Online Resource 1
Fatty Pancreas as a Marker of Tumor Dissemination in Pancreatic Cancer: A Systematic Review and Meta-analysis
Journal of Gastrointestinal Cancer

Contents

Table S1 Complete database-specific search strategies and retrieval counts

Search date: June 19, 2026. All databases were searched from inception. No language restriction was applied.

Database	Search string	Records
MEDLINE/PubMed	("Pancreatic Neoplasms"[Mesh] OR "pancreatic cancer"[tiab] OR "pancreatic neoplasm*"[tiab] OR "pancreatic ductal adenocarcinoma"[tiab] OR PDAC[tiab] OR "pancreatic adenocarcinoma"[tiab] OR "pancreas cancer"[tiab]) AND ("pancreatic steatosis"[tiab] OR "fatty pancreas"[tiab] OR "fatty pancreatic"[tiab] OR "pancreatic fat"[tiab] OR "pancreatic fatty infiltration"[tiab] OR "fatty infiltration"[tiab] OR "intrapancreatic fat"[tiab] OR "intrapancreatic fat deposition"[tiab] OR IPFD[tiab] OR NAFPD[tiab] OR "non-alcoholic fatty pancreas disease"[tiab] OR "nonalcoholic fatty pancreas disease"[tiab] OR "pancreatic lipomatosis"[tiab] OR "pancreatic adiposity"[tiab] OR "pancreatic attenuation"[tiab] OR "pancreatic fat fraction"[tiab] OR "hyperechoic pancreas"[tiab])	209
Embase	('pancreas cancer'/exp OR 'pancreatic neoplasm'/exp OR 'pancreatic ductal adenocarcinoma'/exp OR 'pancreatic cancer':ti,ab,kw OR 'pancreatic neoplasm*':ti,ab,kw OR 'pancreatic ductal adenocarcinoma':ti,ab,kw OR PDAC:ti,ab,kw OR 'pancreatic adenocarcinoma':ti,ab,kw OR 'pancreas cancer':ti,ab,kw) AND ('pancreatic steatosis':ti,ab,kw OR 'fatty pancreas':ti,ab,kw OR 'fatty pancreatic':ti,ab,kw OR 'pancreatic fat':ti,ab,kw OR 'pancreatic fatty infiltration':ti,ab,kw OR 'fatty infiltration':ti,ab,kw OR 'intrapancreatic fat':ti,ab,kw OR 'intrapancreatic fat deposition':ti,ab,kw OR IPFD:ti,ab,kw OR NAFPD:ti,ab,kw OR 'non-alcoholic fatty pancreas disease':ti,ab,kw OR 'nonalcoholic fatty pancreas disease':ti,ab,kw OR 'pancreatic lipomatosis':ti,ab,kw OR 'pancreatic adiposity':ti,ab,kw OR 'pancreatic attenuation':ti,ab,kw OR 'pancreatic fat fraction':ti,ab,kw OR 'hyperechoic pancreas':ti,ab,kw)	416
Scopus	TITLE-ABS-KEY("pancreatic cancer" OR "pancreatic neoplasm*" OR "pancreatic ductal adenocarcinoma" OR PDAC OR "pancreatic adenocarcinoma" OR "pancreas cancer") AND TITLE-ABS-KEY("pancreatic steatosis" OR "fatty pancreas" OR "fatty pancreatic" OR "pancreatic fat" OR "pancreatic fatty infiltration" OR "fatty infiltration" OR "intrapancreatic fat" OR "intrapancreatic fat deposition" OR IPFD OR NAFPD OR "non-alcoholic fatty pancreas disease" OR "nonalcoholic fatty pancreas disease" OR "pancreatic lipomatosis" OR "pancreatic adiposity" OR "pancreatic attenuation" OR "pancreatic fat fraction" OR "hyperechoic pancreas")	265
Web of Science Core Collection	TS=("pancreatic cancer" OR "pancreatic neoplasm*" OR "pancreatic ductal adenocarcinoma" OR PDAC OR "pancreatic adenocarcinoma" OR "pancreas cancer") AND TS=("pancreatic steatosis" OR "fatty pancreas" OR "fatty pancreatic" OR "pancreatic fat" OR "pancreatic fatty infiltration" OR "fatty infiltration" OR "intrapancreatic fat" OR "intrapancreatic fat deposition" OR IPFD OR NAFPD OR "non-alcoholic fatty pancreas disease" OR "nonalcoholic fatty pancreas disease" OR "pancreatic lipomatosis" OR "pancreatic adiposity" OR "pancreatic attenuation" OR "pancreatic fat fraction" OR "hyperechoic pancreas")	334
Cochrane Library	#1 MeSH descriptor [Pancreatic Neoplasms] explode all trees; #2 ("pancreatic cancer" OR "pancreatic neoplasm*" OR "pancreatic ductal adenocarcinoma" OR PDAC OR "pancreatic adenocarcinoma" OR "pancreas cancer"):ti,ab,kw; #3 ("pancreatic steatosis" OR "fatty pancreas" OR "pancreatic fat" OR "intrapancreatic fat" OR "intrapancreatic fat deposition" OR IPFD OR NAFPD OR "pancreatic lipomatosis" OR "pancreatic attenuation" OR "pancreatic fat fraction" OR "hyperechoic pancreas"):ti,ab,kw; #4 (survival OR mortality OR prognosis OR recurrence OR metastasis OR "lymph node" OR stage):ti,ab,kw; #5 (#1 OR #2) AND #3; #6 (#1 OR #2) AND #3 AND #4	3
Total records identified		1,227
Duplicate records removed		675
Records screened after removal of duplicates		552

