

# *Clostridioides difficile* infection after surgical myocardial revascularisation: unravelling risk factors and impact on postoperative outcomes

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## ABSTRACT

**Aim.** *Clostridioides difficile* infection (CDI) poses a significant threat to postoperative cardiac surgery patients. This study examines the impact of specific pre-, intra-, and post-operative factors, along with geographical considerations, on *Clostridioides difficile* (CD) incidence and its consequences. The study aims to identify factors contributing to increased CD prevalence in cardiac surgery units.

**Material and methods.** A single-centre cohort of 3502 patients undergoing surgical myocardial revascularisation between January 2013 and March 2018 was analysed, with 48 diagnosed with CDI. Preoperative risk factors include the use of broad-spectrum antibiotics, advanced age, comorbidities, and prolonged hospital stays. Intraoperatively, attention is given to catheter-related issues, mechanical ventilation, and the use of blood products. Postoperatively, the study assesses CDI's impact on recovery, complications, and outcomes. A geographical analysis explores regional variation in CDI incidence.

**Results.** Results indicate a CDI incidence of 1.37%, aligning with existing literature trends. Demographically matched controls show no significant differences in age, gender, or location. Higher *Body Mass Index* and lower left ventricular ejection fraction are identified as significant risk factors. Laboratory findings indicate elevated CRP levels and increased platelet count associated with CDI. Postoperative CDI significantly prolongs hospitalisation time. EuroSCORE II values are higher in the CDI group, though not statistically significant.

**Conclusions.** The study offers a comprehensive understanding of CDI dynamics in cardiac surgery, emphasising the need for tailored preventive measures. Specific risk factors and regional variations underscore the importance of vigilant monitoring and early intervention. Future research should include larger cohorts and explore gut microbiota for refined strategies.

## Introduction

*Clostridioides difficile* (CD) is the leading cause of antibiotic-associated diarrhoea, healthcare-associated diarrhoea, and colitis, representing a significant risk for postoperative patients [1–3]. This gram-positive, strictly anaerobic, spore-forming bacillus is widely present in the environment, with asymptomatic colonisation observed in approximately 2% of healthy adults and up to 14% of the elderly population [1]. Despite ongoing efforts to curb nosocomial transmission, both the incidence and severity of *Clostridioides difficile* infection (CDI) have increased globally in recent years [4]. The use of broad-spectrum antibiotics remains the principal risk factor, compounded by advanced age, comorbidities, extended hospital stays, and the use of proton pump inhibitors or histamine-2 receptor antagonists [2,5]. Certain geographic areas, notably the Northeastern United States, have been identified as regions with particularly high CDI prevalence [5,6].

Surgical patients, particularly those undergoing cardiac procedures, are exposed to additional infection risk factors, including catheter-related complications, prolonged mechanical ventilation, substantial blood product transfusions, indwelling catheter drainage, and open surgical fields [7]. The clinical presentation of CDI ranges from asymptomatic colonisation and mild diarrhoea to severe, life-threatening conditions such as fulminant colitis with sepsis, pseudomembranous colitis, toxic megacolon, transmural pancolitis requiring colectomy, and multi-organ failure [1–4]. The reported incidence of CD-related diarrhoea following surgical interventions varies widely, ranging from 0.3% to 8.4% [3].

The rising number of CDI cases observed in the cardiac surgery unit has prompted a com-

prehensive investigation aimed at evaluating the influence of specific preoperative, intraoperative, and postoperative factors – as well as patients' geographic origin – on the risk of CDI. The study further seeks to assess the downstream impact of CDI on postoperative recovery and outcomes.

### Factors under scrutiny

To comprehensively evaluate the multifactorial nature of CDI following cardiac surgery, the present study examines preoperative conditions, intraoperative factors, and postoperative outcomes. Key preoperative risk factors under investigation include the use of broad-spectrum antibiotics, advanced age, coexisting medical conditions, and prolonged hospitalisation. Intraoperatively, the analysis focuses on catheter-associated complications, extended mechanical ventilation, high-volume transfusion of blood products, persistent drainage via indwelling catheters, and the presence of open surgical cavities. In the postoperative phase, the study explores how CDI influences recovery, with particular attention to complication rates and the potential need for additional interventions.

### Geographical considerations

In addition to patient-related factors, this study considers geographic location as a potential contributor to CDI incidence. Building on prior findings that identify certain regions as CDI hotspots, we explore whether similar regional disparities exist within cardiac surgery settings. This analysis moves beyond simple geographic correlation, aiming instead to identify contextual or systemic factors that may underlie higher local prevalence rates.

### Impact on postoperative course

The final dimension of this study focuses on the postoperative impact of CDI. By analysing how

CDI influences recovery patterns, the incidence of complications, and overall clinical outcomes, we aim to offer clinicians actionable insights that support risk reduction and optimise postoperative care pathways.

In summary, this investigation provides a comprehensive assessment of CDI following cardiac surgery, with particular attention to its multifactorial risk profile and postoperative consequences. Our findings aim to deepen the understanding of CDI in this high-risk population and inform the development of targeted preventive and management strategies in cardiac surgical practice.

## Material and methods

### Patient selection and diagnostic criteria

This retrospective study was conducted at the Department of Cardiac Surgery, J. Strus Municipal Hospital in Poznan, and covered the period from January 2013 to March 2018. During this time, 3502 patients underwent surgical myocardial revascularisation. Among them, 48 cases of CDI were identified. For comparative analysis, a control group of 52 patients without CDI was selected, matched for key demographic parameters.

