"CAROL DAVILA" UNIVERSITY OF MEDICINE AND PHARMACY BUCHAREST DOCTORAL SCHOOL MEDICINE



Impact of Abdominal Surgical Procedures on Cardiovascular Functional Dynamics PhD THESIS SUMMARY

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Introduction

Annually, over 300 million surgical procedures are performed worldwide. One third of reported deaths occur within the first 30 postoperative days due to complications [1], [2]. Cardiovascular diseases account for more than one third of deaths in Romania, with 19% of total deaths attributed to ischemic heart disease—this percentage being double the European average. Mortality from stroke is the second leading cause of death, responsible for 16% of total deaths. One third of deaths caused by stroke and myocardial infarction occur prematurely in people under 70 years of age, with the most impactful risk factors being poor diet, smoking, and excessive alcohol consumption [3], [4]. Postoperative cardiovascular complications account for a significant proportion of total complications following abdominal surgery. However, current literature data are heterogeneous, reporting rates that vary widely from 2% to 35% [5], [6], [7].

Digestive surgery has significantly advanced in recent decades, allowing the treatment of a growing number of pathologies and, consequently, patients. Although technological advancements and modern surgical procedures have brought substantial benefits, a series of risks to which patients are exposed still remain. The cardiovascular system is most frequently associated with these risks, as complications in this domain have high rates of morbidity and mortality, also incurring additional costs. While cardiovascular complications following cardiothoracic surgery have been extensively studied, data on the occurrence of perioperative cardiac complications in abdominal surgical pathology remain limited.

Complications occurring during a surgical intervention or in the immediate postoperative period can be major non-fatal events but with significant impact on the patient's clinical course during hospitalization and in the long term. Given this, identifying patients at risk for cardiovascular complications and, more importantly, the associated modifiable risk factors, is imperative. Improving postoperative outcomes and reducing cardiac complications is possible only by identifying these risk factors and implementing appropriate countermeasures. Preventive strategies and appropriate, individualized management will be dictated by early risk detection, thus allowing early intervention in case of complications. This approach ensures faster and safer recovery for the patient. A personalized approach based on individual risk factors will significantly impact the quality of medical care and, naturally, patient outcomes.

Among the most frequent pathologies arising in the preoperative period are tachyarrhythmias. These are most often benign and do not pose a life-threatening risk. However, certain conditions, causes, and factors play a role in the occurrence and development of rhythm or conduction disorders during the preoperative period.

Cardiac electrical activity and the occurrence of tachyarrhythmias can be influenced by pharmacological and anesthetic agents administered preoperatively. There are also non-pharmacological stimuli related to surgical preparation and performance that can affect electrical activity, triggering rhythm disturbances such as stress, anxiety, pain, or physical discomfort.

Although the number of deaths and postoperative complications has significantly decreased over recent decades, it is important to note the extreme variability in how such complications are reported globally. This creates real barriers to evaluating how they are managed and assessing the true magnitude of postoperative cardiovascular complications. The development of comprehensive and rigorous assessments, individualized risk scores tailored to each patient, and prognostic models for cardiovascular risk are future necessities in achieving complete perioperative evaluation aimed at reducing postoperative morbidity and mortality.

The main goal of our study is to assess the functional parameters of the cardiovascular system during the perioperative period in patients undergoing abdominal surgery. Our objectives include the creation of a database comprising monitored perioperative patients, performing functional tests to evaluate cardiovascular activity, identifying anesthetic and surgical management factors that may influence cardiovascular function, and ultimately proposing prophylactic measures to reduce cardiovascular risk in patients undergoing abdominal surgery.

This work aims to emphasize the importance of a multidisciplinary approach to patients requiring non-cardiac surgery. The occurrence of cardiovascular events during the perioperative period increases patient morbidity and mortality, with profound implications for the healthcare system. Many of the triggering factors can be considered modifiable or at least avoidable. In cases where preventing such events is not possible due to the emergency nature of the surgical intervention, cardiac and biological monitoring of the patient, as well as interdisciplinary collaboration, often represent the key to success in each individual case. Further studies are necessary to deepen the understanding of monitoring and cardiac-targeted therapy in patients undergoing non-cardiac surgery.

