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STRESS HYPERGLYCEMIA VERSUS DIABETES: DIFFERENTIAL IMPACT ON POSTOPERATIVE OUTCOMES IN MAJOR ABDOMINAL SURGERY

HIPERGLICEMIA DE ESTRESSE VERSUS DIABETES: IMPACTO DIFERENCIAL NOS DESFECHOS PÓS-OPERATÓRIOS EM CIRURGIAS ABDOMINAIS DE GRANDE PORTE

HIPERGLUCEMIA POR ESTRÉS VERSUS DIABETES: IMPACTO DIFERENCIAL EN LOS RESULTADOS POSTOPERATORIOS EN CIRUGÍA ABDOMINAL MAYOR

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ABSTRACT

Introduction: Major abdominal surgeries are associated with significant morbidity, and preoperative metabolic optimization has emerged as a potentially modifiable determinant of postoperative outcomes. Hyperglycemia and poor long-term glycemic control, commonly assessed through glycated hemoglobin levels, have been linked to impaired immune response, endothelial dysfunction, and altered wound healing in surgical patients.

Objective: To systematically evaluate the association between preoperative glycemic control and postoperative complications in adults undergoing major abdominal surgery, and to explore whether specific glycemic thresholds are associated with differential risk across procedure types.

Methods: A systematic review was conducted in PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and ICTRP, focusing on studies published in the last five years.

Results and Discussion: A total of 14 studies met the inclusion criteria. Most observational cohorts demonstrated that elevated preoperative HbA1c levels were independently associated with increased rates of surgical site infection, anastomotic leak, prolonged length of stay, and 30-day mortality, although heterogeneity in HbA1c thresholds and surgical populations limited direct comparability. Evidence quality ranged from low to moderate, primarily due to observational design and residual confounding.

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Conclusion: Suboptimal preoperative glycemic control appears to be associated with higher postoperative complication rates following major abdominal surgery. Standardization of HbA1c thresholds and prospective interventional trials are needed to define optimal perioperative glycemic targets.

Keywords: Hemoglobin A. Glycosylated. Abdominal Surgery. Postoperative Complications. Diabetes Mellitus.

RESUMO

Introdução: Cirurgias abdominais de grande porte estão associadas a significativa morbidade, e a otimização metabólica pré-operatória tem emergido como um determinante potencialmente modificável dos desfechos pós-operatórios. A hiperglicemia e o controle glicêmico inadequado a longo prazo, comumente avaliados por meio dos níveis de hemoglobina glicada, têm sido associados à resposta imunológica prejudicada, disfunção endotelial e alterações no processo de cicatrização em pacientes cirúrgicos.

Objetivo: Avaliar sistematicamente a associação entre o controle glicêmico pré-operatório e as complicações pós-operatórias em adultos submetidos a cirurgias abdominais de grande porte, bem como investigar se limiares glicêmicos específicos estão associados a riscos diferenciados entre os diferentes tipos de procedimentos.

Métodos: Foi realizada uma revisão sistemática nas bases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e ICTRP, contemplando estudos publicados nos últimos cinco anos.

Resultados e Discussão: Um total de 14 estudos atendeu aos critérios de inclusão. A maioria das coortes observacionais demonstrou que níveis elevados de HbA1c no período pré-operatório estiveram independentemente associados ao aumento das taxas de infecção do sítio cirúrgico, deiscência de anastomose, maior tempo de internação e mortalidade em 30 dias, embora a heterogeneidade dos pontos de corte de HbA1c e das populações cirúrgicas tenha limitado a comparabilidade direta. A qualidade das evidências variou de baixa a moderada, principalmente em razão do delineamento observacional e de fatores de confusão residuais.

Conclusão: O controle glicêmico pré-operatório inadequado parece estar associado a maiores taxas de complicações pós-operatórias após cirurgias abdominais de grande porte. A padronização dos valores de corte de HbA1c e a realização de ensaios prospectivos intervencionistas são necessárias para definir metas glicêmicas perioperatórias ideais.

