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REVIEW ARTICLE

Findings from the RAW Study: a narrative review of postoperative complications, patient factors, venous resection, and adjuvant treatment

Resultados del estudio RAW: revisión narrativa de complicaciones postoperatorias, características del paciente, resección venosa y tratamiento adyuvante

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Abstract

This review synthesizes the findings of the four studies derived from the Recurrence After Whipple's (RAW) project, which examine postoperative complications, patient-related factors, surgical technique, and access to adjuvant therapy after pancreatoduodenectomy. Published evidence from 2023 to 2025 was integrated into a conceptual framework aimed at identifying the key determinants of oncologic success. The studies show that grade C postoperative pancreatic fistula and post-pancreatectomy hemorrhage are the complications with the greatest impact on morbidity and mortality, whereas delayed gastric emptying has limited clinical relevance. Diabetes mellitus did not influence recurrence, survival, or the benefit of adjuvant therapy, in contrast to independent prognostic predictors such as positive margins, metastatic lymph nodes, tumor size greater than 3 cm, and elevated CA19-9 levels. Venous resection was shown to be safe and oncologically equivalent when performed in experienced centers. Major complications significantly decreased the likelihood of receiving adjuvant treatment, thereby worsening survival. Overall, the RAW project reframes clinical priorities in pancreatoduodenectomy, highlighting the prevention of critical complications, preservation of the therapeutic window for adjuvancy, and decision-making driven by tumor biology.

Keywords: *Pancreaticoduodenectomy. Postoperative complications. Pancreatic fistula. Adjuvant therapy. Venous surgical.*

Resumen

Este trabajo sintetiza y analiza los hallazgos de los cuatro estudios derivados del proyecto Recurrence After Whipple's (RAW), enfocados en complicaciones postoperatorias, factores del paciente, técnica quirúrgica y acceso a terapia adyuvante después de pancreatoduodenectomía. La revisión integró la evidencia publicada entre 2023 y 2025 dentro de un marco conceptual orientado a identificar los determinantes del éxito oncológico. Los estudios muestran que la fístula pancreática postoperatoria de grado C y la hemorragia pospancreatectomía representan las complicaciones de mayor impacto en morbilidad y mortalidad, mientras que el retraso en el vaciamiento gástrico tiene una relevancia clínica limitada. La diabetes mellitus no modificó la recurrencia, la supervivencia ni el beneficio de la adyuvancia, en contraste con predictores adversos como márgenes positivos, ganglios metastásicos, tumores mayores de 3 cm y niveles elevados de CA19-9. La resección venosa demostró ser segura y oncológicamente equivalente cuando es realizada en centros con experiencia. Asimismo, las complicaciones mayores reducen la probabilidad de recibir tratamiento adyuvante, comprometiendo la supervivencia. En conjunto, RAW redefine las

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prioridades clínicas en pancreatoduodenectomía, enfatizando la prevención de complicaciones críticas, la conservación de la ventana terapéutica para adyuvancia y la toma de decisiones guiada por la biología tumoral.

Palabras clave: *Pancreatoduodenectomía. Complicaciones postoperatorias. Fístula pancreática. Terapia adyuvante. Procedimientos quirúrgicos venosos. Diabetes mellitus.*

Introduction

Pancreatic cancer is among the leading causes of cancer-related mortality worldwide, with a sustained increase in the absolute number of reported cases over recent decades.[1] Pancreatoduodenectomy (PD) remains the potentially curative treatment for resectable tumours of the pancreatic head, but it is one of the most complex procedures in major abdominal surgery, with morbidity rates ranging from 40% to 60% even at highly experienced centres.[2,3] Although postoperative mortality has decreased significantly and is usually between 1% and 5% at specialised institutions, considerable variability in outcomes persists among hospitals, attributable to differences in surgical volume, institutional experience, and standardisation of perioperative care.[3] In addition, much of the available evidence comes from single-centre series or relatively small cohorts, making it difficult to robustly identify the clinical and oncological factors that influence outcomes after PD.[4]

The Recurrence After Whipple's (RAW) study is an international multicentre initiative developed to overcome the limitations of the traditional evidence on PD, which has historically been based on single-centre series and small sample sizes. Its collaborative design, with standardised definitions and systematic collection of perioperative and oncological data, enables more precise analysis of the factors influencing morbidity, recurrence, and survival after surgery.[5]

Four independent analyses derived from this cohort have been published, exploring key dimensions of PD management: the differential impact of postoperative complications, the influence of patient characteristics such as diabetes mellitus (DM) on recurrence and survival, outcomes associated with venous resection, and the effect of major complications on timely access to adjuvant therapy.[6-9]

Although the RAW study has generated multiple publications addressing specific aspects of PD, these analyses have been reported independently and remain scattered throughout the literature. The absence of a synthesis integrating these findings limits their overall interpretation and hinders their application to clinical practice. Therefore, a narrative review bringing together and analysing the published findings from the RAW study is needed to provide a unified and updated overview of the factors influencing outcomes after PD.