Chapter 1. Cardiovascular Risks Associated with Non-Cardiac Surgeries

Non-cardiac surgeries can be associated with significant cardiovascular risks, particularly during the perioperative period. These complications may include arrhythmias, myocardial ischemia, hemodynamic dysfunction, and secondary complications induced by anesthesia. A thorough preoperative cardiovascular risk assessment is essential for reducing related morbidity and mortality. For this purpose, various clinically validated scoring systems are employed, such as the Revised Cardiac Risk Index (RCRI), ACS NSQIP, SORT, AUBHAS2, among others, which integrate factors like functional status, comorbidities, type of surgery, and patient age [8–13].

In addition to individual risk evaluation, the specific risk associated with the surgical procedure must also be considered. Surgeries can be classified by risk (low, intermediate, high) based on the type, duration, urgency, and anatomical location of the procedure [14–15]. Laparoscopic surgery has significantly reduced complication rates compared to traditional open surgery, but it introduces its own risks, such as intra-abdominal hypertension induced by pneumoperitoneum, which has a major hemodynamic impact [16].

Perioperative arrhythmic risk is a frequent complication, occurring in 4–20% of patients undergoing non-cardiac surgery. It includes supraventricular arrhythmias (especially atrial fibrillation) and ventricular arrhythmias [17]. New-onset postoperative atrial fibrillation is associated with an increased risk of stroke and myocardial infarction, requiring anticoagulation, rate control, and sometimes electrical cardioversion. Predisposing factors include advanced age, male sex, vascular disease, and heart failure. According to the 2024 ESC Guidelines, postoperative atrial fibrillation is not only a common complication but also an important predictor of long-term atrial fibrillation recurrence—patients with postoperative atrial fibrillation have a 4–5 times higher risk of developing recurrent episodes within the following five years. It is also associated with multiple adverse events, including hemodynamic instability, prolonged hospital stay, infections, renal complications, increased risk of bleeding, and higher in-hospital mortality. Ventricular arrhythmias, though rarer, may require emergency treatment in the context of hemodynamic instability. Regarding complex ventricular tachyarrhythmias, these represent medical emergencies due to their potentially life-threatening nature and require prompt intervention. Identifying and correcting reversible causes is the first step in their management. Continuous rhythm monitoring, optimization of electrolyte balance,

and hemodynamic support are essential, while in severe cases, intravenous administration of antiarrhythmic agents (such as amiodarone) and electrical cardioversion may be necessary. [18]. Bradyarrhythmias are common in the perioperative period, especially in elderly patients, those with pre-existing conduction disorders, or those receiving beta-blockers, calcium channel blockers, or class III antiarrhythmics. They may be caused or exacerbated by hypoxia, hypothermia, hyperkalemia, hypothyroidism, myocardial ischemia, and surgical manipulation near cardiac structures or the vagus nerve.

Perioperative myocardial ischemia is caused by an imbalance between myocardial oxygen demand and supply, worsened by surgical stress, systemic inflammation, and interruption of antiplatelet therapies. Clinical presentations can vary from silent ischemia to acute myocardial infarction and require a personalized approach depending on pre-existing risk and the type of surgery.

Anesthesia also contributes to cardiovascular complications through mechanisms including reduced sympathetic tone, vasodilation, hypotension, and decreased tissue perfusion. Prolonged intraoperative hypotension is associated with vital organ dysfunction, particularly in patients with pre-existing cardiovascular disease. Strategies for maintaining hemodynamic stability and optimizing circulating volume are crucial in preventing such events [19], [20].

Besides cardiovascular risks, anesthesia may induce respiratory complications (atelectasis, pneumonia, respiratory failure) [21], neurological issues (delirium, encephalopathy, malignant hyperthermia) [22], and renal complications (acute kidney injury), especially in the context of hypotension and hypoperfusion [23]. Modern monitoring techniques and interventions such as protective ventilation or the use of specific pharmacological agents (e.g., sugammadex) can help reduce these risks [24], [25].

In conclusion, the evaluation and management of perioperative cardiovascular risk are essential components of care in patients undergoing non-cardiac surgery. The integration of risk scores, close monitoring, and multidisciplinary collaboration allows for optimization of postoperative outcomes and reduction of severe complications.

Chapter 2. Postoperative Atrial Fibrillation and Mortality

Postoperative atrial fibrillation (AF) is a commonly encountered complication following major surgeries, including gastrointestinal procedures, and is associated with increased morbidity. The current study presents a systematic review and meta-analysis of the existing literature, aiming to evaluate the relationship between atrial fibrillation and mortality after gastrointestinal surgeries. The research was exclusively based on randomized controlled trials (RCTs), ensuring methodological rigor by adhering to the PRISMA guidelines and assessing study quality using tools developed by the Cochrane Collaboration.

