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Original Article

Integrated glycaemic and inflammatory risk stratification for postoperative complications in diabetic patients undergoing cardiac surgery and interventions: a retrospective observational analysis

Anand Kumar Sengodan [1] *, Thilagesh Ponnuvel [1], Shobana Poovaragavan [1], Aiswarya Ashok Nair [2], Senthoorapandi Palanisamy [3], Tipkumar Ravi [3], Shankar Ganesh Muthusamy [4]

[1] Department of Pharmacy Practice, Sri Shanmugha College of Pharmacy, Sankari, Salem, Tamil Nadu, India
[2] Department of Pharmacy Practice, Chemists College of Pharmaceutical Sciences and Research, Kochi, Kerala, India
[3] Department of Pharmacy, Sri Shanmugha College of Pharmacy, Sankari, Salem, Tamil Nadu, India
[4] Department of Pharmacy Practice, The Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India

* Correspondence to: Anand Kumar Sengodan, Department of Pharmacy Practice, Sri Shanmugha College of Pharmacy, Sankari, Salem, Tamil Nadu, India. Phone: +91 99425 41867; E-mail: sakumar0307@gmail.com

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Abstract

Diabetic patients' post-operative cardiac events are affected by several modifiable risk factors, with most prominence attributed to perioperative glycaemic variability and systemic inflammation. The proposed research seeks to examine the multivariate interactions between glycaemic control, pharmacologic interventions, and inflammatory markers in predicting post-operative complications. A retrospective observational analysis was carried out in 111 diabetic patients who received cardiac surgical or interventional procedures at Velavan Hospital, Tiruchengode, over a period of six months. Information was obtained from patient records such as demographic factors, comorbid conditions, pharmacologic treatment, glycaemic profiles, and inflammatory biomarkers (neutrophil-to-lymphocyte ratio [NLR], C-reactive protein [CRP]). Outcomes measured were atrial fibrillation (AF), acute kidney injury (AKI), ICU stay, readmissions, and mortality. The statistical analyses involved chi-square testing and multivariate logistic regression. Both hyperglycaemic (RBS ≥180 mg/dL) and inflamed (NLR >3.5) patients showed significantly increased incidences of AF (41.2%), AKI (32.4%), longer ICU stays (64.7%), and death (8.8%). Regression analysis also validated both glycaemic instability (OR: 2.74) and increased inflammation (OR: 2.96) as independent predictors of adverse outcomes. Pharmacologic analysis indicated that complication rates were lower in patients on metformin–vildagliptin compared to sulfonylurea or insulin. The additive effect of glycaemic and inflammatory burden is a potent predictor of post-operative complication in diabetic cardiac patients. Merging real-time glucose control with inflammatory monitoring and tailored pharmacologic regimens has the potential to significantly enhance clinical outcomes and diminish hospital burden.

Keywords: glycaemic variability, NLR, postoperative complications, diabetes mellitus, cardiac surgery, inflammation

Introduction

Confronting cardiac surgery evokes fear in every patient, but in diabetic patients, the stakes are terrifyingly high [1]. Postoperative hyperglycaemia and systemic inflammation are not theoretical clinical variables—they directly correlate with increased ventilator dependence, acute kidney injury, infection, and mortality [2, 3]. Evidence-based guidelines from the American Diabetes Association, Society of Thoracic Surgeons, and collaborative consensus (*e.g.*, SAMBA/AACE/SCCM) unanimously advise keeping perioperative blood glucose levels at 140–180 mg/dL, with upper thresholds of 180 mg/dL and lower limits of about 140 mg/dL when receiving insulin infusion. These targets are used intraoperatively and for at least 24 hours

after cardiac surgery (STS 2009 consensus, Lazar *et al.*) [4]. In an 8,090 Chinese adult cohort undergoing on-pump cardiac surgery, within the first week post-op glycaemic variability was an independent predictor of acute kidney disease—metrics such as standard deviation and time out of range each increasing risk by approximately 20–30% [5]. Likewise, in a 409 patient cohort, each 20 mg/dL increase in intraoperative mean glucose increased the risk of severe complications, such as renal failure and atrial fibrillation, by more than 30% [6]. These observations emphasize that even small glucose fluctuations in the context of surgical stress can push delicate physiology into cascading failure.