Outcome terms were not required in MEDLINE/PubMed, Embase, Scopus or Web of Science because preliminary testing showed that incorporating prognosis, survival, metastasis or lymph-node terminology reduced retrieval sensitivity. In the Cochrane Library, both a broad disease–exposure set (#5) and a supplementary outcome-focused set (#6) were run. Reference lists of included studies and of relevant reviews were hand-searched. IPFD, intrapancreatic fat deposition; NAFPD, non-alcoholic fatty pancreas disease; PDAC, pancreatic ductal adenocarcinoma

Table S2 Reports excluded at full text, with reasons.

No.	Report	Author, year	Reason for exclusion
1	An imaging biomarker for prediction of malignancy in pancreas: CT-based pancreas composition analysis	Kim et al. 2026	Conference abstract
2	Clinical, oncological and metabolic effects of pancreatic mass loss after pancreatectomy in patients with preoperative diabetes	Registry record, 2026	Registry or protocol record without extractable results
3	Excessive intrapancreatic fat deposition: a missing metabolic driver of pancreatic carcinogenesis in type 2 diabetes?	Souza et al. 2026	Commentary or narrative review
4	Significant intrapancreatic fat deposition as an independent prognostic factor in high-grade pancreatic neuroendocrine neoplasms	Gao et al. 2026	Pancreatic neuroendocrine population
5	Fatty pancreas correlates with larger cyst size and worrisome features in presumed IPMN and MCN	Tang et al. 2025	Conference abstract
6	Fatty pancreas on EUS: risk factors, correlation with CT/MRI, and implications for pancreatic cancer screening	Ibrahim et al. 2025	Cancer risk or screening outcome only
7	Clinicopathological features and prognosis of patients with pancreatic cancer complicated with NAFPD	Dong et al. 2024	Conference abstract
8	Identification of SMAD4-mutated PDAC using preoperative contrast-enhanced MRI and clinical characteristics	Li et al. 2024	Exposure not pancreatic steatosis
9	Intra-pancreatic fat promotes the progression of PDAC by activating thermogenesis	Yin et al. 2024	Conference abstract
10	Non-alcoholic fatty pancreas disease outcomes: not as benign as it seems	Chatterjee et al. 2024	Conference abstract
11	Characteristics of FABP4 expression in pancreatic cancer and correlation with clinicopathological features and prognosis	Liu et al. 2024	Exposure not pancreatic steatosis
12	Pancreatic steatosis and post-operative pancreatic fistula after pancreatectomy	Cortes et al. 2025	Mixed pancreatectomy cohort; PDAC data not separable
13	The emerging issue: pancreatic steatosis prevalence in pancreatic cystic neoplasms and adenocarcinoma	Single-center report, 2024	Commentary or narrative review
14	Pancreatic steatosis and correlation with clinicopathological features in pancreatic neuroendocrine neoplasms	Li et al. 2023	Pancreatic neuroendocrine population
15	Estimating fatty pancreas: a preoperative bedside assessment by bioelectric impedance analysis	Angrisani et al. 2022	Postoperative outcomes only
16	The thermogenic activity of intra-pancreatic fat fuels the progression of pancreatic cancer	Yin et al. 2022	Conference abstract
17	Impact of abdominal composition CT profile on postoperative complications after curative resection for pancreatic cancer	Belyaev et al. 2019	Postoperative outcomes only
18	Prognostic importance of quantitative MRI for evaluation of pancreatic steatosis in patients with pancreatic cancer	Registry record, 2015	Registry or protocol record without extractable results
19	Adipocytes in the pancreatic tumor microenvironment promote dissemination of human pancreatic cancer	White et al. 2010	Conference abstract

The individual full-text exclusion reasons are reported in Table S2. Figure 1 summarizes these exclusions using broader grouped categories. CT, computed tomography; EUS, endoscopic ultrasound; IPMN, intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm; MRI, magnetic resonance imaging; NAFPD, non-alcoholic fatty pancreas disease; PDAC, pancreatic ductal adenocarcinoma