The results of the meta-analysis, which included five randomized studies, did not reveal a statistically significant association between postoperative AF and mortality. The overall mortality rate did not differ significantly between patients with and without AF (OR = 1.03; 95% CI [0.24–4.41]; p = 0.97). However, the high heterogeneity among studies ($I^2 = 88\%$) necessitates cautious interpretation of these results. Regarding the incidence of AF, it was significantly higher in the experimental groups (patients undergoing GI surgery) compared to control groups, with an OR of 0.42 (95% CI [0.18–0.99]; p = 0.05).

The discussion highlights the complexity of the relationship between AF and mortality. Some observational studies suggested a significant increase in mortality risk following the onset of AF, particularly in lower gastrointestinal surgeries. Others, however, did not identify such a relationship, attributing the occurrence of AF to secondary factors such as hyperthyroidism, pre-existing cardiac conditions, or postoperative inflammatory states.

The relevance of this research lies in its emphasis on the need for larger-scale studies involving diverse populations and in-depth investigations into the pathophysiological mechanisms and clinical implications of postoperative AF. Furthermore, the findings have the potential to influence clinical practice guidelines, contributing to a more accurate perioperative risk assessment and better care for patients undergoing gastrointestinal surgery.

Study limitations include the small number of available RCTs, potential publication bias, exclusion of non-English studies, and inconsistent reporting of other clinical variables. In conclusion, although current data do not support a clear link between postoperative AF and mortality in gastrointestinal surgery, the complexity of this topic justifies further rigorous research [26].

Personal Contributions

Chapter 3. Research Hypothesis and General Objectives

This thesis represents an in-depth study of cardiovascular events that may occur during the perioperative period of non-cardiac surgeries. The primary aim was to identify cardiovascular complications during the perioperative period and the factors that contribute to their occurrence. Identifying and highlighting the relationship between the presence of these triggering factors and specific cardiovascular events emerging during the surgical period—which contribute to increased morbidity and mortality—lays the foundation for a multidisciplinary approach to surgical patients in an attempt to reduce the risks associated with surgery.

Specific objectives of the study were:

- To evaluate the variations in biological and clinical parameters—blood pressure, heart rate, ECG interpretation, and the like—recorded before, during, and after surgery, whether clinically evident or asymptomatic;
- To conduct peri-operative Holter ECG monitoring in order to identify rhythm or conduction disturbances and ischemic changes;
- To correlate comorbidities, medical history, and the pre-operative cardiovascular drug regimen with postoperative cardiovascular changes and the accompanying biological parameters;
- To perform a statistical analysis of the significant differences between pre- and postoperative parameters.

The findings were distilled into two separate studies. The first study analyzed the triggering and predisposing factors of cardiac events during the peri-operative period in non-cardiac surgery. The second study examined the role of pre-operative β -blocker therapy, highlighting both its benefits and its associated risks. Together, these investigations resulted in the publication of two original articles in peer-reviewed specialist journals.

The complexity and variability of the monitored parameters enabled the identification of factors that may contribute to peri-operative cardiovascular complications in general surgery.

Subsequent data processing likewise culminated in two original publications: the first elucidated the triggering and predisposing factors for peri-operative cardiac events in non-cardiac surgery, while the second underscored the role, advantages, and potential hazards of β -blocker therapy in the peri-operative management of cardiac pathology.

Chapter 4. General Research Methodology

The present work constitutes a clinical, analytic-observational, prospective, single-centre, non-interventional, descriptive, and correlational study involving 100 consecutive patients admitted to the Department of General Surgery and Emergency III at the Bucharest University Emergency Hospital.

Study design and data collection

- A dedicated digital platform was used to construct the database, which included the following variables:
- Demographics and baseline characteristics: age, sex, body-mass index, smoking status;
- Surgical profile: underlying surgical pathology, emergency versus elective setting, type of anaesthesia, operative time;
- Medical history: arterial hypertension, diabetes mellitus, paroxysmal or permanent atrial fibrillation, dyslipidaemia;
- Chronic cardiovascular medication: oral anticoagulants, statins, angiotensin-converting-enzyme inhibitors or angiotensin-receptor blockers;
- β-blocker therapy—recorded together with its indication (symptomatic extrasystoles, atrial fibrillation with rapid ventricular response, arterial hypertension, or secondary prevention of chronic coronary syndrome).

