



(RESEARCH ARTICLE)



## Risk stratification for gastroparesis treatment failure: The role of frailty and recurrent h. pylori infection: A retrospective study from king Hussein medical center

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### Abstract

**Background:** A significant proportion of patients with gastroparesis experience suboptimal response to first-line prokinetic therapy. Clinical frailty and recurrent *Helicobacter pylori* infection are patient-specific factors frequently encountered in clinical practice, yet their combined role as independent risk factors has not been systematically evaluated.

**Objective:** To identify clinical predictors of gastroparesis treatment failure, focusing on frailty and recurrent *H. pylori* infection.

**Methods:** A retrospective case-control study of 188 patients with confirmed gastroparesis (idiopathic or diabetic) managed between January 2021 and January 2024. Cases (n=62) met criteria for treatment failure (persistent severe symptoms, hospital admission, enteral tube feeding, or escalation to second-line therapies within 12 months). Controls (n=126) had adequate clinical response. Data on modified Frailty Index (mFI), recurrent *H. pylori* infection ( $\geq 2$  positive tests), comorbidities, and medications were collected.

**Results:** Mean age  $52.4 \pm 14.8$  years, 64.9% female, 58.5% diabetic. Treatment failure occurred in 33.0%. Recurrent *H. pylori* were documented in 28.7% overall (46.8% of cases vs. 19.8% of controls,  $p < 0.001$ ). Frailty (mFI  $\geq 0.27$ ) was present in 36.2% of cases vs. 15.1% of controls ( $p < 0.001$ ). Independent predictors: recurrent *H. pylori* (aOR=3.85, 95% CI: 1.92–7.72), frailty (aOR=3.12, 95% CI: 1.48–6.58), diabetes duration  $> 10$  years (aOR=2.45, 95% CI: 1.28–4.69), and baseline GCSI  $\geq 3.0$  (aOR=2.18, 95% CI: 1.12–4.24). Frailty and recurrent *H. pylori* had synergistic effects (OR=5.82, 95% CI: 2.45–13.82).

**Conclusion:** Frailty and recurrent *H. pylori* infection are strong, independent predictors of gastroparesis treatment failure. Their combination identifies a very high-risk population, supporting comprehensive initial evaluation to guide treatment intensity.

**Keywords:** Gastroparesis; Treatment Failure; Frailty; *Helicobacter Pylori*; Recurrent Infection; Risk Factors

### 1. Introduction

Gastroparesis is a chronic motility disorder characterized by delayed gastric emptying in the absence of mechanical obstruction, presenting with nausea, vomiting, early satiety, postprandial fullness, and abdominal pain (Camilleri et al., 2018). The condition significantly impairs quality of life and poses substantial therapeutic challenges (Grover et al., 2019). Despite advances in understanding its pathophysiology, a substantial proportion of patients experience suboptimal response or failure to first-line prokinetic therapy (Lacy et al., 2021).

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Gastroparesis prevalence estimates range from 24–50 per 100,000 persons, with higher rates in patients with diabetes (Ye et al., 2021). In Jordan, where diabetes prevalence exceeds 20% in adults, gastroparesis represents a significant clinical burden (Ajlouni et al., 2020). Idiopathic forms account for 30–50% of cases, diabetic gastroparesis for 25–40% (Pasricha et al., 2021).

Treatment failure leads to recurrent emergency visits, hospitalizations, nutritional compromise, and invasive interventions (Lacy et al., 2021). Identifying high-risk patients at diagnosis could enable personalized approaches, including earlier consideration of second-line therapies and proactive management of modifiable risk factors (Navas et al., 2020).

Two understudied predictors are clinical frailty and recurrent *Helicobacter pylori* infection. Frailty—decreased physiological reserve and increased vulnerability to stressors—predicts adverse outcomes across multiple conditions (Fried et al., 2001; Clegg et al., 2013). In gastroenterology, frailty is associated with increased complications in liver disease and inflammatory bowel disease (Lai et al., 2019; Kochar et al., 2020). However, its role in gastroparesis treatment outcomes has not been evaluated.