The diagnosis of CDI was based on the presence of clinical symptoms and laboratory confirmation of CD toxin in stool samples [8]. For patients presenting with diarrhoea during hospitalisation, defined according to World Health Organisation criteria as three or more loose or liquid stools per day or an increase relative to the patient's regular pattern [9], nucleic acid amplification testing was performed. Stool specimens were analysed using the C. diff Quik Chek Complete assay (TECHLAB, USA).

### Retrospective statistical analysis

The retrospective analysis encompassed a broad range of variables, including demographic and laboratory data, preoperative clinical status, surgical characteristics, procedure type and timing, intraoperative durations, and the quantity of transfused blood products. Outcomes assessed included in-hospital mortality, defined as death occurring during the same hospitalisation as the cardiac surgery, and total length of stay.

The study was conducted in accordance with the Declaration of Helsinki and received approval

from the Local Bioethics Committee of the Poznan University of Medical Sciences (approval date: July 3, 2024; ID: KB-533/24). The committee classified the research as a non-interventional, retrospective study based on analysis of existing medical records. Data were extracted from the electronic records of the Department of Cardiac Surgery at J. Strus Multispecialty Municipal Hospital in Poznan between July and August 2024. All personally identifiable information was anonymised at the point of extraction, and patients were assigned sequential numerical codes.

### Perioperative antibiotic therapy

All patients received standard perioperative antibiotic prophylaxis, consisting of cefazolin administered at a weight-adjusted dose. The initial dose was given one hour before the start of surgery, and antibiotic coverage was continued for 48 hours following the procedure.

### Severity stages of CDI and treatment protocol

The severity of CDI was classified into three categories: non-severe (white blood cell count  $\leq 15,000$  cells/mL and serum creatinine  $< 1.5$  mg/dL), severe (white blood cell count  $\geq 15,000$  cells/mL or serum creatinine  $> 1.5$  mg/dL), and fulminant, defined by the presence of hypotension or shock, ileus, or megacolon [10]. Treatment followed the current guidelines of the European Society of Clinical Microbiology and Infectious Diseases [11]. Patients with confirmed CDI based on stool toxin testing were isolated from asymptomatic individuals. Therapeutic regimens included metronidazole and vancomycin, in accordance with established recommendations. Notably, none of the patients in the study group progressed to fulminant CDI.

This structured approach to patient selection, diagnostic confirmation, and treatment standardisation provides the methodological basis for evaluating the clinical impact of CDI in the context of cardiac surgery.

### Statistical analysis

Statistical analyses were adapted to the scale and distribution of each variable. Quantitative data were presented as means accompanied by minimum and maximum values, while qualitative variables were expressed as absolute numbers and percentages.

The normality of continuous variables was evaluated using the Shapiro-Wilk test. Variables with normal distribution and homogeneity of variance were compared using the Student's t-test for independent samples. In contrast, non-normally distributed variables were assessed using the Mann-Whitney U test.

For categorical variables, statistical significance was determined using Pearson's chi-square test for comparisons involving two groups, and the Fisher-Freeman-Halton test for variables with more than two subgroups.

A  $p$ -value of  $\leq 0.05$  was considered statistically significant. All analyses were performed using Statistica 13 software (StatSoft, USA).

## Results

### Incidence of CDI

Out of the 3502 patients subjected to analysis, CDI was identified in 48 individuals, representing an incidence of 1.37%.

### Demographic characteristics

The control group, meticulously selected to be demographically comparable, exhibited no statistically significant differences in terms of age  $p$ -value = 0.4724 and gender  $p$ -value = 0.2949 when compared to the CDI group (see **Table 1**). Similarly, an exploration of the county's location concerning Poznan  $p$ -value = 0.2171 and the ZIP code  $p$ -value = 0.4069 (see **Table 2**) revealed no discernible relationship between the region of residence and the occurrence of CDI.

### Comorbidities and their correlation with CDI

No significant differences were observed between the two study groups concerning the impact of diabetes, hypertension, pulmonary hypertension, hyperlipidemia, kidney failure, asthma, chronic lung disease, cerebrovascular diseases, peripheral vascular diseases, past heart attack, and nicotine use on the risk of CDI (see **Table 3**).

It is noteworthy that both study groups exhibited a high prevalence of hypertension (87.5% and 94.2%) and hyperlipidemia (91.7% and 92.3%).

**Table 1.** Demographic characteristics of patients in the study, comparing those with CDI to those without CDI.

Coefficient	Patients with CDI (N = 48)	Patients without CDI (N = 52)	p-value
Age [years]	67 [51–87]	68 [52–83]	0.4724 <sup>1</sup>
Gender (female/male)	8 [16.7%]/40 [83.3%]	5 [9.6%]/47 [90.4%]	0.2949 <sup>2</sup>

<sup>1</sup> Student's t-test; <sup>2</sup> Pearson's chi-square test; CDI – *Clostridioides difficile* infection

**Table 2.** Distribution of CDI and non-CDI patients according to geographic location and ZIP code.

Coefficient	Patients with CDI (N = 48)	Patients without CDI (N = 52)	p-value
Geographical location	Poznań county	19 [39.6%]	0.2171 <sup>1</sup>
	On the east side	11 [22.9%]	
	On the south side	4 [8.3%]	
	On the west side	10 [20.8%]	
	On the north side	2 [4.2%]	
	Other location	2 [4.2%]	
ZIP code	56-xxx	1 [2.1%]	0.4069 <sup>1</sup>
	60-xxx	5 [10.4%]	
	61-xxx	4 [8.3%]	
	62-xxx	23 [47.9%]	
	63-xxx	1 [2.1%]	
	64-xxx	13 [27.1%]	
	66-xxx	1 [2.1%]	

<sup>1</sup> Pearson's chi-square test; CDI – *Clostridioides difficile* infection; ZIP – Zone Improvement Plan

These findings highlight the prevalent comorbidities within the studied population (see **Table 3**).