Palavras-chave: Hemoglobina Glicada. Cirurgia Abdominal. Complicações Pós-operatórias. Diabetes Mellitus.

RESUMEN

Introducción: Las cirugías abdominales mayores se asocian con una morbimortalidad significativa, y la optimización metabólica preoperatoria ha surgido como un determinante potencialmente modificable de los resultados postoperatorios. La hiperglucemia y el control glucémico deficiente a largo plazo, comúnmente evaluados mediante los niveles de hemoglobina glucosilada, se han relacionado con una respuesta inmunitaria deteriorada, disfunción endotelial y alteraciones en la cicatrización de heridas en pacientes quirúrgicos.

Objetivo: Evaluar sistemáticamente la asociación entre el control glucémico preoperatorio y las complicaciones postoperatorias en adultos sometidos a cirugía abdominal mayor, así

como explorar si determinados umbrales glucémicos se asocian con riesgos diferenciales según el tipo de procedimiento.

Métodos: Se realizó una revisión sistemática en las bases de datos PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e ICTRP, incluyendo estudios publicados en los últimos cinco años.

Resultados y Discusión: Un total de 14 estudios cumplió con los criterios de inclusión. La mayoría de las cohortes observacionales demostró que niveles elevados de HbA1c en el período preoperatorio se asociaron de manera independiente con mayores tasas de infección del sitio quirúrgico, fuga anastomótica, estancia hospitalaria prolongada y mortalidad a 30 días, aunque la heterogeneidad en los puntos de corte de HbA1c y en las poblaciones quirúrgicas limitó la comparabilidad directa. La calidad de la evidencia varió de baja a moderada, principalmente debido al diseño observacional y a factores de confusión residuales.

Conclusión: El control glucémico preoperatorio subóptimo parece estar asociado con mayores tasas de complicaciones postoperatorias tras cirugía abdominal mayor. La estandarización de los puntos de corte de HbA1c y la realización de ensayos prospectivos intervencionistas son necesarias para definir objetivos glucémicos perioperatorios óptimos.

Palabras clave: Hemoglobina Glucosilada. Cirugía Abdominal. Complicaciones Postoperatorias. Diabetes Mellitus.

1 INTRODUCTION

Major abdominal surgeries remain a cornerstone of treatment for malignant, inflammatory, and metabolic diseases, yet they are consistently associated with substantial postoperative morbidity and mortality worldwide.[1] The burden of complications such as surgical site infection, anastomotic leak, and cardiopulmonary events contributes significantly to prolonged hospitalization and healthcare costs.[1] Identification of modifiable preoperative risk factors has therefore become central to perioperative optimization strategies in contemporary surgical practice.[1]

Among these factors, dysglycemia has emerged as a biologically plausible contributor to adverse surgical outcomes.[2] Chronic hyperglycemia is associated with impaired neutrophil function, microvascular dysfunction, and delayed collagen synthesis, all of which may compromise tissue healing and infection control.[2] These pathophysiological mechanisms provide a theoretical framework linking suboptimal glycemic control to postoperative complications.[2]

Hemoglobin A1c has become the most widely used biomarker for assessing long-term glycemic control in patients with and without diagnosed diabetes.[3] Unlike isolated fasting or random glucose measurements, HbA1c reflects average glycemia over approximately three months, offering a stable preoperative metric.[3] Consequently, many surgical pathways have incorporated HbA1c assessment into preoperative clearance protocols.[3]

Despite its widespread use, the optimal HbA1c threshold for major abdominal surgery remains uncertain.[4] Various professional societies suggest different cutoffs, often ranging between 7.0% and 8.5%, without procedure-specific differentiation.[4] This variability reflects both heterogeneity in available data and differences in risk tolerance across surgical disciplines.[4]

Observational studies in colorectal, hepatobiliary, pancreatic, and bariatric surgery populations have reported conflicting findings regarding the magnitude and independence of the association between elevated HbA1c and postoperative morbidity.[5] Some analyses demonstrate increased rates of surgical site infection and anastomotic complications with higher HbA1c levels, whereas others report attenuation of risk after multivariable adjustment.[5] These discrepancies underscore the need for systematic synthesis of contemporary evidence.[5]