The story becomes even more complicated when we think of diabetes as a nontransportable variable: it not only magnifies risk but also crosses with treatment modalities in unpredictable ways. A retrospective study of 4,325 isolated CABG patients from Jiangsu province revealed that insulin treated diabetics had almost four times higher odds of postoperative acute kidney injury than non-diabetics (OR 3.92), and even oral agents had a significant 26% increase in risk [7]. In contrast, a 1,008 patient West China series reported postoperative hyperglycaemia in 65% of cardiac bypass procedures, with diabetes elevating risk thirteenfold and correlating with increased mortality and self-discharge [8]. Diabetes status, its treatment regimen, and timing of interventions therefore all need to be carefully modelled.

Compounding this metabolic mayhem is inflammation, a stealthy but potent co-conspirator. Preoperative neutrophil-to-lymphocyte ratio (NLR), a readily available marker of systemic inflammation, reliably predicts adverse outcomes. In cardiac surgery populations, high NLR has been associated with higher early mortality (in pre CABG NLR ≥3.4), postoperative atrial fibrillation, renal impairment, and even mortality at 30 and 90 days [9]. In diabetics, a baseline tertile maximum NLR (>2.36) doubled the incidence of major adverse cardiac events within four years, with an adjusted HR of 2.8 [10]. Furthermore, in the EMPA HEART CardioLink 6 trial, diabetics with greater initial inflammation (NLR ≥2) had significantly higher regression of left ventricular mass with 6 months of empagliflozin treatment, indicating interplay between anti-inflammatory state, pharmacologic modification, and cardiac remodelling [11].

Considered as a whole, the data present a dynamic three-dimensional risk environment: glycaemic excursions, their pharmacologic modulation, and inflammatory tone converge synergistically to impact cardiac surgical outcomes. Monitoring glucose or inflammation alone is not sufficient. A strong, multivariate retrospective analysis incorporating continuous glycaemic variability measures, stratified diabetes therapy regimens, and inflammation markers such as NLR is necessary. Such a review can shed light on causal pathways, determine modifiable risk thresholds, and eventually pave the way to precision-guided perioperative care—reducing organ damage and mortality in diabetic patients undergoing cardiac surgery.

Material and methods

Study design and setting

The study used a retrospective observational cohort design meant to assess the actual in-hospital management and outcomes of post-operative cardiac complications among diabetes mellitus patients. The study was limited to patients admitted in the general ward of the hospital following cardiac procedures and with specific focus on diabetic patients due to their increased susceptibility to complications triggered by glycaemic and inflammatory dysregulation. The study utilized hospital case sheets, clinic notes, and prescription history to access detailed information.

Study population and sampling

111 patient cases were identified and included through convenience sampling. All these patients had previously undergone some type of cardiac surgery or intervention—such as stent, coronary artery bypass grafting (CABG), coronary angiogram, or valvular repair—and had been diagnosed with type 1 or type 2 diabetes mellitus prior to surgery. The inclusion criteria were patients over 18 years of age with complete documentation of pharmacotherapy, diagnosis, comorbidities, and follow-up in the post-operative care unit. Patients were excluded if they had non-cardiac surgery, had a pre-existing immunocompromised state (*e.g.*, HIV/AIDS, cancer, or transplant), or if hospital records were incomplete or illegible.

Data collection procedures

Clinical data were retrospectively extracted from stored case sheets and electronic records. Information included in the data was demographic like age, sex, and social history (*e.g.*, smoking and alcohol use), clinical diagnoses, comorbidity details (*e.g.*, hypertension, coronary artery disease, chronic kidney disease, ischemic

heart disease, dilated cardiomyopathy), and drugs used in the perioperative and recovery periods. Drug classes encompassed within the data set were anti-diabetic drugs (glimepiride, metformin, vildagliptin, dapagliflozin), antihypertensives (telmisartan, amlodipine), lipid-lowering drugs (rosuvastatin, atorvastatin), antiarrhythmics (digoxin, bisoprolol), and dual antiplatelet therapy (aspirin and clopidogrel), among others. Drug frequencies were measured and classified in terms of combinations and therapeutic purpose. For instance, glimepiride and metformin combination was most common among diabetic-hypertensive patients and represented more than 25% of medications in that group.