Methods

We conducted a narrative review of the literature based on studies derived from the multicentre RAW database. The search was performed in PubMed, identifying all original publications related to the RAW study from its initial registration through 2025. Articles were included if they met the following criteria: they were based on the RAW cohort and had been published in peer-reviewed journals. Articles not derived directly from the RAW database were excluded. Overall, 4 published studies corresponding to the main lines of research generated from RAW were analysed: postoperative complications, patient characteristics, venous resection, and adjuvant therapy.

The synthesis was performed through narrative integration of the findings because of the methodological heterogeneity of the included studies and the absence of comparable metrics that would allow a formal meta-analysis.

Results

The findings of the RAW study have been published in 4 independent analyses addressing different dimensions of PD (Table 1). The main results of each study are presented individually below. Their implications are subsequently integrated to provide a global and unified perspective.

Postoperative complications after PD[6]

The complications with the greatest clinical impact were grade C postoperative pancreatic fistula and postpancreatectomy haemorrhage, both of which were associated with significant increases in severe morbidity and mortality. In contrast, delayed gastric

Table 1. Publications derived from the RAW study

Study	Main topic	Conclusions
Russell et al.[6]	Postoperative complications after PD	Grade C postoperative pancreatic fistula and postpancreatectomy haemorrhage were the complications with the greatest clinical impact. Delayed gastric emptying was not associated with mortality or severe complications.
Rajagopalan et al.[7]	Impact of DM on recurrence and survival	Pre-existing DM did not affect recurrence, overall survival, disease-free survival, or the probability of receiving adjuvant therapy.
Bellotti et al.[8]	Safety and oncological outcomes of venous resection	Venous resection did not increase morbidity or mortality and was equivalent to PD without venous resection.
Russell et al.[9]	Serious complications and their impact on access to adjuvant therapy	Major complications (Clavien-Dindo≥IIIa) significantly reduced access to adjuvant chemotherapy.

DM, diabetes mellitus; PD, pancreatoduodenectomy.

emptying, despite its frequency, was not associated with higher mortality or severe complications. Independent factors associated with major complications were advanced age, high body mass index, American Society of Anesthesiologists classification, hypoalbuminaemia, and prolonged operative times.

Central message: not all complications carry the same weight; grade C postoperative pancreatic fistula and postpancreatectomy haemorrhage are the complications that truly determine prognosis.

Patient characteristics and their impact on recurrence and survival[7]

Pre-existing DM had no significant impact on recurrence, overall survival, the probability of receiving adjuvant therapy, or the benefit derived from it. In contrast, independent predictors of poorer prognosis were variables related to tumour biology: positive lymph nodes, R1 margins, elevated CA19-9, and tumours > 3 cm.

Central message: prognosis is determined by tumour biology; DM does not modify the oncological behaviour of the disease.

Impact of surgical technique: venous resection[8]

Comparison between PD with and without venous resection showed that venous resection did not increase morbidity or mortality and maintained similar rates of major complications. No differences were observed in overall survival, disease-free survival, or recurrence patterns.

Central message: venous resection is safe and oncologically equivalent; its success depends primarily on institutional experience.

Serious complications and access to adjuvant therapy[9]

Major complications (Clavien-Dindo ≥ IIIa) significantly reduced the probability of receiving adjuvant chemotherapy. The absence of adjuvant treatment was associated with poorer overall survival, indicating that the negative clinical impact arises from loss of the oncological window rather than from the complication *per se*.

Central message: a severe complication does not affect survival by itself; it does so by preventing timely access to adjuvant therapy.

Discussion

The published results of the RAW study provide a contemporary perspective that supports previously established concepts while simultaneously questioning and redefining other aspects of PD.