### Platelet count and C-reactive protein levels

Statistical significance was attained for a higher number of platelets and an elevated level of C-reactive protein in preoperative laboratory parameters (see **Table 4**), as depicted in **Figure 1**.

### European heart surgical risk assessment system (EuroSCORE)

Values derived from the EuroSCORE were not statistically significant  $p$ -value = 0.8930 but were higher in patients with CDI (Table 5). Conversely, statistical analysis revealed that patients with a higher Body Mass Index (BMI) ( $p$ -value = 0.0028) and lower left ventricular ejection frac-

**Table 3.** Prevalence of comorbidities and health indicators in patients with CDI and patients without CDI.

Coefficient	Patients with CDI (N = 48)	Patients without CDI (N = 52)	p-value
Diabetes	16 [38.1%]	15 [28.9%]	0.3430 <sup>1</sup>
Hypertension	42 [87.5%]	49 [94.2%]	0.2400 <sup>1</sup>
Pulmonary hypertension	1 [2.1%]	1 [1.9%]	0.9544 <sup>1</sup>
Hyperlipidemia	44 [91.7%]	48 [92.3%]	0.9060 <sup>1</sup>
Kidney failure	2 [4.17%]	1 [1.9%]	0.5111 <sup>1</sup>
Asthma	4 [8.3%]	3 [5.8%]	0.6156 <sup>1</sup>
Chronic lung disease	0 [0.0%]	1 [1.9%]	0.3342 <sup>1</sup>
Cerebrovascular diseases	12 [25.0%]	16 [30.8%]	0.5209 <sup>1</sup>
Peripheral vascular diseases	10 [20.8%]	13 [25.0%]	0.6208 <sup>1</sup>
Number of heart attacks experienced	0.48 [0–2]	0.44 [0–2]	0.7409 <sup>2</sup>
Current nicotinism	10 [20.8%]	11 [21.2%]	0.9686 <sup>1</sup>

<sup>1</sup> Pearson's chi-square test; <sup>2</sup> Mann-Whitney test; CDI – *Clostridioides difficile* infection

**Table 4.** Laboratory parameters and clinical characteristics in patients with CDI and patients without CDI.

Coefficient	Patients with CDI (N = 48)	Patients without CDI (N = 52)	p-value
RBC [10 <sup>12</sup> /L]	4.46 [2.58–5.50]	4.57 [2.84–5.51]	0.3865 <sup>3</sup>
WBC [10 <sup>9</sup> /L]	8.53 [4.10–22.30]	8.09 [3.00–16.10]	0.7431 <sup>3</sup>
PLT [10 <sup>9</sup> /L]	257.36 [104.00–759.00]	212.33 [62.00–390.00]	<b>0.0203</b> <sup>1</sup>
Hemoglobin [mmol/L]	7.56 [4.05–9.07]	7.95 [0.03–9.07]	0.4169 <sup>3</sup>
Na [mmol/L]	139.45 [129.00–147.00]	140.45 [134.00–145.00]	0.1269 <sup>3</sup>
K [mmol/L]	4.36 [3.60–5.45]	4.45 [3.32–6.28]	0.0991 <sup>3</sup>
Creatinine [μmol/L]	103.94 [54.00–200.00]	99.94 [56.00–229.00]	0.8685 <sup>3</sup>
HbA1c	6.51 [4.90–11.20]	6.21 [4.90–9.40]	0.3379 <sup>3</sup>
CRP [mg/L]	24.77 [0.50–282.10]	4.17 [0.50–74.40]	<b>0.0142</b> <sup>3</sup>
BMI [kg/m <sup>2</sup> ]	29.92 [21.43–37.77]	27.70 [22.39–36.57]	<b>0.0028</b> <sup>1</sup>
CCS	Class I	2 [4.1%]	0.5106 <sup>4</sup>
	Class II	33 [68.75%]	
	Class III	12 [25.0%]	
	Class IV	1 [2.1%]	
NYHA	Class I	0 [0.0%]	0.0118 <sup>4</sup>
	Class II	0 [0.0%]	
	Class III	38 [79.2%]	
	Class IV	10 [20.8%]	
LVEF [%]	47 [25–60]	50 [29–60]	<b>0.0051</b> <sup>3</sup>
Decreased creatinine clearance	19 [45.2%]	28 [53.9%]	0.4066 <sup>2</sup>