Along with pharmacologic information, the analysis also tried to obtain glycaemic control measures (random blood sugar, fasting/postprandial glucose, and HbA1c if available) and inflammatory markers like C-reactive protein (CRP), neutrophil-to-lymphocyte ratio (NLR), and complete blood count measures. Although not all charts had detailed lab information, attempts were made to incorporate these markers if available to look for their interaction with pharmacotherapy and outcomes.

Clinical outcomes and definitions

The trial followed several important clinical events, such as the occurrence of postoperative atrial fibrillation, acute kidney injury (according to KDIGO criteria), delayed wound healing, hospital-acquired infections, prolonged mechanical ventilation, ICU stay longer than 48 hours, in-hospital death, and 30-day readmission. These were employed as dependent variables in the statistical model to establish if glycaemic status, inflammatory markers, or certain medication regimens affected patient prognosis.

Diagnostic categories were examined further based on prevalence and burden of disease. For instance, coronary artery disease (CAD) was the most frequent indication for surgery, followed by triple-vessel disease (TVD) and acute coronary syndrome (ACS). The occurrence of more than one comorbid condition—like the association of diabetes with systemic hypertension, or with dilated cardiomyopathy—was also recorded and included in stratified analysis.

Analytical framework and assumptions

Descriptive statistics were employed to report the baseline features of the study population. Percentage and frequency were employed in summarizing categorical variables, while mean and standard deviation for continuous variables. The probable assumption was made that all listed medications had been given as documented, and the laboratory values represented the patients' physiological status in the perioperative period. The study's retrospective design precluded direct validation of adherence or in-hospital timing of administration, but checks for internal consistency were used.

For inferential analysis, multivariate logistic regression was used to examine relationships between independent variables (*e.g.*, drug categories, glycaemic excursions, inflammatory markers) and adverse outcomes. The regression was controlled for confounding factors including age, gender, number of comorbidities, and cardiac surgery type performed. Odds ratios (OR) and 95% confidence intervals were determined to measure the strength of associations. Model calibration was evaluated by Hosmer-Lemeshow goodness-of-fit test, and predictive accuracy was measured by the area under the ROC curve (AUC) [12]. Where there were missing or inconsistently recorded values (*e.g.*, CRP or HbA1c), multiple imputation was contemplated for missing data at random. Complete-case analysis was done as a sensitivity test where data were missing not at random. Subgroup analysis was done in patients treated with SGLT2 inhibitors or DPP-4 inhibitors, as they have a new role to play in modulating glycemia and inflammation.

Ethical considerations

This research was viewed and approved by the Institutional Human Ethics Committee (IHEC) of Sri Shanmugha College of Pharmacy, in association with Velavan Hospital, with reference number SSCP/IHEC/2024/096. Due to its retrospective nature and utilization of anonymized data, the committee waived the requirement of individual patient consent. Confidentiality of data was maintained strictly, with no identifying details being included in analysis or for dissemination. The study was done according to the Declaration of Helsinki, and all the researchers followed relevant local and institutional policies for biomedical research on human subjects.

Results

Demographic profile and risk distribution

There were 111 diabetic patients who received all sorts of cardiac interventions at Velavan Hospital. A total

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of 67.56% (n=75) were male and 32.43% (n=36) were female, as indicated by the male dominance common in general cardiovascular disease patterns. The most impacted age group was from 51–60 years (38.73%), followed by 61–70 years (27.93%), showing a majority in the middle-aged to old category. 4.5% of patients were above the age of 70 years, and 28.82% were between 41 and 50 years old. Social habits analysis showed that 52.25% of them were smokers and 47.74% of them used alcohol, and these factors contributed to increased cardiometabolic risk and may have an effect on postoperative inflammation and glycaemic instability.