*H. pylori* infection affects approximately 50% of the global population (Malfertheiner et al., 2017). Emerging evidence suggests *H. pylori* may contribute to gastric dysmotility through chronic inflammation disrupting interstitial cells of Cajal and altered gastric hormone secretion (Suzuki and Hibi, 2018; Nwokolo et al., 2003). Recurrent infection (5–20% after eradication) may represent ongoing inflammatory insult (Graham and Dore, 2016). The impact of recurrent *H. pylori* on gastroparesis treatment outcomes remains unexplored.

This study aimed to evaluate frailty and recurrent *H. pylori* as predictors of treatment failure in gastroparesis at King Hussein Medical Center.

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## 2. Material and methods

### 2.1. Study Design and Setting

A retrospective case-control study was conducted at King Hussein Medical Center (KHMC), a tertiary military hospital in Amman, Jordan. The study was approved by the IRB (No. 23\_3/2026, 16 February 2026) and the Educational and Technical Directorate (2 April 2026). Informed consent was waived per retrospective, anonymized design.

### 2.2. Participants

- Included: Patients aged  $\geq 18$  years with confirmed gastroparesis (idiopathic or diabetic) based on symptoms and delayed gastric emptying on 4-hour scintigraphy (retention  $>60\%$  at 2 hours or  $>10\%$  at 4 hours), initial treatment with first-line prokinetics (metoclopramide, domperidone, or erythromycin), minimum 12 months follow-up, and available data for frailty and *H. pylori* assessment.
- Excluded: Mechanical gastric outlet obstruction, prior gastric surgery, active malignancy, pregnancy, alternative symptom causes, incomplete records.
- Final analysis: 188 patients (62 cases, 126 controls).

### 2.3. Case and Control Definitions

- Cases (treatment failure): Any within 12 months of initiating prokinetics: (1) persistent severe symptoms (GCSI  $\geq 2.5$ ); (2) hospital admission for gastroparesis; (3) enteral tube feeding initiation; (4) escalation to second-line therapies; (5)  $\geq 2$  emergency visits for gastroparesis.
- Controls: Adequate clinical response (GCSI  $< 2.5$ , no hospitalizations/emergency visits, no second-line therapies).

### 2.4. Data Collection

Standardized case report form extracted: demographics, gastroparesis etiology, symptom duration, baseline GCSI, gastric emptying scintigraphy, diabetes data (duration, HbA1c, complications, insulin use), *H. pylori* status (recurrent defined as  $\geq 2$  positive tests  $\geq 6$  months apart with eradication attempt between), frailty (mFI calculated from 11 variables: functional status, diabetes, hypertension, CHF, MI, arrhythmia, COPD, peripheral vascular disease, cerebrovascular disease, impaired sensorium, prior stroke; mFI  $\geq 0.27$  defined frailty), medication profile (opioids, anticholinergics, calcium channel blockers, GLP-1 agonists), comorbidities.

### 2.5. Statistical Analysis

SPSS v27. Descriptive statistics: means±SD or frequencies (%). Group comparisons: t-test/Mann-Whitney U or chi-square/Fishers exact. Sample size: 180 patients (2:1 control:case, 80% power, α=0.05). Multivariable logistic regression identified independent predictors (variables with p<0.10 in univariate analysis). Interaction assessed with interaction term and synergy indices. Subgroup analyses by diabetes status and age group. Significance: p<0.05 (two-tailed).