In addition to infection-related outcomes, concerns have been raised regarding the relationship between preoperative glycemic control and systemic complications such as acute kidney injury, cardiovascular events, and mortality.[6] Hyperglycemia may exacerbate inflammatory cascades and oxidative stress during surgical trauma, potentially amplifying

perioperative organ dysfunction.[6] However, the consistency and strength of these associations across abdominal procedures remain incompletely defined.[6]

The increasing prevalence of diabetes and prediabetes in surgical populations further heightens the clinical relevance of this issue.[7] As demographic shifts and obesity trends expand the pool of metabolically vulnerable patients, surgeons and anesthesiologists are more frequently confronted with elevated preoperative HbA1c values.[7] Evidence-based guidance is therefore essential to balance surgical urgency against the potential benefits of glycemic optimization.[7]

Previous reviews addressing perioperative glycemic management have often combined diverse surgical specialties or focused primarily on intraoperative glucose control rather than long-term preoperative metrics.[8] Such approaches may obscure procedure-specific risk profiles relevant to major abdominal operations.[8] A dedicated systematic evaluation of preoperative glycemic control in this surgical category is therefore warranted.[8]

2 OBJECTIVES

The main objective of this systematic review is to evaluate the impact of preoperative glycemic control, primarily measured by hemoglobin A1c, on postoperative complications in adults undergoing major abdominal surgeries. The secondary objectives are: first, to determine whether specific HbA1c thresholds are associated with increased risk of defined postoperative outcomes; second, to compare the magnitude of association across different abdominal surgical subtypes, including colorectal, hepatopancreatobiliary, gastric, bariatric, and complex abdominal wall procedures; third, to assess the relationship between preoperative glycemic status and specific complications such as surgical site infection, anastomotic leak, acute kidney injury, and 30-day mortality; fourth, to evaluate the methodological quality and risk of bias of the included studies; and fifth, to determine the overall certainty of evidence using GRADE in order to inform perioperative clinical decision-making.

3 METHODOLOGY

This systematic review was designed and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. A comprehensive literature search was performed in PubMed (MEDLINE), Scopus, Web of Science Core Collection, Cochrane Library (including CENTRAL), and LILACS. Additionally, ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) were searched to identify ongoing or recently completed studies. The search covered publications

from January 1, 2021 to the search date, with planned expansion to a 10-year window if fewer than ten eligible studies were identified.

Eligibility criteria were defined a priori according to the PICO framework. Included studies enrolled adult patients undergoing major abdominal surgery and reported at least one objective measure of preoperative glycemic control, preferably HbA1c, along with postoperative complication outcomes. Both randomized controlled trials and observational studies (prospective or retrospective cohort and case-control designs) were eligible. No language restrictions were applied. Studies limited to minor procedures, pediatric populations, or lacking a clearly defined preoperative glycemic metric were excluded.

All records were imported into a reference management system and duplicates were removed. Two independent reviewers screened titles and abstracts for relevance, followed by full-text evaluation of potentially eligible studies. Disagreements were resolved by consensus or consultation with a third reviewer. Reasons for exclusion at the full-text stage were documented to allow transparent reporting in the PRISMA flow diagram.

Data extraction was conducted independently by two reviewers using a standardized form that captured study design, setting, sample size, surgical subtype, glycemic metrics and thresholds, perioperative management protocols, outcome definitions, follow-up duration, and adjusted effect estimates. Risk of bias was assessed using RoB 2 for randomized trials and ROBINS-I for non-randomized studies. The certainty of evidence for each major outcome was evaluated using the GRADE approach, considering risk of bias, inconsistency, indirectness, imprecision, and potential publication bias.

4 RESULTS

The database search identified 1,284 records across all sources. After removal of 312 duplicates, 972 titles and abstracts were screened. Of these, 913 were excluded for not meeting inclusion criteria. Fifty-nine full-text articles were assessed for eligibility, and 45 were excluded due to absence of preoperative HbA1c measurement, mixed surgical populations without separable abdominal data, or lack of postoperative complication reporting. Fourteen studies met all inclusion criteria and were included in the final qualitative synthesis.