Table S3 QUIPS domain-level risk-of-bias judgements

Study	Study participation	Study attrition	Prognostic-factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Overall
Dong et al. 2025	Moderate	High	Moderate	Low	High	High	High
Fukuda et al. 2025	Low	Low	Moderate	Low	Moderate	Moderate	Moderate
Chan et al. 2024	Moderate	Moderate	Moderate	Moderate	High	Moderate	High
Tróchez-Mejía et al. 2019	High	Low	Moderate	Moderate	High	High	High
Mathur et al. 2011	Moderate	Low	Moderate	Low	High	Moderate	High
Mathur et al. 2009	Moderate	Low	Low	Low	Moderate	Moderate	Moderate

Judgements reflect the risk that each domain could bias the association between fatty pancreas and the review outcomes. Overall judgements were not computed as a sum of domains; studies at high risk in confounding, prognostic-factor measurement, attrition for survival outcomes, or statistical analysis and reporting were generally rated high overall. Attrition was rated high for Dong et al. because follow-up data were available for 80 of 116 patients and the group sizes reported for the survival analysis could not be reconciled with those of the main cohort. The threshold applied by Fukuda et al. was derived by receiver operating characteristic analysis within the study and is described as a ROC-derived study threshold. QUIPS, Quality In Prognosis Studies; ROC, receiver operating characteristic

Table S4 GRADE certainty assessment of the two pooled outcomes
Population: adults with established pancreatic cancer, prioritizing histologically confirmed pancreatic ductal adenocarcinoma.
Exposure: fatty pancreas, pancreatic steatosis or intrapancreatic fat deposition.
Comparator: no fatty pancreas or a lower pancreatic-fat category according to each study definition.
Study design: observational prognostic studies.

Panel A Summary of findings

Outcome	Patients (studies)	Assumed risk without fatty pancreas	Corresponding risk with fatty pancreas	Relative effect (95% CI)	Certainty
Lymph node metastasis or nodal positivity	275 (four studies)	478 per 1,000[a]	607 per 1,000 (492 to 750)[b]	RR 1.27 (1.03–1.57)	Very low[c],[d]
Overall survival or all-cause mortality	268 (three studies)	Not estimable from the pooled data[e]	Not estimable[e]	HR 1.23 (0.64–2.38)	Very low[c],[d]

[a]The assumed risk was estimated from the pooled comparator arms of the four contributing studies (76/159 = 478 per 1,000). [b]Corresponding risks were obtained by applying the pooled risk ratio and its 95% confidence limits, as reported to two decimal places, to the assumed risk. [c]Observational prognostic studies start at low certainty in GRADE; no criterion for rating up was met. [d]Normal-approximation prediction intervals were 1.01–1.59 for nodal positivity and 0.37–4.07 for overall survival; they are exploratory descriptors and were not used as evidence of robustness. [e]Absolute effects were not estimated for overall survival because baseline hazards, follow-up duration and survival reporting varied across studies. CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HR, hazard ratio; RR, risk ratio

Panel B Certainty domains and reasons for rating down

Outcome	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty
Lymph node metastasis or nodal positivity	Serious	Not serious	Not serious	Serious	Not assessed	Very low
Overall survival or all-cause mortality	Serious	Very serious	Not serious	Very serious	Not assessed	Very low

Risk of bias was rated down because QUIPS identified moderate-to-high or high overall risk of bias in most contributing studies, chiefly from residual confounding, heterogeneous measurement of fatty pancreas, small samples and incomplete adjusted reporting. Inconsistency was not rated down for nodal positivity because statistical heterogeneity was low, although important clinical and measurement heterogeneity remained; overall survival was rated down as very serious because I^2 was 77%, individual estimates pointed in opposite directions, and the pooled direction depended on whether the single adjusted estimate was included. Indirectness was not rated down because population, exposure, comparator and outcomes matched the review question; measurement heterogeneity was handled under risk of bias. Imprecision was rated down for nodal positivity because the lower confidence bound lay close to the null, few small studies contributed, and statistical significance was lost in three of four leave-one-out analyses; it was rated down as very serious for overall survival because the confidence interval was compatible with both appreciable benefit and appreciable harm. Publication bias was not formally assessed because fewer than 10 studies contributed to either outcome; not assessed does not imply absence of bias, and this domain was not used as a basis for rating down. GRADE, Grading of Recommendations Assessment, Development and Evaluation; QUIPS, Quality In Prognosis Studies