First, the study confirms previous reviews identifying grade C postoperative pancreatic fistula and postpancreatectomy haemorrhage as the complications with the greatest impact on mortality, reintervention, and clinical deterioration.[3,6] Nevertheless, it challenges the importance historically attributed to delayed gastric emptying; although the literature had identified it as a relevant complication because of its frequency and association with prolonged hospital stays,[3] it was shown not to increase mortality.[6]

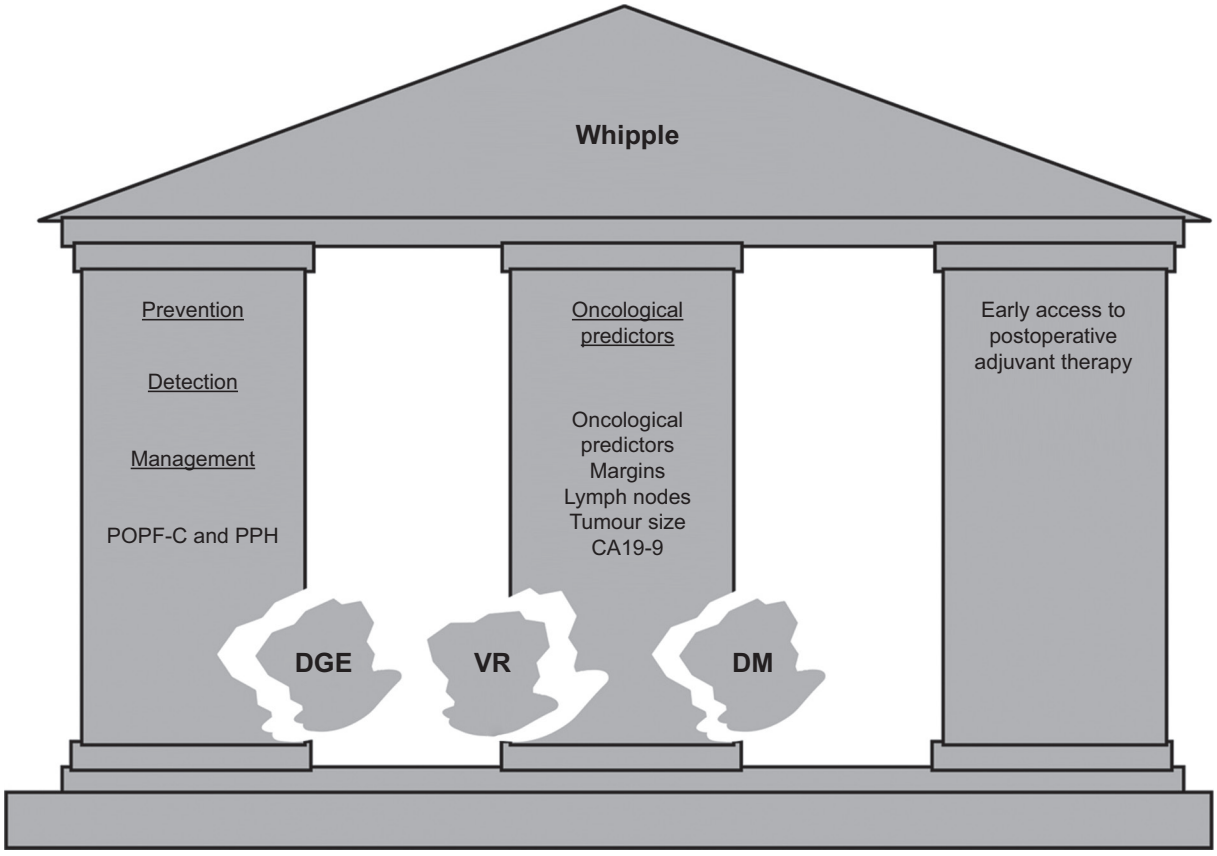


Figure 1. *Conceptual Whipple Parthenon model derived from the RAW project, illustrating the pillars determining oncological success after pancreatoduodenectomy and the factors shown to have less prognostic impact. DGE, delayed gastric emptying; DM, diabetes mellitus; POPF-C, grade C postoperative pancreatic fistula; PPH, postpancreatectomy haemorrhage; VR, venous resection.*

Furthermore, in relation to the findings on access to adjuvant therapy, the limited physiological impact of delayed gastric emptying means that it does not significantly compromise the oncological window for initiation of adjuvant chemotherapy, unlike grade C postoperative pancreatic fistula and postpancreatectomy haemorrhage, which do lead to substantial delays or even permanent loss of adjuvant treatment.[9] In this context, the true clinical impact of a complication should be measured not only by its frequency or immediate mortality, but also by its ability to prevent timely oncological treatment.