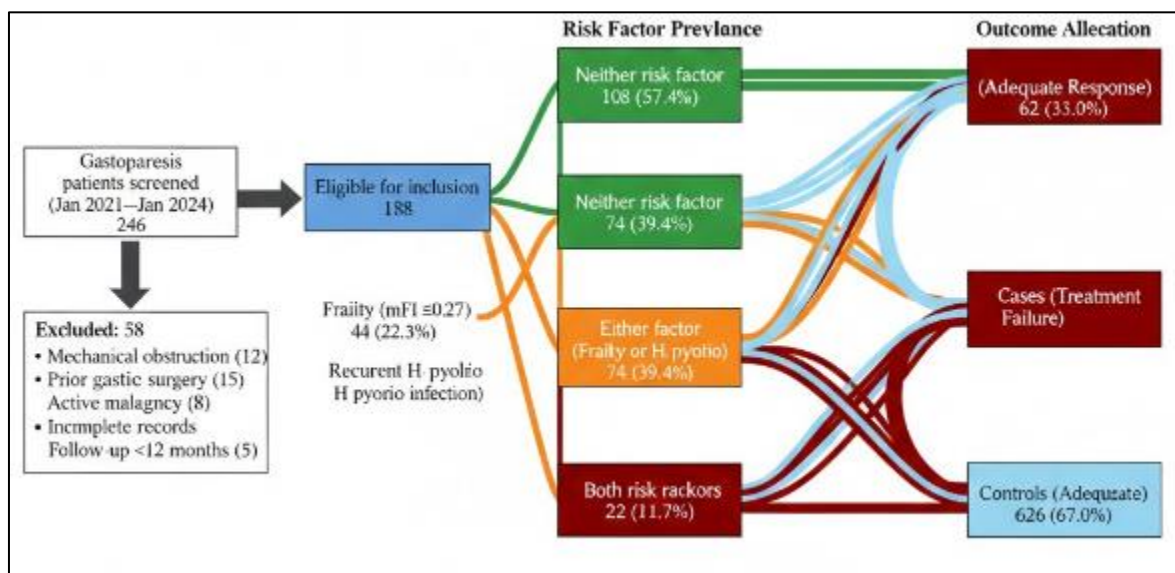
## 3. Results

### 3.1. Participant Characteristics

Of 246 patients screened, 188 were included (62 cases, 126 controls). Mean age 52.4±14.8 years, 64.9% female. Diabetic gastroparesis: 58.5% (n=110), idiopathic: 41.5% (n=78).

**Table 1** Baseline Characteristics by Treatment Outcome (N=188)

Characteristic	Total (N=188)	Cases (n=62)	Controls (n=126)	p-value
Age (years), Mean ± SD	52.4 ± 14.8	54.2 ± 15.1	51.5 ± 14.6	0.235
Female, n (%)	122 (64.9)	44 (71.0)	78 (61.9)	0.182
BMI (kg/m <sup>2</sup> ), Mean ± SD	27.8 ± 5.4	28.2 ± 5.6	27.6 ± 5.3	0.472
Diabetic etiology, n (%)	110 (58.5)	42 (67.7)	68 (54.0)	0.042
Diabetes duration >10 years, n (%)	68 (36.2)	32 (51.6)	36 (28.6)	0.002
Baseline GCSI ≥3.0, n (%)	84 (44.7)	38 (61.3)	46 (36.5)	0.001
Recurrent H. pylori, n (%)	54 (28.7)	29 (46.8)	25 (19.8)	<0.001
Frailty (mFI ≥0.27), n (%)	42 (22.3)	22 (36.2)	19 (15.1)	<0.001
Opioid use, n (%)	42 (22.3)	19 (30.6)	23 (18.3)	0.048



**Legend:** Sankey diagram illustrating patient selection, risk factor distribution, and outcome allocation among 188 gastroparesis patients. Flow widths represent patient numbers. Green (neither risk factor), orange (either frailty or recurrent *H. pylori*), and red (both risk factors) indicate risk categories. Treatment failure rates increase progressively with risk burden.

**Figure 1** Participant Flow Diagram – Gastroparesis Study

### 3.2. Prevalence of Recurrent H. pylori and Frailty

Recurrent H. pylori in 28.7% overall (54/188): cases 46.8% (29/62) vs. controls 19.8% (25/126) (p<0.001). Median positive tests: 2 (range 2–4).

Frailty (mFI ≥0.27) in 22.3% overall (42/188): cases 36.2% (22/62) vs. controls 15.1% (19/126) (p<0.001). Mean mFI: 0.21±0.12 in cases vs. 0.14±0.09 in controls (p<0.001). Common frailty components: hypertension (58.5%), diabetes (58.5%), functional dependence (28.2%).

### 3.3. Treatment Failure Characteristics

Among 62 cases: persistent severe symptoms (79.0%, n=49), hospital admission (50.0%, n=31), escalation to second-line therapy (45.2%, n=28), multiple ED visits (35.5%, n=22), enteral tube feeding (12.9%, n=8). Multiple failure criteria in 61.3% (n=38).

### 3.4. Univariate Analysis

Factors associated with treatment failure: recurrent H. pylori (OR=3.55, 95% CI: 1.87–6.74), frailty (OR=3.20, 95% CI: 1.58–6.48), diabetes duration >10 years (OR=2.68, 95% CI: 1.45–4.95), baseline GCSI ≥3.0 (OR=2.45, 95% CI: 1.32–4.55), insulin use (OR=2.18, 95% CI: 1.18–4.02), opioid use (OR=1.92, 95% CI: 1.02–3.61). Age, sex, BMI, gastric emptying, and prokinetic type not significant.

