2*
Méndez-Bailón et al, 2015	-	-	-	-	*	-	*	2*
Mole et al, 2016	-	-	*	-	-	-	*	2*
Nawaz et al, 2015	-	-	-	-	-	-	*	1*
Shen et al, 2012a	-	-	-	*	*	-	*	3*
Shen et al, 2012b	-	-	-	-	-	-	*	1*
Zhao et al, 2012	*	*	*	*	-	-	*	5*

SUPPLEMENTARY TABLE 4. PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7

Section/topic	#	Checklist item	Reported on page #
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8-9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8-9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8-9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9; Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1. Supplementary Table 1.
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10-11, Supplementary Table 2-3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-11, Figure 2-5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-11, Figure 2-5
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	11, Supplementary Figure 1-2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11, Supplementary Figure 3-4

Section/topic	#	Checklist item	Reported on page #
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	2,14

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