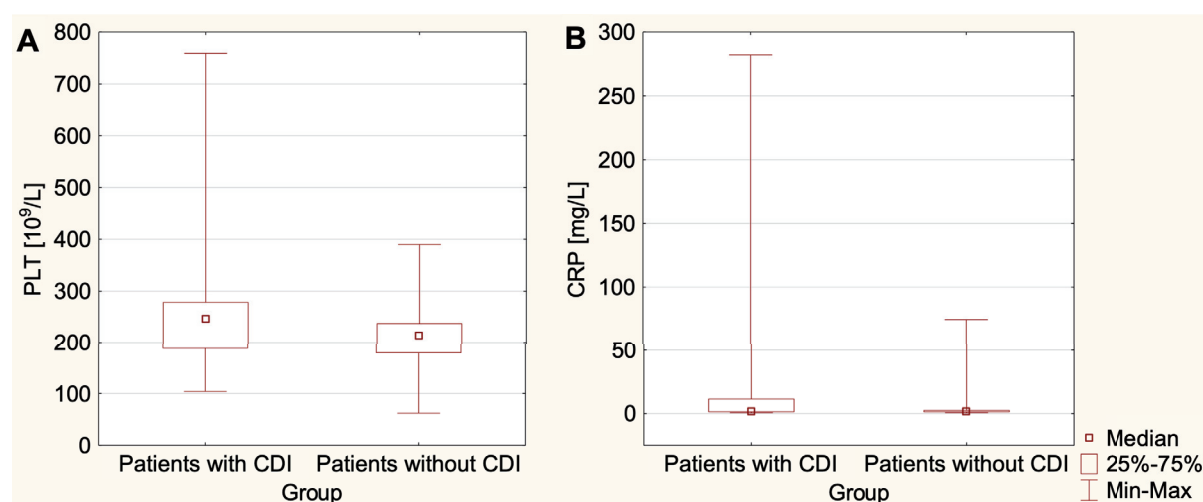
<sup>1</sup> Student's t-test; <sup>2</sup> Pearson's chi-square test; <sup>3</sup> Mann-Whitney test; <sup>4</sup> Fisher-Freeman-Halton test; BMI – Body Mass Index; CCS – Canadian Cardiovascular Society Angina Grading Scale; CDI – *Clostridioides difficile* infection; CRP – C-reactive protein; HbA1c – glycated hemoglobin; K – potassium; LVEF – left ventricular ejection fraction; Na – sodium; NYHA – New York Heart Association classification; PLT – platelet; RBC – red blood cells; WBC – white blood cells

tion (LVEF) ( $p$ -value = 0.0051) in the preoperative period were more prone to developing CDI during hospitalisation, as illustrated in **Figure 2** (see **Table 4**).

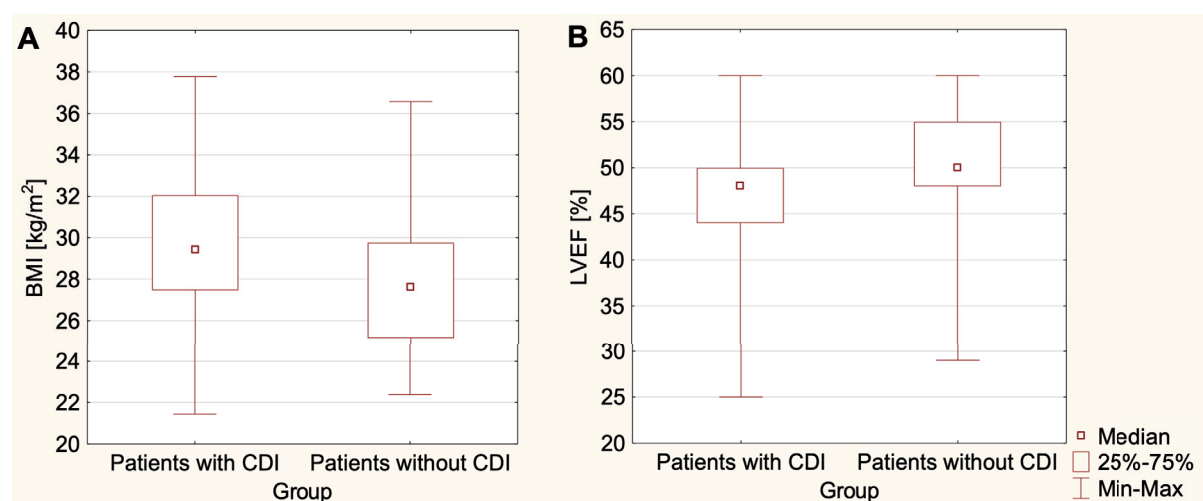
### New York Heart Association (NYHA) scale of heart failure

The NYHA degree of heart failure was significantly higher in patients with CDI,  $p$ -val-

ue = 0.0118 (see **Table 4**). Conversely, parameters related to surgical characteristics, type and timing of surgery, intraoperative times, the number of transfused blood products, and in-hospital mortality did not exhibit statistical significance. However, postoperative CDI significantly extended the total hospitalisation time ( $p$ -value = 0.0001), as depicted in **Figure 3** and **Table 5**.

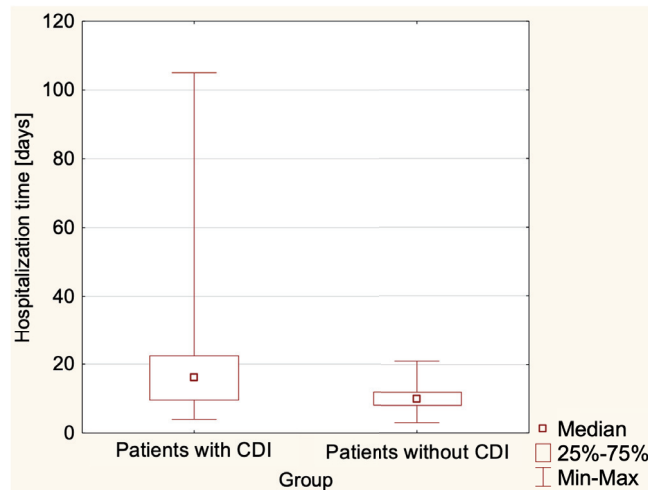


**Figure 1. A:** Platelet Counts (PLT [10<sup>9</sup>/L]) in patients with CDI and patients without CDI. The boxplots depict the distribution of platelet counts, with median values and interquartile ranges indicated. The platelet count is significantly different between the two groups ( $p$ -value = 0.0203). **B:** C-reactive protein levels (CRP [mg/L]) in patients with CDI and patients without CDI. The boxplots illustrate the distribution of CRP levels, showing median values and interquartile ranges. A statistically significant difference is observed between the two groups ( $p$ -value = 0.0142).