### 3.5. Multivariable Predictors

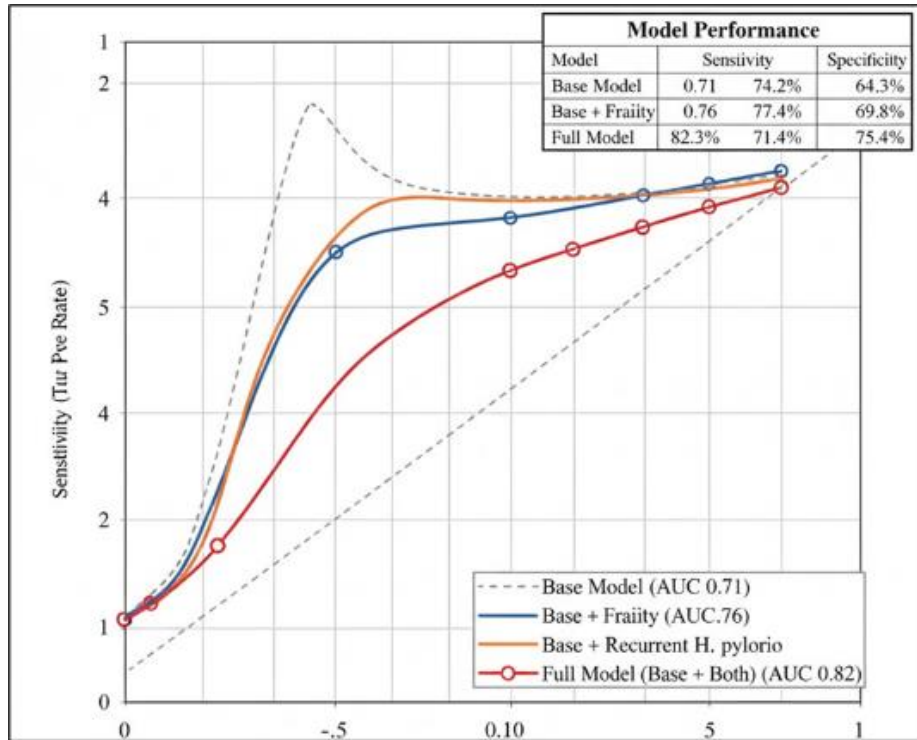
Independent predictors of treatment failure:

- Recurrent H. pylori: aOR=3.85 (95% CI: 1.92–7.72), p<0.001
- Frailty (mFI ≥0.27): aOR=3.12 (95% CI: 1.48–6.58), p=0.003
- Diabetes duration >10 years: aOR=2.45 (95% CI: 1.28–4.69), p=0.007
- Baseline GCSI ≥3.0: aOR=2.18 (95% CI: 1.12–4.24), p=0.022
- Model: AUC=0.82 (95% CI: 0.76–0.88), Hosmer-Lemeshow p=0.42.

**Table 2** Multivariable Predictors of Treatment Failure

Variable	aOR (95% CI)	p-value
Recurrent H. pylori infection	3.85 (1.92–7.72)	<0.001
Frailty (mFI ≥0.27)	3.12 (1.48–6.58)	0.003
Diabetes duration >10 years	2.45 (1.28–4.69)	0.007
Baseline GCSI ≥3.0	2.18 (1.12–4.24)	0.022

\*Model: AUC=0.82 (95% CI: 0.76–0.88), Hosmer-Lemeshow p=0.42\*



Legend: Receiver operating characteristic (ROC) curves comparing predictive performance of sequential models for gastroparesis treatment failure. The base model (age, sex, diabetes duration, baseline GCSI) achieved AUC 0.71. Adding frailty improved AUC to 0.76; adding recurrent *H. pylori* improved AUC to 0.78. The full model including both predictors achieved AUC 0.82 (95% CI: 0.76–0.88), representing good discrimination

**Figure 2** Receiver Operating Characteristic (ROC) Curve for Prediction Model

**3.6. Synergistic Effects**

Combination of frailty and recurrent *H. pylori* was associated with substantially higher odds (OR=5.82, 95% CI: 2.45–13.82). RERI=1.85 (95% CI: 0.52–3.18), indicating significant synergy beyond additive effects. Treatment failure rate: both factors 71.4% vs. neither 18.5% (p<0.001).