Table S5 PRISMA 2020 checklist

Section/topic	Item	Checklist item	Location in manuscript
Title	1	Identify the report as a systematic review.	Title, p. 1
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract, pp. 1–2
Introduction	3	Describe the rationale for the review in the context of existing knowledge.	Introduction, pp. 2–3, paragraphs 1–4
Introduction	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction, p. 3, final paragraph
Methods	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods: Eligibility criteria, pp. 3–4; Exposure and outcome definitions, pp. 4–5
Methods	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies.	Methods: Search strategy, p. 3; Online Resource 1, Table S1
Methods	7	Present the full search strategies for all databases and registers, including any filters applied.	Online Resource 1, Table S1
Methods	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and title/abstract, how they were calibrated, and any automation tools used.	Methods: Study selection and data extraction, p. 4
Methods	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they were calibrated, any processes for obtaining or confirming data from study investigators, and if applicable any automation tools used.	Methods: Study selection and data extraction, p. 4
Methods	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought.	Methods: Exposure and outcome definitions, pp. 4–5; Online Resource 1, Table S8
Methods	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources).	Methods: Study selection and data extraction, p. 4; Tables 1–2, pp. 9–10; Online Resource 1, Table S7
Methods	11a	Specify the statistical methods used to synthesise results, and if meta-analysis was done, the rationale for the chosen model(s) and method(s).	Methods: Statistical analysis, pp. 5–6
Methods	11b	If quantitative synthesis was performed, specify any methods used to explore possible causes of heterogeneity (e.g. subgroup analysis, meta-regression).	Methods: Statistical analysis, p. 6; Online Resource 1, Table S9
Methods	11c	Specify any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Methods: Statistical analysis, p. 6 (not assessed because fewer than 10 studies contributed)
Methods	11d	Specify any additional analyses (e.g. sensitivity or subgroup analyses, meta-regression) which were planned before or after the review was conducted.	Methods: Statistical analysis, p. 6; Online Resource 1, Table S9
Methods	12	Specify the methods used to assess risk of bias in the included studies.	Methods: Risk-of-bias assessment, p. 5; Online Resource 1, Table S3; Supplementary Figs. S1a–S1b
Methods	13	Describe the methods of certainty assessment, if any.	Methods: Certainty of evidence, p. 6; Online Resource 1, Table S4
Results	14	Describe the results of the search and selection process, including reasons for exclusions from full-text screening, ideally using a flow diagram.	Results: Study selection, pp. 6–7; Fig. 1, p. 7; Online Resource 1, Table S2
Results	15a	Cite each included study and present its characteristics.	Results: Study characteristics, pp. 8–10; Tables 1–2, pp. 9–10; references 20–25
Results	15b	Cite each excluded study that may appear to meet the inclusion criteria, and explain why it was excluded.	Online Resource 1, Table S2
Results	16	Present assessments of risk of bias for each included study.	Results: Risk of bias, p. 11; Online Resource 1, Table S3; Supplementary Figs. S1a–S1b

Results	17	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision.	Results: Lymph node metastasis, pp. 11–12; Overall survival, pp. 12–13; Figs. 2–3; Table 2; Online Resource 1, Table S8
Results	18	For each synthesis, present the results of each synthesis carried out, including confidence/credible intervals, measures of statistical heterogeneity, and, if applicable, overall certainty of evidence.	Results, pp. 11–13; Figs. 2–3; Online Resource 1, Tables S4 and S9
Results	19	Present results of all investigations of possible causes of heterogeneity among study results.	Results: subgroup analyses, p. 12; Overall survival, pp. 12–13; Online Resource 1, Table S9
Results	20	Present results of all sensitivity analyses conducted to assess the robustness of the synthesised results.	Results: Lymph node metastasis, pp. 11–12; Overall survival, pp. 12–13; Online Resource 1, Table S9
Results	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Methods: Statistical analysis, p. 6; Results: Certainty of evidence, p. 13; Online Resource 1, Table S4 (not assessed)
Results	22	Present results of additional analyses, if any (e.g. sensitivity or subgroup analyses, meta-regression).	Results, pp. 12–13; Online Resource 1, Table S9
Discussion	23	Provide a general interpretation of the results in the context of other evidence.	Discussion, pp. 14–16
Discussion	24	Discuss any limitations of the evidence included in the review.	Discussion, pp. 14–16
Discussion	25	Provide an overall interpretation of the results and implications for practice, policy, and future research.	Discussion, pp. 15–16; Conclusion, p. 16
Other Information	26a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Methods: Protocol and reporting, p. 3 (PROSPERO CRD420261445124)
Other Information	26b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Methods: Protocol and reporting, p. 3; PROSPERO record CRD420261445124
Other Information	26c	Describe and explain any amendments to information provided at registration or in the protocol.	Not reported in the manuscript
Other Information	27	Describe sources of funding or other support (e.g. supply of data); role of funders in review.	Statements and Declarations: Funding, p. 18

From: Page MJ et al. The PRISMA 2020 statement. BMJ. 2021;372:n71. doi:10.1136/bmj.n71