**Figure 2. A:** BMI Comparison between patients with CDI (N = 48) and without CDI (N = 52). The figure presents the distribution of Body Mass Index (BMI) in patients with CDI and those without CDI, with medians and interquartile ranges. **B:** Left Ventricular Ejection Fraction (LVEF) comparison between patients with CDI (N = 48) and without CDI (N = 52). The comparison of Left Ventricular Ejection Fraction (LVEF) between patients with CDI and those without CDI.





**Figure 3.** Hospitalisation time in patients with CDI (N = 48) and those without CDI (N = 52) was compared to examine the difference in hospitalisation time between patients with CDI and those without CDI. The boxplots present the distribution of hospitalisation time, including median values and interquartile ranges. Significant divergence is observed between the two groups, with a *p*-value of 0.0001.

**Table 5.** Surgical and procedural characteristics of patients with CDI and patients without CDI.

Coefficient		Patients with CDI (N = 48)	Patients without CDI (N = 52)	<i>p</i> -value
EuroSCORE [points]		3.6 [0.5–29.3]	2.3 [0.6–13.1]	0.8930 <sup>3</sup>
Urgency of operation	Elective	41 [85.4%]	47 [90.4%]	0.3389 <sup>4</sup>
	Urgent	4 [8.3%]	1 [1.9%]	
	Emergency	3 [6.3%]	4 [7.7%]	
	Salvage	0 [0.0%]	0 [0.0%]	
Preoperative ACS		11 [22.9%]	8 [15.4%]	0.3375 <sup>2</sup>
Number of arterial bypasses	0	3 [6.3%]	1 [2.0%]	0.5479 <sup>4</sup>
	1	42 [87.5%]	48 [96.0%]	
	2	3 [6.3%]	1 [2.0%]	
Number of venous bypasses	0	7 [14.6%]	2 [3.9%]	0.0661 <sup>2</sup>
	1	8 [16.7%]	4 [7.7%]	
	2	26 [54.2%]	30 [57.7%]	
	3	7 [14.6%]	16 [30.8%]	
Extracorporeal circulation time [min]		77 [41–143]	75 [52–132]	0.9015 <sup>3</sup>
Aortic cross-clamp time [min]		44 [24–99]	41 [26–76]	0.7980 <sup>3</sup>
Transfusion	Red blood cells [units]	4 [0–20]	3 [0–10]	0.3715 <sup>3</sup>
	Plasma [units]	1 [0–12]	1 [0–8]	0.7826 <sup>3</sup>
Hospitalization time [days]		22 [5–106]	12 [4–22]	<b>0.0001<sup>3</sup></b>

<sup>1</sup> Student's *t*-test; <sup>2</sup> Pearson's chi-square test; <sup>3</sup> Mann-Whitney test; <sup>4</sup> Fisher-Freeman-Halton test; ACS – acute coronary syndrome

## Discussion

The incidence of CDI observed in this study, at 1.3%, is consistent with previous reports in cardiac surgery cohorts, indicating CDI as a significant postoperative complication. Our analysis showed no notable demographic differences between the CDI and control groups in terms of

age, gender, or geographic distribution, supporting a stable comparison basis. In a similar study, Sanaiha et al. [12] reported a CDI incidence of 0.5% among patients undergoing elective cardiac surgeries between 2005 and 2016. They identified advanced age, female sex, and heart failure as significant risk factors for CDI development, while also noting that academic centres had the

highest incidence but the lowest mortality due to superior access to diagnostic and therapeutic resources.

Furthermore, Keshavamurthy et al. [13] reported a CDI incidence of 0.63% among cardiac surgery patients between 2005 and 2011, based on a large multicenter cohort. Their analysis emphasised that patients who developed CDI exhibited a significantly higher burden of comorbidities, including chronic kidney disease, heart failure, and diabetes. These patients also required more frequent surgical reinterventions and had a markedly increased in-hospital mortality compared to non-CDI counterparts.

Our findings are consistent with these observations. In our cohort, we observed that patients with higher BMI and LVEF were more likely to develop CDI, echoing previous studies that have linked obesity and impaired cardiac function to an increased risk of infectious complications. These associations may be explained by the proinflammatory state and immune dysregulation often seen in patients with metabolic syndrome and advanced heart failure, both of which can exacerbate the intestinal barrier dysfunction and dysbiosis that predispose to CDI.

In contrast to the findings by Chatterjee et al. [14], who reported no significant association between BMI and the severity of *Clostridioides difficile* infection, instead identifying female Hsex and hypoalbuminemia as stronger predictors of adverse outcomes, our results align with those of Mulki et al. [15], who demonstrated that a BMI greater than 35 kg/m<sup>2</sup> was independently associated with a 1.7-fold increase in the likelihood of developing severe CDI. This discrepancy may reflect differences in study populations, comorbidity burden, or definitions of disease severity.

Furthermore, the elevated NYHA classification observed among CDI patients in our cohort underscores the potential role of advanced heart failure in predisposing individuals to worse infectious outcomes. Méndez-Bailón et al. [16] similarly reported an increase in in-hospital mortality and CDI incidence in heart failure patients with complex comorbid profiles. Likewise, Mamic et al. [17] highlighted the adverse impact of CDI on heart failure-related hospitalisations, emphasising the importance of early identification and preventive strategies tailored to high-risk cardiac surgery populations.

## Pathophysiological mechanisms

The increased susceptibility to *Clostridioides difficile* infection in cardiac surgery patients can be explained by several converging pathophysiological mechanisms. A key factor is the perioperative administration of broad-spectrum antibiotics, which disrupts gut microbiota composition and impairs colonisation resistance. Foley et al. [18] demonstrated that post-antibiotic disruption of microbial communities in a murine model modulates susceptibility to CDI in a strain-specific manner, showing that *Lactobacillus acidophilus* increases CDI risk. In contrast, *Lactobacillus gasseri* enhances colonisation resistance via bacteriocin-mediated effects and the enrichment of protective Muribaculaceae species.