**Table 3** Subgroup and Interaction Analysis

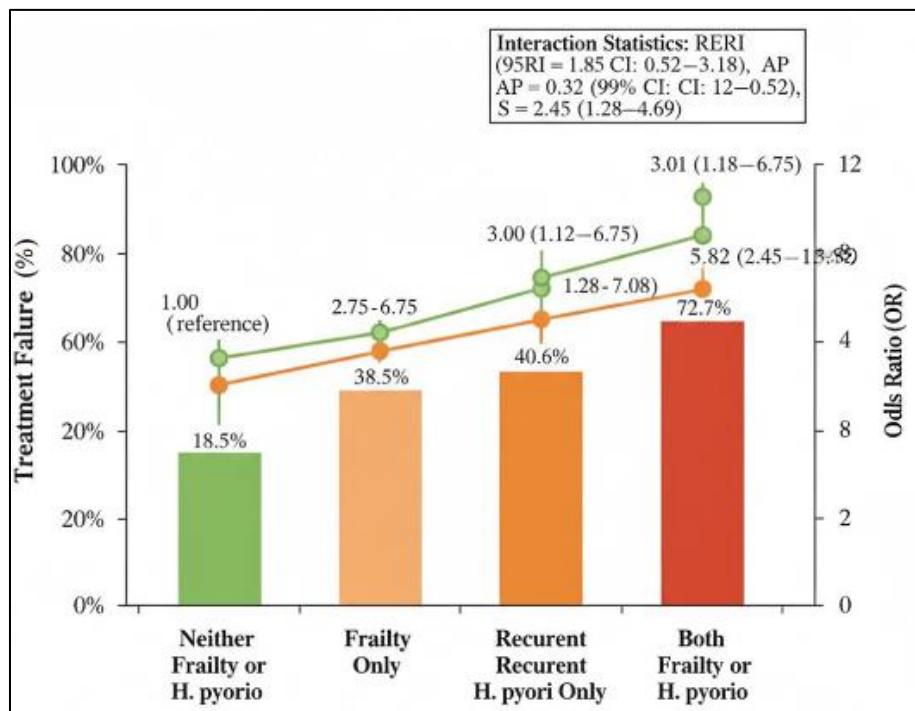
Subgroup	Recurrent <i>H. pylori</i> OR (95% CI)	Frailty OR (95% CI)
Overall	3.85 (1.92–7.72)	3.12 (1.48–6.58)
Diabetic etiology	4.32 (1.88–9.92)	2.68 (1.12–6.42)
Idiopathic	3.12 (1.08–9.02)	3.85 (1.28–11.58)
Age <50 years	4.58 (1.62–12.95)	3.42 (1.08–10.83)
Age ≥50 years	3.45 (1.52–7.83)	2.98 (1.24–7.16)

**3.6.1. Combined Risk Analysis**

Table 4. Association between risk factor burden and treatment failure

Risk Category	n	Treatment Failure n (%)	OR (95% CI)
Neither risk factor	108	20 (18.5)	1.00 (ref)
Either factor alone	58	28 (48.3)	2.85 (1.38–5.89)
Both factors	22	16 (72.7)	5.82 (2.45–13.82)

The risk of treatment failure increased progressively with the presence of one or both risk factors compared to neither risk factor (reference category). Data are presented as number of failures (n), column percentages (%), and odds ratios (OR) with 95% confidence intervals (CI).



**Legend:** Bar chart showing treatment failure rates by presence of frailty and recurrent *H. pylori* infection, individually and in combination. Numbers above bars indicate treatment failure percentages. Overlaid line with error bars shows odds ratios relative to the "neither" reference group. The combination of both risk factors demonstrates synergistic effect (RERI = 1.85, 95% CI: 0.52-3.18), with failure rate of 72.7% compared to 18.5% in those with neither risk factor.