Table S6 MOOSE checklist

Section	Item	Recommendation	Location in the manuscript
Background	1	Problem definition	Introduction, paragraphs 1–3
Background	2	Hypothesis statement	Introduction, paragraphs 3–5; Abstract
Background	3	Description of study outcomes	Methods, Exposure and outcome definitions; Table S8
Background	4	Type of exposure used	Methods, Exposure and outcome definitions; Table 2
Background	5	Type of study designs used	Methods, Eligibility criteria
Background	6	Study population	Methods, Eligibility criteria; Table 1
Search	7	Qualifications of searchers	Methods, Study selection and data extraction (two reviewers, independent and in duplicate)
Search	8	Search strategy, time period and keywords	Methods, Search strategy; Table S1
Search	9	Effort to include all available studies	Methods, Search strategy (no language restriction; hand-searching of reference lists)
Search	10	Databases and registries searched	Methods, Search strategy; Table S1
Search	11	Search software used, name and version, including special features	Searches were run in the native database interfaces. Records were exported, deduplicated, and screened using a structured electronic review workflow (Methods, Study selection and data extraction)
Search	12	Use of hand searching	Methods, Search strategy
Search	13	List of citations located and those excluded, with justification	Table S2
Search	14	Method of addressing articles published in languages other than English	Methods, Search strategy and Eligibility criteria (no language restriction); one Chinese-language article was translated and checked against the original (Methods, Use of AI-assisted translation tools)
Search	15	Method of handling abstracts and unpublished studies	Methods, Eligibility criteria; Table S2 (conference abstracts and registry records excluded)
Search	16	Description of any contact with authors	No contact with authors was required; all extracted data were available in the published reports
Methods	17	Description of relevance or appropriateness of studies assembled	Methods, Eligibility criteria; Results, Study characteristics
Methods	18	Rationale for the selection and coding of data	Methods, Study selection and data extraction; Exposure and outcome definitions
Methods	19	Documentation of how data were classified and coded	Methods, Study selection and data extraction (independent duplicate extraction, third-reviewer adjudication)
Methods	20	Assessment of confounding	Methods, Risk-of-bias assessment; Table S7; Discussion
Methods	21	Assessment of study quality	Methods, Risk-of-bias assessment; Table S3; Supplementary Figs. S1a, S1b
Methods	22	Assessment of heterogeneity	Methods, Statistical analysis (Cochran Q, τ^2, I^2, normal-approximation prediction intervals); Results
Methods	23	Description of statistical methods in sufficient detail to be replicated	Methods, Statistical analysis; Supplementary Note 1
Methods	24	Provision of appropriate tables and graphics	Tables 1 and 2; Figs. 1–3; Tables S1–S9; Supplementary Figs. S1a, S1b
Results	25	Graph summarising individual study estimates and the overall estimate	Figs. 2 and 3

Section	Item	Recommendation	Location in the manuscript
Results	26	Table giving descriptive information for each study	Tables 1 and 2; Table S7
Results	27	Results of sensitivity testing	Results, Lymph node metastasis and Overall survival; Table S9 (fixed-effect, leave-one-out, exclusion of the reconstructed estimate, subgroup analyses)
Results	28	Indication of statistical uncertainty of findings	Figs. 2 and 3 (confidence and prediction intervals); Table S9
Discussion	29	Quantitative assessment of bias	Formal assessment of small-study effects was not performed because fewer than 10 studies contributed to any outcome (Methods, Statistical analysis; Table S4). Sensitivity and subgroup analyses were performed and are reported in Table S9
Discussion	30	Justification for exclusion	Methods, Eligibility criteria; Table S2
Discussion	31	Assessment of quality of included studies	Results, Risk of bias; Table S3
Conclusions	32	Consideration of alternative explanations for observed results	Discussion (reverse causation and residual confounding)
Conclusions	33	Generalisation of the conclusions	Discussion; Conclusion
Conclusions	34	Guidelines for future research	Discussion, final paragraph
Conclusions	35	Disclosure of funding source	Statements and Declarations, Funding; Title page