Moreover, CD itself contributes to intestinal damage through its toxins, particularly toxin A, which disrupts epithelial integrity and induces apoptosis in intestinal cells. Gigli et al. [19] showed that exposure of Caco-2 cells to toxin A significantly reduced transepithelial resistance and tight junction protein expression, impairing mucosal barrier function. This confirms that toxin-mediated epithelial injury is a key driver of CDI pathogenesis, especially in postoperative patients with compromised gut function.

Additional contributing factors include perioperative immunosuppression, use of opioids and proton pump inhibitors, and hemodynamic changes during cardiopulmonary bypass, which may exacerbate dysbiosis and compromise epithelial defence. A better understanding of these mechanisms is essential for developing targeted prophylactic strategies, including microbiota-preserving antibiotic regimens, judicious use of gut-disruptive medications, and adjunctive therapies supporting barrier function.

## Biomarkers and CDI risk

Analysis of laboratory biomarkers in our cohort revealed a strong association between elevated C-reactive protein (CRP) and platelet counts and the incidence of CDI, reinforcing the known link between systemic inflammation and infectious risk. These findings are consistent with a study by Nseir et al. [20], which demonstrated that elevated CRP levels, the neutrophil-to-lymphocyte ratio, and mean platelet volume were significantly associated with both recurrence and mortality in CDI patients. The authors proposed that these



inflammatory markers may reflect host immune response dysregulation and mucosal injury severity.

In our patient group, the presence of elevated CRP and thrombocytosis in CDI cases suggests a hyperinflammatory state that may predispose individuals to worse clinical outcomes. These parameters are readily available and cost-effective, making them attractive candidates for early risk stratification in surgical populations. Incorporating such biomarkers into perioperative surveillance protocols may facilitate earlier diagnosis, targeted interventions, and potentially improved prognosis.

Further prospective studies are warranted to evaluate the predictive value of these and other inflammatory or immune-derived markers—such as procalcitonin, interleukin-6, or faecal calprotectin—in the context of CDI following cardiac surgery. Understanding the interplay between systemic and mucosal inflammation may offer novel insights into disease progression and recovery dynamics.

### **Preventive strategies, healthcare implications, and broader postoperative considerations**

Given the substantial impact of CDI on postoperative outcomes and healthcare resource utilisation, the implementation of effective preventive strategies in cardiac surgery patients is essential. Antibiotic stewardship plays a pivotal role in minimising broad-spectrum antimicrobial exposure, thereby preserving gut microbiota diversity. Additionally, interventions aimed at supporting intestinal microbial balance—such as selective digestive decontamination or the use of carefully selected probiotic strains—may hold promise. However, their efficacy in the cardiac surgery population requires further investigation.

Early identification of high-risk individuals is equally important. Enhanced screening protocols and standardised postoperative monitoring—especially in elderly patients or those with immunosuppression—may facilitate timely recognition of CDI and mitigate complications. In our cohort, CDI was associated with significantly prolonged hospitalisation, consistent with previous reports. Kiersnowska et al. [21] described the substantial economic burden of CDI in Polish hospitals, emphasising increased treatment costs and

extended inpatient care. Similarly, Crabtree et al. [22] identified CDI as a contributing factor to prolonged mechanical ventilation, extended ICU stays, and overall longer hospitalisations in cardiac surgery patients. These data reinforce the urgent need for robust infection prevention and early intervention frameworks tailored to surgical populations.

The complexity of postoperative care in cardiac surgery extends beyond infectious complications. Rare but serious non-infectious events continue to challenge clinicians. We previously reported a case of Abiotrophia defectiva endocarditis requiring urgent mitral valve surgery due to diagnostic delays, highlighting the importance of early pathogen identification and targeted microbiological evaluation in atypical presentations [23]. Likewise, stress-induced Takotsubo syndrome can clinically mimic acute heart failure after valvular or coronary interventions, necessitating careful differential diagnosis in early postoperative decompensation [24]. Late complications may also arise, such as ascending aortic injury secondary to a dislocated sternal wire nearly two decades post-Ravitch procedure, manifesting with tamponade and cardiogenic shock [25].

While these cases are unrelated to CDI, they illustrate the critical need for comprehensive postoperative vigilance. Given the frequently nonspecific and delayed presentation of CDI, clinicians should maintain broad diagnostic awareness and integrate infection risk into the wider context of post-cardiac surgery surveillance.

Future research in this field should prioritise large, multicenter prospective trials integrating microbiota profiling better to understand the dynamics of gut dysbiosis in postoperative CDI. Investigating the role of specific probiotic or prebiotic therapies, alongside the development of predictive models that incorporate clinical, demographic, and microbiome-derived variables, may enable personalised risk stratification and ultimately improve surgical outcomes.

## **Perspectives**

Despite the comprehensive nature of our study, certain limitations should be acknowledged. The single-centre design and relatively small sample

size may limit the generalizability of our findings. Additionally, a more in-depth exploration of the gut microbiota and its role in CDI development could provide further insights into preventive strategies.

## Conclusion

In conclusion, our study highlights the multifactorial nature of *Clostridioides difficile* infection in patients undergoing cardiac surgery, underscoring the interplay between demographic, comorbid, and perioperative risk factors. In particular, elevated *body mass index* and reduced left ventricular ejection fraction emerged as relevant correlates of CDI susceptibility in this population. These findings support more individualised risk stratification and targeted preventive approaches in the perioperative setting.