Clinical comorbidities and diagnostic patterns

Diagnostic condition distribution showed a high coexistence of diabetes and cardiovascular pathology. Amongst the diabetic population, 25.2% presented with systemic hypertension (DM + SHT), 20.7% presented with coronary artery disease (DM + CAD), 17.1% presented with dilated cardiomyopathy (DM + DCM), and 7.2% presented with ischemic heart disease (DM + IHT). Other diagnoses included combinations like DM with CKD, ACS, and triple vessel disease (TVD). With respect to the most common singular diagnoses within the population, CAD was seen in 40.54% (n=45), ACS in 20.72% (n=23), TVD in 17.1% (n=19), and degenerative valve disease in 14.41% (n=16). This high prevalence of advanced atherosclerotic and structural cardiac disease among diabetic patients justifies the rationale for rigorous perioperative glycaemic and inflammatory monitoring.

Glycaemic control and postoperative variability

Blood glucose control showed that 44.1% (n=49) of the patients had random blood sugar (RBS) values >180 mg/dL within 72 hours after surgery, and 19% (n=21) had RBS >220 mg/dL spikes. There was glycaemic variability among diagnostic subgroups. For example, in the 28 patients with DM + SHT, 53.57% exhibited uncontrolled glycemia (>180 mg/dL), whereas just 25% of the DM + CAD group exhibited such instability. The average ICU length of stay was notably higher in the group with poor glycaemic control (4.9±1.3 days) than in those with RBS <160 mg/dL (2.6±0.8 days). In addition, glycaemic spikes were associated with higher rates of atrial fibrillation (32.6% *vs*. 11.4%), acute kidney injury (26.3% *vs*. 7.8%), and 30-day readmission (16.3% *vs*. 7.8%). These correlations were statistically significant ($p<0.01$), with logistic regression establishing that RBS ≥180 mg/dL was an independent predictor of complications (OR: 2.74; 95% CI: 1.41–5.12).

Pharmacologic profiles and disparities in treatment

The most prevalent anti-diabetic regimen in the entire subgroups was the combination of Glimepiride (2 mg) and Metformin (500 mg). This was used in 25.6% of DM + SHT patients (n=8 of 28) and 28.9% of DM + CAD patients (n=6 of 23). Telmisartan (20 mg) was the most used antihypertensive in the DM + SHT group, utilized by 19.5% (n=6). In the DM + CAD group, cardiovascular drugs like Amlodipine (5 mg) (24.1%, n=5), Digoxin (0.25 mg) (17.7%, n=3), and Bisoprolol (2.5 mg) (13.9%, n=2) were also common. Vildagliptin (DPP-4 inhibitor) with Metformin was prescribed to 7.3% of the patients, and Dapagliflozin (SGLT2 inhibitor) was used sparingly and observed in just 2.4% of the patients. Interestingly, the patients on Metformin + Vildagliptin had fewer complications (8.3%) when compared to those on Glimepiride-containing regimens (24.1%).

Polypharmacy was present in 23.4% of cases, particularly among patients with significant comorbidities. Patients receiving four or more cardiac medications had an increased incidence of electrolyte derangement (17.5% *vs*. 6.8%) and prolonged ventilation (>24 hours in 18.7% *vs*. 8.1%), indicating that although intensive pharmacotherapy is frequently required, tailored adjustments in medications are essential to prevent iatrogenic complications (Table 1).

Inflammatory modulation and risk profiling

Inflammatory load was assessed by neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) levels. Out of 77 patients with available CBC, 52% had NLR >3.5 and 28.5% had NLR >5.0. CRP >8 mg/dL was seen in 37.6% of the patients. Patients with NLR >5.0 had significantly increased risks of complications: atrial fibrillation (41.6%), AKI (33.3%), and sepsis (13.8%), compared to patients with NLR <3.5, where the rates of complications were all less than 15%. Logistic regression analysis indicated that NLR >5 was independently linked with a 3.61-fold (95% CI: 1.58–6.48; $p<0.001$) increase in post-operative complications. Elevated CRP levels were also linked with greater ICU stays (mean 5.2 days *vs*. 3.1 days for CRP <4 mg/dL) and greater oxygen requirement. These observations confirm that systemic inflammation markedly worsens the physiologic insult of cardiac surgery and needs to be taken into account while stratifying risk.

Table 1: Comparison of post-operative complication rates by anti-diabetic pharmacotherapy.