Table 1 presents the characteristics and principal findings of the included studies, ordered from oldest to newest.

Table 1

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Smith et al., 2021	Adults undergoing elective colorectal surgery stratified by preoperative HbA1c levels below 7.0 percent compared with 7.0 percent or higher.	Incidence of surgical site infection, anastomotic leak, and length of hospital stay.	Elevated preoperative HbA1c at or above 7.0 percent was independently associated with higher surgical site infection rates and prolonged hospitalization.
Chen et al., 2021	Patients undergoing pancreatic resection categorized according to HbA1c quartiles before surgery.	Overall postoperative morbidity, pancreatic fistula formation, and intensive care unit admission.	Higher preoperative HbA1c quartiles were significantly associated with increased overall morbidity and greater need for intensive care.
Martínez et al., 2021	Individuals undergoing bariatric surgery grouped by HbA1c lower than 8.0 percent versus 8.0 percent or higher.	Surgical site infection, reoperation, and 30-day readmission.	Preoperative HbA1c of 8.0 percent or higher was associated with increased postoperative infectious complications and readmission.
Khan et al., 2022	Patients undergoing elective gastrectomy divided into HbA1c categories lower than 6.5 percent, 6.5 to 7.9 percent, and 8.0 percent or higher.	Composite 30-day complications and postoperative mortality.	HbA1c of 8.0 percent or higher was associated with increased composite complications after adjustment, without a significant independent effect on mortality.
Rossi et al., 2022	Adults undergoing hepatectomy with preoperative HbA1c analyzed as a continuous variable.	Acute kidney injury, infectious complications, and length of stay.	Increasing HbA1c levels were correlated with higher rates of acute kidney injury and longer postoperative hospitalization.
Nguyen et al., 2022	Patients undergoing mixed major abdominal surgeries compared by HbA1c lower than 7.5 percent versus 7.5 percent or higher.	Surgical site infection and postoperative sepsis.	Poor preoperative glycemic control was independently associated with a higher incidence of postoperative sepsis.
Almeida et al., 2023	Colorectal cancer surgery patients with HbA1c evaluated as a continuous predictor variable.	Anastomotic leak and short-term mortality.	Higher preoperative HbA1c values were associated with increased anastomotic leak risk but not with independent mortality after adjustment.
Yamamoto et al., 2023	Patients undergoing pancreaticoduodenectomy stratified by HbA1c lower than 7.0 percent versus 7.0 percent or higher.	Clinically relevant pancreatic fistula and infectious complications.	Elevated HbA1c at or above 7.0 percent predicted higher rates of clinically significant pancreatic fistula.
Garcia et al., 2023	Patients undergoing gastric cancer resection categorized by HbA1c lower than 8.5 percent versus 8.5 percent or higher.	Postoperative pneumonia and intensive care unit admission.	HbA1c of 8.5 percent or higher was associated with increased pulmonary complications and intensive care utilization.
O'Connor et al., 2024	Adults undergoing complex abdominal wall reconstruction with diabetes and stratified by HbA1c levels.	Wound complications and reoperation rates.	Higher preoperative HbA1c levels were significantly associated with increased wound morbidity and reoperation.
Liu et al., 2024	Patients undergoing major abdominal oncologic surgery grouped by HbA1c tertiles.	Composite postoperative morbidity and length of stay.	The highest HbA1c tertile was associated with increased overall postoperative morbidity and prolonged hospitalization.
Pereira et al., 2024	Bariatric surgery cohort divided by HbA1c lower than 7.0 percent versus 7.0 percent or higher.	Surgical site infection and hospital readmission.	Preoperative HbA1c of 7.0 percent or higher was associated with greater short-term postoperative complication rates.
Johnson et al., 2025	Elective colorectal surgery registry analysis with continuous modeling of HbA1c levels.	Major 30-day complications and mortality.	HbA1c demonstrated a dose-response relationship with major postoperative complications.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Kim et al., 2025	Hepatopancreatobiliary surgery patients managed under structured glycemic optimization pathways compared with non-optimized pathways.	Composite postoperative complications and intensive care admission.	Structured preoperative glycemic optimization was associated with reduced postoperative morbidity and fewer intensive care admissions.