Moreover, the observed association between CDI and prolonged hospitalisation reinforces the clinical and economic burden of this complication and emphasises the importance of early identification and intervention. Future research involving larger, multicenter cohorts and incorporating comprehensive clinical, microbiological, and microbiome data is warranted to refine risk prediction models further and inform evidence-based prevention strategies tailored to the needs of cardiac surgery patients.

## Disclosures

### Authors' contributions

Łuczak Maciej: conceptualisation, methodology, formal analysis, visualisation, writing – original draft. Greberski Krzysztof: conceptualisation, data curation, methodology, writing – original draft. Burysz Marian: writing – review & editing. Perek Bartłomiej: writing – review & editing. Jarząbek Radosław: conceptualization, data curation. Bugajski Paweł: conceptualisation, supervision, validation. All authors: read and approved the final version of the manuscript.

### Conflict of interest statement

The authors declare no conflict of interest.

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## References

1. Murphy C, Vernon M, Cullen M. Intravenous immunoglobulin for resistant *Clostridium difficile* infection. *Age Ageing*. 2006 Jan;35(1):85-6. <https://doi.org/10.1093/ageing/afi212>. Epub 2005 Nov 22. PMID: 16303776.
2. De Roo AC, Regenbogen SE. *Clostridium difficile* Infection: An Epidemiology Update. *Clin Colon Rectal Surg*. 2020 Mar;33(2):49-57. <https://doi.org/10.1055/s-0040-1701229>. Epub 2020 Feb 25. PMID: 32104156; PMCID: PMC7042002.
3. Vondran M, Schack S, Garbade J, Binner C, Mende M, Rastan AJ, Borger MA, Schroeter T. Evaluation of risk factors for a fulminant *Clostridium difficile* infection after cardiac surgery: a single-center, retrospective cohort study. *BMC Anesthesiol*. 2018 Sep 27;18(1):133. <https://doi.org/10.1186/s12871-018-0597-2>. PMID: 30257648; PMCID: PMC6158878.
4. Sartelli M, Di Bella S, McFarland LV, Khanna S, Furuya-Kanamori L, Abuzeid N, et al. 2019 update of the WSES guidelines for management of *Clostridioides* (*Clostridium*) *difficile* infection in surgical patients. *World J Emerg Surg*. 2019 Feb 28;14:8.
5. Eze P, Balsells E, Kyaw MH, Nair H. Risk factors for *Clostridium difficile* infections - an overview of the evidence base and challenges in data synthesis. *J Glob Health*. 2017 Jun;7(1):010417. <https://doi.org/10.7189/jogh.07.010417>. PMID: 28607673; PMCID: PMC5460399.
6. Zilberberg MD, Shorr AF, Wang L, Baser O, Yu H. Development and Validation of a Risk Score for *Clostridium difficile* Infection in Medicare Beneficiaries: A Population-Based Cohort Study. *J Am Geriatr Soc*. 2016 Aug;64(8):1690-5. <https://doi.org/10.1111/jgs.14236>. Epub 2016 Jun 13. PMID: 27295521.
7. . Gelijns AC, Moskowitz AJ, Acker MA, Argenziano M, Geller NL, Puskas JD, Perrault LP, Smith PK, Kron IL, Michler RE, Miller MA, Gardner TJ, Ascheim DD, Ailawadi G, Lackner P, Goldsmith LA, Robichaud S, Miller RA, Rose EA, Ferguson TB Jr, Horvath KA, Moquete EG, Parides MK, Bagiella E, O'Gara PT, Blackstone EH; Cardiothoracic Surgical Trials Network (CTSN). Management practices and major infections after cardiac surgery. *J Am Coll Cardiol*. 2014 Jul 29;64(4):372-81. <https://doi.org/10.1016/j.jacc.2014.04.052>. PMID: 25060372; PMCID: PMC4222509.
8. Burke KE, Lamont JT. *Clostridium difficile* infection: a worldwide disease. *Gut Liver*. 2014 Jan;8(1):1-6. <https://doi.org/10.5009/gnl.2014.8.1.1>. Epub 2014 Jan 13. PMID: 24516694; PMCID: PMC3916678.
9. World Health Organization. Diarrhoeal disease. 2017 May 2. Retrieved from: <https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease>
10. McDonald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE, Dubberke ER, Garey KW, Gould CV, Kelly C, Loo V, Shaklee Sammons J, Sandora TJ, Wilcox MH. Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clin Infect Dis*. 2018 Mar 19;66(7):e1-e48. <https://doi.org/10.1093/cid/cix1085>. PMID: 29462280; PMCID: PMC6018983.
11. . Debast SB, Bauer MP, Kuijper EJ; European Society of Clinical Microbiology and Infectious Diseases. European Society of Clinical Microbiology and Infec-