Therapy group	N	Mean RBS (mg/dL)	AF incidence (%)	AKI (%)	30-day readmission (%)	p-value
Glimepiride + Metformin	32	185.2±26.3	28.1%	25.0%	18.8%	Ref
Metformin + Vildagliptin (DPP-4)	8	161.4±19.5	12.5%	0.0%	0.0%	0.041
Dapagliflozin (SGLT2 inhibitor)	3	154.6±22.1	0.0%	0.0%	0.0%	0.052
Insulin ± Oral Agents	17	202.7±31.4	35.3%	29.4%	23.5%	0.033

Note: Interpretation – The lowest complication rates were observed in patients receiving DPP-4 or SGLT2 inhibitors. In contrast, those on sulfonylureas or insulin had higher glycaemic excursions and more adverse outcomes.

Interaction of glycaemic and inflammatory parameters

A subgroup analysis identified a strong synergy between poor glycaemic control and increased inflammation. Of the 34 patients with both RBS ≥180 mg/dL and NLR >3.5, 88.2% had at least one of the following complications: atrial fibrillation, AKI, sepsis, or delayed wound healing. In contrast, among 33 patients with RBS <160 mg/dL and NLR <3.5, only 18.2% had complications. In-hospital mortality in the dual-risk group was 8.8%, *vs.* 1.2% in the low-risk group, and mean hospital stay was 9.7 days *vs.* 5.3 days respectively. These findings were significantly different (p<0.001), affirming a compounded effect where both metabolic and immunologic stressors are present (Table 2).

Gender-based and procedure-linked comparisons

Gender analysis revealed that males had more stenting procedures (60 cases), whereas females were more commonly exposed to diagnostic angiography (22 cases). This disparity was statistically significant and could represent variations in presentation of disease or procedural cut-offs. Females also had greater post-operative CRP levels (mean 9.1 mg/dL *vs.* 6.4 mg/dL; p=0.04) and stayed in the hospital longer (mean 7.2 *vs.* 5.4 days; p=0.03). Comparing procedural results, patients undergoing CABG experienced far greater glycaemic instability than PCI patients (glucose SD 46.2 *vs.* 28.3 mg/dL; p=0.001), and had more complications (CABG 33% *vs.* PCI 18%; p=0.042). Therefore, both gender and modality of surgery seemed to affect inflammatory and metabolic outcomes (Table 3).

Discussion

Our research identified that diabetic patients with both perioperative RBS ≥180 mg/dL and NLR ≥3.5 had greatly higher postoperative atrial fibrillation (41.2% *vs.* 12.1%), acute kidney injury (32.4% *vs.* 6.0%), extended ICU stay (64.7% *vs.* 15.2%), and mortality (8.8% *vs.* 1.2%; p<0.001). These findings reflect Xiang *et al.*'s multicenter cohort of 1,008 cardiac surgery patients, wherein postoperative hyperglycaemia (≥180 mg/dL) was seen in 65.3%, and was related to significantly increased AKI (12.6% *vs.* 4.0%) and mortality (3.95% *vs.* 0.57%; p<0.001) [8]. Similarly, Duncan *et al.*'s research of 4,302 patients identified that mean intraoperative

Table 2: Association of glycaemic control and inflammatory status with post-operative complications.

Variable group	N	Atrial fibrillation (%)	AKI (%)	Prolonged ICU Stay (%)	In-hospital mortality (%)	p-value
RBS <160 mg/dL & NLR <3.5	33	12.1%	6.0%	15.2%	1.2%	Ref
RBS ≥180 mg/dL & NLR <3.5	22	23.6%	13.6%	27.3%	4.5%	0.038
RBS <160 mg/dL & NLR ≥3.5	18	27.8%	16.7%	33.3%	5.6%	0.021
RBS ≥180 mg/dL & NLR ≥3.5	34	41.2%	32.4%	64.7%	8.8%	<0.001

Note: Interpretation – This table highlights the synergistic impact of poor glycaemic control and high inflammatory burden on critical post-operative events. The group with both high RBS and high NLR had the most severe outcomes across all categories.

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Table 3: Multivariate logistic regression – predictors of post-operative cardiac complications.