On the other hand, although epidemiological studies had suggested that DM might be associated with poorer oncological outcomes because of its relationship with chronic inflammation and metabolic dysfunction,[1] DM was found not to affect recurrence, overall survival, disease-free survival, or the benefit of adjuvant therapy.[7] This finding challenges previous interpretations and shifts the focus towards the true independent prognostic predictors: tumour biology variables, particularly R1 margins, positive lymph nodes, tumours larger than 3 cm, and elevated CA19-9.[1,3,7]

Finally, regarding surgical technique and the historical concern that venous resection might increase mortality or compromise oncological outcomes, propensity score analysis demonstrated that it does not increase morbidity or mortality and provides oncological outcomes equivalent to those of PD without venous resection, provided that it is performed at experienced centres.[8]

Overall, these findings allow an integrated reinterpretation of the determinants of oncological success after PD. Based on these results, a Parthenon model can be conceptualised, in which the upper vertex represents the final oncological outcome (survival and disease control), while the columns correspond to the elements that truly support it: reduction of critical

complications, timely access to adjuvant therapy, and tumour biology variables (Fig. 1).

Limitations

Although the 4 RAW analyses provide valuable information, inherent limitations remain. The multicentre nature of the study entails heterogeneity in surgical technique, patient selection, and perioperative protocols. In addition, although the RAW-derived studies are robust, they do not constitute a meta-analysis and do not allow definitive causality to be established.

Future directions

- Determine standardised "rescue after complication" strategies and their impact on the oncological window.
- Validate predictive models combining tumour biology, critical complications, and timing of adjuvant therapy.

These issues could guide future phases of the RAW study or future multicentre investigations.

Conclusions

The analyses derived from the RAW study allow an integrated reinterpretation of the determinants of oncological success after PD by demonstrating that critical complications – grade C postoperative pancreatic fistula and postpancreatectomy haemorrhage – and timely access to adjuvant therapy are the main factors influencing survival and tumour control. In contrast, factors traditionally overemphasised, such as delayed gastric emptying, DM, and venous resection, show limited prognostic impact. These findings reinforce the need for strategies aimed at preventing and promptly treating major complications, preserving the oncological window for adjuvant therapy, and focusing decision-making on tumour biology. Additional studies are required to standardise rescue algorithms and validate combined prognostic models that further optimise PD outcomes at specialised centres.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments involving humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve personal data, medical records, or human biological samples and therefore does not require ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no type of generative artificial intelligence was used in the writing or creation of content for this manuscript.

References

1. Hu J, Zhang Z. Pancreatic cancer epidemiology and burden. Gastroenterol Rep (Oxf). 2021;9(1):1-10.
2. Giuliano K, Ejaz A, He J. Technical aspects of pancreaticoduodenectomy and their outcomes. Chin Clin Oncol. 2017;6(6):64. doi: 10.21037/cco.2017.09.01.
3. Zhang H, Lu J, Shen Y. Benchmarking pancreatoduodenectomy postoperative outcomes: a systematic review. Ann Surg. 2022;275(3):e540-e552.
4. Gazivoda VP, Lee MK, Khan S. Current evidence in pancreaticoduodenectomy: impact of hospital volume, technique and perioperative management. World J Gastrointest Surg. 2024;16(6):1843-1860.
5. National Cancer Institute. Recurrence After Whipple's (RAW) Study. ClinicalTrials.gov identifier: NCT04596865.
6. Russell TB, Labib PL, Denson J, Streeter A, Ausania F, Pando E, et al. Postoperative complications after pancreatoduodenectomy for malignancy: results from the Recurrence After Whipple's (RAW) study. BJS Open. 2023;7(6):zrad106. doi: 10.1093/bjsopen/zrad106.
7. Rajagopalan A, Aroori S, Russell TB, Labib PL, Ausania F, Pando E, et al. Five-year recurrence/survival after pancreatoduodenectomy for pancreatic adenocarcinoma: does pre-existing diabetes matter? Results from the Recurrence After Whipple's (RAW) study. HPB (Oxford). 2024;26(8):981-989. doi: 10.1016/j.hpb.2024.04.010.
8. Bellotti R, Aroori S, Cardini B, Ponholzer F, Russell TB, Labib PL, et al. Venous resection during pancreatoduodenectomy for pancreatic ductal adenocarcinoma: a multicentre propensity score matching analysis of the Recurrence After Whipple's (RAW) study. Cancers (Basel). 2025;17(7):1223. doi: 10.3390/cancers17071223.
9. Russell TB, Labib PL, Ausania F, Pando E, Roberts KJ, Kausar A, et al. Serious complications of pancreatoduodenectomy correlate with lower rates of adjuvant chemotherapy: results from the Recurrence After Whipple's (RAW) study. Eur J Surg Oncol. 2023;49(9):106919. doi: 10.1016/j.ejso.2023.04.018.