Table S7 Contribution matrix, analytic sample sizes and covariate adjustment

Study	Total cohort, N	Qualitative synthesis	Nodal meta-analysis (patients)	Survival meta-analysis (patients)	Narrative or exploratory contribution	Covariates adjusted for
Dong et al. 2025	116	Yes	Yes (n = 116)	Yes (n = 80 with follow-up)	T stage, N stage, lymphovascular invasion, perineural invasion, differentiation, CA19-9, tumor location, lipid profile	None (crude event counts and unadjusted Cox model)
Fukuda et al. 2025	87	Yes	Yes (n = 87)	Yes (n = 87)	Recurrence-free survival, T stage, lymphatic, vascular and neural invasion, differentiation, CA19-9, R status, postoperative pancreatic fistula	CA19-9, T stage, nodal status, lymphatic invasion, adjuvant chemotherapy (survival only)
Chan et al. 2024	101	Yes	No	Yes (n = 101)	Stage, chronic pancreatitis, hepatic steatosis, surgery, death	None for the extracted estimate (univariable Cox)
Tróchez-Mejía et al. 2019	30	Yes	Yes (n = 30)	No	Clinical stage, distant metastasis, tumor size, resectability, palliative chemotherapy, Karnofsky score, diabetes	None (crude event counts)
Mathur et al. 2011	42	Yes	Yes (n = 42)	No	Visceral (perirenal) fat, hepatic attenuation, survival by visceral-adiposity stratum	None (crude event counts)
Mathur et al. 2009	40	Yes	No	No	Pancreatic fat-cell count and fibrosis score by nodal status, mean survival	Matched for age, sex, body mass index, comorbidity, tumor size and resection status

N denotes the number of patients enrolled; n denotes the analytic sample contributing to each pooled estimate. The two differ only for Dong et al. 2025, in which 80 of 116 patients had follow-up data available for the survival analysis. Totals contributing to synthesis: nodal meta-analysis, 275 patients from four studies; survival meta-analysis, 268 patients from three studies; qualitative synthesis, 416 patients from six studies. CA19-9, carbohydrate antigen 19-9

Table S8 Complete accounting of all outcomes evaluated in the review

Outcome domain	Specific outcome	Reported by	Synthesis status	Reason not pooled
Dissemination	Lymph node metastasis or nodal positivity	Dong 2025; Fukuda 2025; Tróchez-Mejía 2019; Mathur 2011	Meta-analyzed (primary outcome)	Not applicable
Dissemination	Distant metastasis	Tróchez-Mejía 2019	Narrative (10/12 vs 5/18, P = 0.004)	Reported by one study only
Dissemination	Advanced clinical stage	Tróchez-Mejía 2019; Chan 2024	Narrative	Stage categories and thresholds not comparable across studies
Survival	Overall survival or all-cause mortality	Dong 2025; Fukuda 2025; Chan 2024	Meta-analyzed (secondary outcome)	Not applicable
Survival	Recurrence-free or progression-free survival	Fukuda 2025	Narrative	Reported by one study only
Recurrence	Any, local, distant, hepatic or peritoneal recurrence; time to recurrence	None	Not estimable	Not reported by any included study
Tumor biology	T stage	Dong 2025; Fukuda 2025	Narrative	Different categorisations (T3 vs T1–2 and T3–4 vs T1–2)
Tumor biology	Tumor size	Tróchez-Mejía 2019; Mathur 2009	Narrative	Continuous data reported without dispersion by exposure group
Tumor biology	Tumor location	Dong 2025	Narrative	Reported by one study only
Tumor biology	Histological grade or poor differentiation	Dong 2025; Fukuda 2025	Narrative	Different grade groupings and denominators
Tumor biology	Lymphatic or lymphovascular invasion	Dong 2025; Fukuda 2025	Narrative	Lymphovascular tumor thrombus and ly0 vs ly1–3 are not equivalent definitions
Tumor biology	Vascular or venous invasion	Fukuda 2025	Narrative	Reported by one study only
Tumor biology	Perineural or neural invasion	Dong 2025; Fukuda 2025	Narrative	Different denominators owing to missing data
Tumor biology	CA19-9	Dong 2025; Fukuda 2025	Narrative	One study reported a dichotomised threshold and the other a median with range
Surgical	R0 versus R1 or R2 resection	Fukuda 2025	Narrative	Reported for the whole cohort, not by exposure group
Surgical	Clinically relevant postoperative pancreatic fistula	Fukuda 2025	Narrative	Reported by one study only
Surgical	Major postoperative morbidity	Fukuda 2025	Narrative	Reported by one study only
Surgical	30-day and 90-day mortality, length of stay, readmission	None	Not estimable	Not reported by any included study
Treatment	Palliative or first-line chemotherapy assignment	Tróchez-Mejía 2019	Narrative	Reported by one study only
Treatment	Neoadjuvant or adjuvant chemotherapy exposure	Fukuda 2025	Narrative	Reported as a covariate rather than as an outcome by exposure group
Treatment	Pathological response, downstaging, conversion to resectability, RECIST response, grade 3–4 toxicity	None	Not estimable	Not reported by any included study