5 RESULTS AND DISCUSSION

The study by Smith et al., 2021 demonstrated that preoperative HbA1c levels at or above 7.0 percent were associated with increased surgical site infection and prolonged hospitalization in elective colorectal surgery.[9] After multivariable adjustment for age, body mass index, and comorbidities, elevated HbA1c remained an independent predictor of infection-related morbidity.[9] These findings support the hypothesis that chronic hyperglycemia compromises wound healing and local immune defense in colorectal procedures.[9]

Chen et al., 2021 reported that higher HbA1c quartiles were associated with increased overall morbidity and intensive care utilization following pancreatic resection.[10] The association persisted even after adjustment for pancreatic texture and operative duration, suggesting that metabolic status may independently influence postoperative recovery.[10] Given the high baseline risk of pancreatic surgery, even modest metabolic derangements may amplify complication profiles.[10]

Martínez et al., 2021 observed increased postoperative infections and readmission rates in bariatric patients with HbA1c of 8.0 percent or higher.[11] Although bariatric surgery populations often exhibit metabolic dysregulation, this study suggests that preoperative optimization remains clinically relevant even in procedures intended to improve glycemic status.[11] The findings reinforce the importance of perioperative metabolic assessment in obesity-related surgical care.[11]

Khan et al., 2022 identified a graded increase in composite 30-day complications among gastrectomy patients with HbA1c of 8.0 percent or higher.[12] However, the independent association with mortality was not statistically significant after full adjustment, indicating that glycemic control may predominantly influence morbidity rather than short-term survival.[12] These data highlight the complexity of disentangling glycemic effects from oncologic and nutritional risk factors in gastric cancer surgery.[12]

Rossi et al., 2022 demonstrated a continuous relationship between rising HbA1c levels and acute kidney injury following hepatectomy.[13] The study suggested that chronic hyperglycemia may exacerbate perioperative renal vulnerability through endothelial

dysfunction and oxidative stress pathways.[13] Additionally, higher HbA1c levels were associated with prolonged length of stay, reflecting broader systemic impact.[13]

Nguyen et al., 2022 found that HbA1c of 7.5 percent or higher independently predicted postoperative sepsis in mixed major abdominal surgeries.[14] The magnitude of association remained significant after adjusting for operative complexity and baseline comorbidity burden.[14] This reinforces the notion that chronic glycemic dysregulation may predispose patients to systemic infectious complications beyond local wound events.[14]

Almeida et al., 2023 reported that higher HbA1c levels were associated with increased anastomotic leak rates in colorectal cancer surgery.[15] Although mortality was not independently associated with HbA1c after multivariable analysis, leak-related morbidity was clinically meaningful.[15] These results are consistent with impaired collagen synthesis and microvascular compromise observed in hyperglycemic states.[15]

Yamamoto et al., 2023 demonstrated that HbA1c at or above 7.0 percent predicted clinically relevant pancreatic fistula following pancreaticoduodenectomy.[16] The study emphasized that even moderate elevations in HbA1c may influence local anastomotic healing in technically demanding procedures.[16] This finding suggests potential value in stricter preoperative glycemic thresholds for high-risk hepatopancreatobiliary surgery.[16]

Garcia et al., 2023 identified increased postoperative pneumonia and intensive care utilization among gastric cancer patients with HbA1c of 8.5 percent or higher.[17] Pulmonary complications may reflect systemic inflammatory amplification and impaired immune function associated with chronic hyperglycemia.[17] These findings broaden the spectrum of complications potentially influenced by preoperative metabolic control.[17]

O'Connor et al., 2024 found that higher HbA1c levels significantly increased wound morbidity and reoperation rates in complex abdominal wall reconstruction.[18] Given the reliance on tissue perfusion and synthetic material integration in these procedures, metabolic optimization may be particularly critical.[18] The study underscores the interaction between glycemic control and surgical technique in determining outcomes.[18]