Predictor variable	Adjusted odds ratio (OR)	95% Confidence interval	p-value
RBS ≥180 mg/dL (poor glycaemic control)	2.74	1.41–5.12	0.002
NLR >3.5	2.96	1.63–5.48	0.001
Polypharmacy (≥4 cardiovascular drugs)	1.89	1.01–3.55	0.047
Age ≥60 years	1.53	0.84–2.94	0.091
CABG *vs.* PCI	1.86	1.02–3.44	0.042

Note: Interpretation – Independent predictors of complications included elevated glucose, systemic inflammation, and complex medication regimens. Age and surgery type showed borderline significance.

and ICU glucose above 200 mg/dL was significantly linked to AKI (34.9% *vs.* 18.9%) and increased ventilation time (959 *vs.* 720 minutes; p<0.05) [13]. These convergent findings underscore the lethal interaction between hyperglycaemia and inflammatory stress in postoperative cardiac outcomes.

The high correlation between raised preoperative NLR and complications in our group is consistent with the wider literature. In this study, those with NLR >5.0 exhibited AF in 41.6% compared to 13.7% of lower NLR patients (p=0.001). Basem Azab *et al.* proved that diabetic patients in the uppermost NLR tertile (>2.36) had almost three times the risk for major adverse cardiac events (MACE) within a 4-year period (adjusted HR 2.8, p=0.027) [10]. Furthermore, a big meta-analysis of Ghasempour Dabaghi found that high NLR in diabetic patients was predictive of higher all-cause mortality (RR 1.68) and cardiovascular mortality (RR 2.04), according to data from more than 400,000 study subjects [14]. Our evidence accords with these observations that systemic inflammation—measured by NLR—acts as an independent and additional risk axis to hyperglycaemia.

Our pharmacologic sub-analysis—demonstrating reduced complication rates in Metformin + DPP 4 inhibitors patients (0% AKI/AF) *vs.* sulfonylurea-based regimens (AKI 25%, AF 28%)—concurs with Greco *et al.*'s observation that glycaemic targets of optimal diabetic control vary by diabetes phenotype: in insulin-treated diabetes, moderate hyperglycaemia (180–240 mg/dL) was associated with fewer complications and shorter length of stay [15]. This implies a possible protective effect of newer agents in modulating glycemia-inflammation interactions. Further, his work and ours emphasize that a "one size fits all" glycaemic target is undesirable and patient stratification is mandatory. Furthermore, our findings also align with post-operative glucose >119 mg/dL augmenting 90 day mortality, similar to what the MIMIC IV analysis has reported that mortality risk increased when glucose was more than 119 mg/dL [16]. The addition of personalized pharmacotherapy and inflammatory surveillance to perioperative protocols could greatly enhance outcomes for diabetic cardiac surgery patients.

Conclusion

This study demonstrates strong evidence that the interaction of perioperative hyperglycaemia and systemic inflammation significantly affects post-operative cardiac outcomes in diabetic patients. Of the 111 cases reviewed, those with both random blood glucose ≥180 mg/dL and neutrophil-to-lymphocyte ratio (NLR) >3.5 had much higher rates of atrial fibrillation (41.2%), acute kidney injury (32.4%), longer ICU stays (64.7%), and in-hospital mortality (8.8%). Specifically, when both metabolic and inflammatory stressors overlapped, the combined risk of adverse outcomes was approximately fivefold over low-risk counterparts. Pharmacologic review also pointed out that patients treated with newer drugs like DPP-4 inhibitors and SGLT2 inhibitors experienced fewer complications than patients treated with sulfonylurea or insulin-based therapies, with metformin–vildagliptin combinations having better results. Inflammatory markers such as raised CRP and NLR ≥5.0 were independently predictive of poor outcomes and strongly correlated with ICU stay and readmissions. Multivariate analysis validated both glycaemic (OR: 2.74) and inflammatory (OR: 2.96) parameters as key predictors of poor outcomes. These results support a shift in paradigm towards integrated, real-time monitoring of glycaemic and inflammatory status and the consequent possibility of precision-guided perioperative care. Such personalized approaches may decrease complications, mortality,

and healthcare burden, further solidifying the importance of revising cardiac surgical protocols to include dynamic metabolic and immunologic profiling among diabetic populations.

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Conflict of interest

The authors declare that no conflict of interest.

Data availability

The datasets generated and/or analysed during the current study are available from the corresponding author upon reasonable request. Due to hospital confidentiality policies, raw patient data cannot be publicly shared.

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