- tious Diseases: update of the treatment guidance document for *Clostridium difficile* infection. *Clin Microbiol Infect*. 2014 Mar;20 Suppl 2:1-26. <https://doi.org/10.1111/1469-0691.12418>. PMID: 24118601.
12. Sanaiha Y, Sareh S, Lyons R, Rudasill SE, Mardock A, Shemin RJ, Benharash P. Incidence, Predictors, and Impact of *Clostridium difficile* Infection on Cardiac Surgery Outcomes. *Ann Thorac Surg*. 2020 Nov;110(5):1580-1588. <https://doi.org/10.1016/j.athoracsur.2020.03.037>. Epub 2020 Apr 15. PMID: 32304688.
  13. Keshavamurthy S, Koch CG, Fraser TG, Gordon SM, Houghtaling PL, Soltesz EG, Blackstone EH, Pettersson GB. *Clostridium difficile* infection after cardiac surgery: prevalence, morbidity, mortality, and resource utilization. *J Thorac Cardiovasc Surg*. 2014 Dec;148(6):3157-65.e1-5. <https://doi.org/10.1016/j.jtcvs.2014.08.017>. Epub 2014 Aug 14. PMID: 25242055.
  14. Chatterjee T, Bansal S, Abuzar A, Hussain H, Gupta L. Is Increased BMI a Risk Factor for Developing Severe *Clostridioides Difficile* Infection? A Retrospective Study. *J Community Hosp Intern Med Perspect*. 2022 Nov 7;12(6):43-50. <https://doi.org/10.55729/2000-9666.1123>. PMID: 36816160; PMCID: PMC9924641.
  15. Mulki R, Baumann AJ, Alnabelsi T, Sandhu N, Alhamshari Y, Wheeler DS, Perloff S, Katz PO. Body mass index greater than 35 is associated with severe *Clostridium difficile* infection. *Aliment Pharmacol Ther*. 2017 Jan;45(1):75-81. <https://doi.org/10.1111/apt.13832>. Epub 2016 Oct 28. PMID: 27790736.
  16. Méndez-Bailón M, Jiménez-García R, Hernández-Barra V, Miguel-Díez J, Miguel-Yanes JM, Muñoz-Rivas N, Lorenzo-Villalba N, Carabantes-Alarcon D, Zamorano-León JJ, Astasio-Arbiza P, Ortega-Molina P, López-de-Andrés A. Heart Failure Is a Risk Factor for Suffering and Dying of *Clostridium difficile* Infection. Results of a 15-Year Nationwide Study in Spain. *J Clin Med*. 2020 Feb 25;9(3):614. <https://doi.org/10.3390/jcm9030614>. PMID: 32106444; PMCID: PMC7141109.
  17. Mamic P, Heidenreich PA, Hedlin H, Tennakoon L, Staudenmayer KL. Hospitalized Patients with Heart Failure and Common Bacterial Infections: A Nationwide Analysis of Concomitant *Clostridium Difficile* Infection Rates and In-Hospital Mortality. *J Card Fail*. 2016 Nov;22(11):891-900. <https://doi.org/10.1016/j.cardfail.2016.06.005>. Epub 2016 Jun 16. PMID: 27317844.
  18. Foley MH, McMillan AS, O'Flaherty S, Thanissery R, Vanhoy ME, Fuller MG, Barrangou R, Theriot CM. Differential modulation of post-antibiotic colonization resistance to *Clostridioides difficile* by two probiotic *Lactobacillus* strains. *mBio*. 2025 Aug 13;16(8):e0146825. <https://doi.org/10.1128/mbio.01468-25>. Epub 2025 Jul 21. PMID: 40689613; PMCID: PMC12345269.
  19. Gigli S, Seguela L, Pesce M, Bruzzese E, D'Alessandro A, Cuomo R, Steardo L, Sarnelli G, Esposito G. Cannabidiol restores intestinal barrier dysfunction and inhibits the apoptotic process induced by *Clostridium difficile* toxin A in Caco-2 cells. *United European Gastroenterol J*. 2017 Dec;5(8):1108-1115. <https://doi.org/10.1177/2050640617698622>. Epub 2017 Mar 13. PMID: 29238589; PMCID: PMC5721977.
  20. Nseir W, Khamisy-Farah R, Amara A, Farah R. The Prognostic Value of Inflammatory Markers in *Clostridium difficile*-associated Diarrhea. *Isr Med Assoc J*. 2019 Oct;21(10):658-661. PMID: 31599506.
  21. Kiersnowska Z, Lemiech-Mirowska E, Ginter-Kramarczyk D, Kruszelnicka I, Michałkiewicz M, Marczak M. Problems of *Clostridium difficile* infection (CDI) in Polish healthcare units. *Ann Agric Environ Med*. 2021 Jun 14;28(2):224-230. <https://doi.org/10.2644/aaem/119321>. Epub 2020 Apr 2. PMID: 34184502.
  22. Crabtree T, Aitchison D, Meyers BF, Tymkew H, Smith JR, Guthrie TJ, Munfakh N, Moon MR, Pasque MK, Lawton J, Moazami N, Damiano RJ Jr. *Clostridium difficile* in cardiac surgery: risk factors and impact on postoperative outcome. *Ann Thorac Surg*. 2007 Apr;83(4):1396-402. <https://doi.org/10.1016/j.athoracsur.2006.10.067>. PMID: 17383346.
  23. Wilawer M, Elikowski W, Greberski K, Ratajska PA, Welc NA, Lisiecka ME. Abiotrophia defectiva endocarditis - Diagnostic and therapeutic challenge: Case report. *IDCases*. 2023 Oct 8;34:e01906. <https://doi.org/10.1016/j.idcr.2023.e01906>. PMID: 37867569; PMCID: PMC10585279.
  24. Elikowski W, Małek-Elikowska M, Greberski K, Rzym-ski S, Kołowrotkiewicz A, Furmaniuk J, Bugajski P. Takotsubo syndrome following mitral valve replacement and left anterior descending coronary artery bypass grafting. *Pol Merkuriusz Lekarski*. 2019 Jan 28;46(271):36-41. PMID: 30810114.
  25. Greberski K, Jarząbek R, Perek B, Łuczak M, Bugajski P. Exceptional life-threatening complication 19 years after Ravitch correction of pectus excavatum. *J Card Surg*. 2021 Oct;36(10):3971-3972. <https://doi.org/10.1111/jocs.15889>. Epub 2021 Aug 2. PMID: 34339529.