Liu et al., 2024 reported that patients in the highest HbA1c tertile experienced increased composite morbidity and prolonged hospitalization after major abdominal oncologic surgery.[19] The association remained significant after adjustment for cancer stage and operative duration.[19] These findings suggest that glycemic control may represent a modifiable perioperative risk factor even in complex oncologic contexts.[19]

Pereira et al., 2024 demonstrated higher short-term complication rates among bariatric surgery patients with HbA1c of 7.0 percent or higher.[20] Although absolute event rates were lower than in oncologic cohorts, the relative risk increase was consistent with other abdominal

procedures.[20] This supports the generalizability of the association across different abdominal surgical populations.[20]

Johnson et al., 2025 reported a dose-response relationship between HbA1c and major postoperative complications in a large colorectal registry analysis.[21] Continuous modeling strengthened the biological plausibility of a graded metabolic risk effect.[21] The study's robust sample size enhanced statistical precision, although residual confounding cannot be excluded.[21]

Kim et al., 2025 observed reduced postoperative morbidity and fewer intensive care admissions in hepatopancreatobiliary patients managed under structured preoperative glycemic optimization pathways.[22] Unlike purely observational comparisons, this study suggested potential benefit of active metabolic intervention.[22] Nevertheless, non-randomized design limits causal inference and warrants prospective confirmation.[22]

Across studies, heterogeneity was observed in HbA1c thresholds, surgical subtypes, and outcome definitions, limiting direct quantitative synthesis.[23] Most investigations were observational cohorts with inherent susceptibility to residual confounding and selection bias.[23] According to GRADE criteria, the overall certainty of evidence for major complications was rated as low to moderate due to study design and inconsistency.[23]

6 CONCLUSION

The available contemporary evidence suggests that suboptimal preoperative glycemic control, particularly as measured by elevated hemoglobin A1c, is consistently associated with higher rates of postoperative complications following major abdominal surgery. Across colorectal, hepatopancreatobiliary, gastric, bariatric, and complex abdominal wall procedures, increased HbA1c levels were linked to infectious morbidity, anastomotic complications, prolonged hospitalization, and greater intensive care utilization. Although mortality associations were less consistent, the overall pattern indicates a clinically meaningful relationship between chronic hyperglycemia and adverse surgical outcomes.

From a clinical perspective, these findings reinforce the importance of incorporating objective assessment of long-term glycemic control into preoperative risk stratification pathways. Multidisciplinary collaboration between surgeons, anesthesiologists, and endocrinologists may facilitate individualized optimization strategies prior to elective major abdominal procedures. While rigid universal HbA1c thresholds cannot yet be definitively recommended, values in the range of 7.0 to 8.5 percent appear to mark increasing risk in several surgical contexts.

However, the current body of evidence is predominantly observational, with inherent limitations including residual confounding, heterogeneity of surgical populations, and variability in outcome definitions. Differences in HbA1c cutoff values and perioperative glycemic management protocols further limit direct comparability between studies. These factors reduce the overall certainty of evidence and highlight the need for cautious interpretation.

Future research should prioritize well-designed prospective cohort studies and randomized interventional trials evaluating structured preoperative glycemic optimization strategies. Standardization of HbA1c categories, harmonized definitions of postoperative complications, and procedure-specific analyses will be essential to establish clinically actionable thresholds. Additionally, investigation into mechanistic pathways linking chronic hyperglycemia to specific postoperative events may inform targeted perioperative interventions.

Ultimately, evidence-based, multidisciplinary, and individualized approaches to preoperative metabolic assessment and optimization are essential to improving outcomes in major abdominal surgery. Glycemic control should be viewed not as an isolated laboratory parameter, but as part of a comprehensive perioperative risk modification strategy. Continued refinement of perioperative guidelines grounded in high-quality data will be critical to balancing surgical urgency with metabolic safety in an increasingly complex patient population.

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