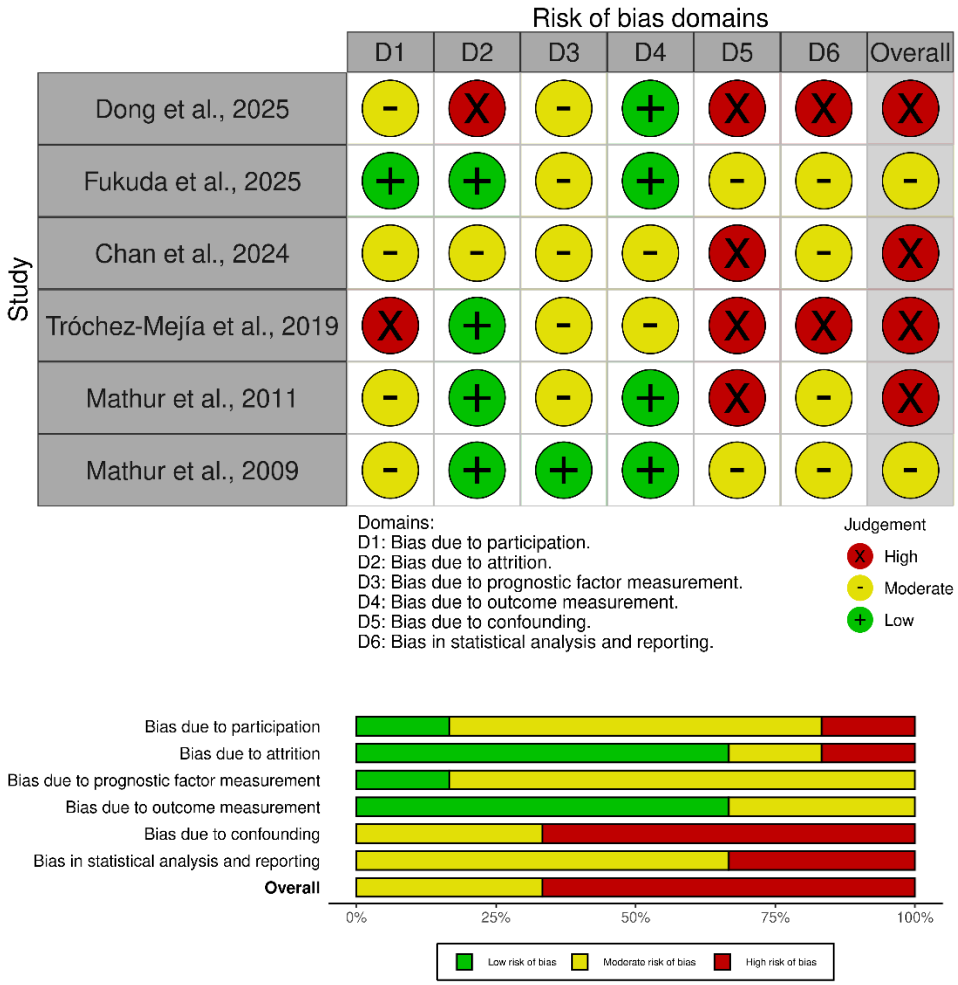
Every outcome evaluated in the review is listed, including those not reported by any included study, which are recorded as not estimable rather than omitted. No outcome was dropped from reporting.
CA19-9, carbohydrate antigen 19-9; RECIST, Response Evaluation Criteria in Solid Tumours

Table S9 Sensitivity and subgroup analyses

Analysis	Studies (patients)	Pooled estimate (95% CI)	P value	I^2	τ^2	Interpretation
Nodal positivity: main random-effects model (REML)	Four (275)	RR 1.27 (1.03–1.57)	0.03	3%	0.00	Reference analysis; normal-approximation prediction interval 1.01–1.59
Nodal positivity: fixed-effect model	Four (275)	RR 1.27 (1.03–1.56)	0.02	–	–	Essentially unchanged
Nodal positivity: omitting Dong et al. 2025	Three (159)	RR 1.37 (1.09–1.74)	0.007	0%	0.00	Significance retained and strengthened
Nodal positivity: omitting Fukuda et al. 2025	Three (188)	RR 1.30 (0.94–1.79)	0.11	36%	0.03	Significance lost
Nodal positivity: omitting Mathur et al. 2011	Three (233)	RR 1.22 (0.95–1.55)	0.12	16%	0.01	Significance lost
Nodal positivity: omitting Tróchez-Mejía et al. 2019	Three (245)	RR 1.17 (0.90–1.52)	0.24	0%	0.00	Significance lost; largest single-study influence
Nodal positivity: pathological nodal ascertainment only	Three (245)	RR 1.17 (0.90–1.52)	0.24	0%	0.00	Same three studies as the resected-cohort analysis
Nodal positivity: clinical or endosonographic ascertainment	One (30)	RR 1.46 (1.04–2.06)	0.03	–	–	Single study; not pooled
Nodal positivity: imaging-defined fatty pancreas	Three (188)	RR 1.30 (0.94–1.79)	0.11	36%	0.03	Not significant
Nodal positivity: histology-defined fatty pancreas	One (87)	RR 1.19 (0.81–1.73)	0.37	–	–	Single study; not pooled
Nodal positivity: CT-defined fatty pancreas only	Two (158)	RR 1.20 (0.69–2.10)	0.52	56%	0.09	Not significant
Overall survival: main random-effects model (REML)	Three (268)	HR 1.23 (0.64–2.38)	0.53	77%	0.26	Reference analysis; normal-approximation prediction interval 0.37–4.07
Overall survival: fixed-effect model	Three (268)	HR 1.24 (0.91–1.69)	0.18	–	–	Remains non-significant
Overall survival: excluding the reconstructed estimate	Two (188)	HR 1.34 (0.46–3.91)	0.59	89%	0.53	Remains non-significant; heterogeneity increases
Overall survival: omitting Chan et al. 2024	Two (167)	HR 1.57 (0.71–3.48)	0.26	74%	0.24	Remains non-significant
Overall survival: omitting Fukuda et al. 2025	Two (181)	HR 0.87 (0.59–1.29)	0.49	0%	0.00	Direction reverses; remains non-significant
Overall survival: unadjusted estimates only	Two (181)	HR 0.87 (0.59–1.29)	0.49	0%	0.00	Same two studies as the analysis omitting Fukuda et al.
Overall survival: adjusted estimate only	One (87)	HR 2.32 (1.38–3.91)	0.0015	–	–	Single study; not pooled