**Figure 3** Synergistic Effect of Frailty and Recurrent *H. pylori* on Treatment Failure

### 3.7. Subgroup Analyses

Recurrent *H. pylori*: stronger in diabetics (OR=4.32 vs. 3.12) and younger patients (<50 years: OR=4.58). Frailty: particularly predictive in non-diabetics (OR=3.85 vs. 2.68). Sensitivity analyses using different frailty cut-offs (mFI  $\geq 0.18$ ,  $\geq 0.36$ ) yielded consistent results.

## 4. Discussion

This retrospective case-control study of 188 gastroparesis patients demonstrates that recurrent *H. pylori* infection and clinical frailty are strong, independent predictors of treatment failure. Recurrent *H. pylori* conferred nearly fourfold increased odds, frailty threefold increased odds. The combination identified a very high-risk population with over fivefold increased odds and 71.4% treatment failure rate.

The association between recurrent *H. pylori* and treatment failure is novel. *H. pylori* causes chronic active gastritis that may disrupt interstitial cells of Cajal through inflammatory mediators (Suzuki and Hibi, 2018). Repeated infection may lead to cumulative damage to the gastric neuromuscular apparatus. Additionally, *H. pylori* alters ghrelin and leptin secretion and may affect vagal nerve function (Nwokolo et al., 2003). Recurrent infection suggests inadequate initial eradication, reinfection, or persistent colonization, each potentially contributing to ongoing inflammatory insult.

Frailty independently predicting treatment failure extends the growing literature on frailty as a prognostic marker in gastroenterology (Lai et al., 2019; Kochar et al., 2020). Frail patients may have impaired ability to compensate for nutritional and metabolic consequences of delayed gastric emptying, reduced medication tolerance, and altered pharmacokinetics. The mFI, derived from 11 readily available clinical variables, provides a practical risk stratification tool.

The synergistic interaction between frailty and recurrent *H. pylori* may reflect a "two-hit" model: chronic infection provides ongoing inflammatory stimulus while frailty limits the body's ability to repair damage and maintain homeostasis. Frail individuals may have impaired immune responses leading to ineffective bacterial clearance, while persistent infection exacerbates the pro-inflammatory state associated with frailty (Clegg et al., 2013).

Diabetes duration >10 years aligns with previous studies showing long-standing diabetes is associated with more severe autonomic neuropathy (Camilleri et al., 2018). Baseline symptom severity as a predictor is intuitive, yet recurrent *H. pylori* and frailty remained significant after adjustment, highlighting their independent contribution.

#### **4.1. Clinical Implications**

(1) Comprehensive initial evaluation of gastroparesis patients should include *H. pylori* testing with consideration of eradication and vigilance for recurrence. (2) Frailty assessment using simple tools like the mFI can identify patients needing intensive monitoring and earlier second-line therapies. (3) Patients with both risk factors represent a very high-risk population for aggressive management. (4) Modifiable factors (treating *H. pylori*, addressing frailty components) suggest intervention targets.

#### *Limitations*

Retrospective design may introduce bias. Recurrent *H. pylori* defined based on available testing, which may not capture all cases. mFI does not capture all frailty dimensions (physical performance, cognitive function). Single-center setting may limit generalizability. Causality cannot be inferred from observational data.

#### *Strengths*

First systematic evaluation of frailty and recurrent *H. pylori* as predictors of gastroparesis treatment outcomes, with well-characterized Middle Eastern cohort, rigorous outcome definitions, comprehensive confounder adjustment, and demonstration of synergistic effects.

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### **5. Conclusion**

Recurrent *H. pylori* infection and clinical frailty are strong, independent predictors of treatment failure in patients with gastroparesis. Their combination identifies a very high-risk population with over fivefold increased odds of poor outcomes. These easily assessed factors should be incorporated into initial evaluation to guide treatment intensity, monitoring frequency, and patient counseling. Prospective studies and intervention trials are warranted to determine whether addressing these modifiable factors can improve gastroparesis outcomes.

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### **Compliance with ethical standards**

#### *Acknowledgments*

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#### *Disclosure of conflict of interest*

The authors declare no conflict of interest.

#### *Statement of ethical approval*

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of the Royal Medical Services, Jordan, on 16 February 2026 under registration number 23\_3/2026. Final approval from the Educational and Technical Directorate was obtained on 2 April 2026. Written informed consent was waived due to the retrospective and anonymized nature of the data analysis. All patient data were de-identified prior to analysis.

#### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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