All analyses used inverse-variance weighting with Wald-type confidence intervals; between-study variance was estimated by restricted maximum likelihood in random-effects analyses. Tests for subgroup differences: pathological versus clinical or endosonographic nodal ascertainment, $\chi^2 = 1.04$, $df = 1$, $P = 0.31$; imaging- versus histology-defined fatty pancreas, $\chi^2 = 0.13$, $df = 1$, $P = 0.72$; adjusted versus unadjusted survival estimates, $\chi^2 = 8.72$, $df = 1$, $P = 0.003$. With one to three studies per subgroup these tests have very low power and a non-significant result does not demonstrate equivalence. An independent restriction based solely on measurement in non-tumoral parenchyma was not feasible because anatomical measurement reporting and nodal-ascertainment categories overlapped. Heterogeneity statistics are not reported for fixed-effect models because between-study variance is constrained to zero under that model. Normal-approximation prediction intervals are exploratory descriptors and were interpreted cautiously because only three or four studies contributed to each synthesis. CI, confidence interval; CT, computed tomography; HR, hazard ratio; REML, restricted maximum likelihood; RR, risk ratio. I^2 was derived from the restricted maximum likelihood estimate of τ^2 relative to the typical within-study variance, as implemented in Review Manager 11.3.1, and therefore differs slightly from the value that would be obtained from Cochran Q alone.

Supplementary figure captions



Supplementary Fig. S1a Quality In Prognosis Studies domain-level risk-of-bias judgments for the six included studies
Supplementary Fig. S1b Distribution of Quality In Prognosis Studies risk-of-bias judgments across the six included studies
Panel A shows the domain-level judgment for each included study across the six QUIPS domains—study participation, study attrition, prognostic-factor measurement, outcome measurement, study confounding, and statistical analysis and reporting—together with the overall judgment. Panel B shows the distribution of judgments across studies for each domain. In Panel A, a plus sign denotes low risk, a minus sign denotes moderate risk, and an X denotes high risk. Colors correspond to low, moderate, and high risk. Percentages in Panel B are calculated across the six included studies. The two panels are provided as separate files and correspond to Table S3.

Supplementary Note 1 Reconstruction of one hazard ratio and rounding check

Dong et al. 2025 reported a hazard ratio for overall survival of 1.031 with a two-sided P value of 0.923 but did not report a confidence interval or standard error. The standard error was reconstructed using the relationships $\log(HR) = \ln(1.031) = 0.030529$; $Z = \Phi^{-1}(1 - P/2) = \Phi^{-1}(0.5385) = 0.096655$; and $SE = |\log(HR)|/Z = 0.030529/0.096655 = 0.315856$. The corresponding estimate is HR 1.03 (95% CI 0.56–1.91), obtained as $\exp(\log(HR) \pm 1.96 \times SE)$.

Because both inputs were reported to a limited number of digits, the derivation was repeated across a half-unit in the last reported digit of each input. Across this range the reconstructed standard error varied from 0.309 to 0.323 and the derived confidence interval from 0.55–1.89 to 0.55–1.94, so rounding did not materially affect the weight assigned to this study in the survival synthesis. The estimate is labelled as reconstructed throughout the manuscript and in Fig. 3, and was excluded in a sensitivity analysis (Table S9). Φ^{-1} denotes the inverse standard normal cumulative distribution function; CI, confidence interval; HR, hazard ratio; SE, standard error.