Cardiovascular monitoring

Rigorous haemodynamic monitoring was carried out, and the following parameters were entered into the database:

- Admission blood pressure;
- Intra-operative maximum and minimum blood pressure;
- Admission heart rate, together with intra- and postoperative minima and maxima.

Twenty-four-hour Holter ECG monitoring—from one hour pre-operatively to 24 h post-operatively—was selected for its non-invasive character, technical accessibility, and rich electrophysiological output. The variables recorded were:

- Newly diagnosed atrial fibrillation;
- Atrioventricular block;
- Sinus pauses exceeding 5 s;
- Left bundle-branch block;
- Ventricular extrasystoles and non-sustained ventricular tachycardia;
- ST-segment elevation or depression.

Automated software interpretation was followed by manual review by a cardiologist to eliminate artefacts and ensure standardised data management. Outcomes analysed included bradycardia (< 60 bpm), tachycardia (> 100 bpm), first-, second-, and third-degree atrioventricular block, left bundle-branch block, ventricular ectopy, non-sustained ventricular tachycardia, sinus pauses > 5 s, ST-segment shifts \ge 1 mm, and the pattern of atrial fibrillation (sustained, paroxysmal, or permanent).

Laboratory parameters

Biochemical variables measured both pre- and post-operatively comprised haemoglobin, leukocyte count, serum creatinine, sodium, potassium, C-reactive protein, and high-sensitivity troponin I on postoperative days 1 and 2.

Statistical analysis

Database management in Microsoft Excel and statistical processing in IBM SPSS v26 provided a robust, coherent analytical framework, enabling the research team to concentrate on the clinical interpretation of results without compromising scientific rigour.

Ethical considerations

Written informed consent was obtained from all participants, upholding autonomy, transparency, and the right to withdraw at any time without prejudice to medical care. Anonymity and data confidentiality were explicitly guaranteed. Ethical approval was granted by the Research Ethics Committee of the "Carol Davila" University of Medicine and Pharmacy, Bucharest. The consent form, drafted in patient-friendly language, detailed the study purpose, methodology, potential risks and benefits, and the confidential nature of all information supplied.

Chapter 5 Study I - Factors Associated with Perioperative Cardiovascular Events in Noncardiac Surgery

We conducted a prospective, observational study aimed at identifying cardiac events occurring in the perioperative period in patients undergoing non-cardiac surgical interventions. Through Holter ECG monitoring, in association with clinical and biochemical parameters (including C-reactive protein and high-sensitivity troponin I), cardiac complications were evaluated in a cohort of 100 patients with a mean age of 54.5 years, admitted for acute or chronic surgical pathologies.

The results highlighted notable incidences of cardiac events: postoperative paroxysmal atrial fibrillation was present in 10% of patients and was associated with longer surgical duration, postoperative anaemia, and elevated CRP levels. Sinus pauses were also recorded (9 cases), in close correlation with advanced age, pre-existing arterial hypertension, and increased intraoperative blood pressure values. ST-segment changes (30% of patients), particularly ST-segment depression, correlated with prolonged operative time, hypertension, and a history of atrial fibrillation and diabetes mellitus.

Statistical analyses (univariate and multivariate logistic regressions) showed that postoperative day-2 troponin is an independent predictor for the occurrence of atrial fibrillation, while pre-existing hypertension and the duration of the intervention are relevant predictors for ST-segment changes. In addition, non-sustained ventricular tachycardia was significantly associated with increased troponin values and elevated intraoperative arterial pressures.

These data underscore the importance of personalised cardiovascular assessment in the perioperative period, with an emphasis on continuous and early monitoring, especially in patients with pre-existing risk factors (advanced age, hypertension, atrial fibrillation). Holter monitoring proved to be a valuable tool for detecting arrhythmias and conduction changes or silent ischaemia, many of which are subclinical and therefore would go undetected in the absence of specialised surveillance.

The conclusion of the study supports the need to integrate advanced perioperative monitoring and biological markers (troponin, CRP) into risk assessment protocols. This approach can considerably improve postoperative prognosis by providing clinicians with essential information for the prevention of major complications. The results suggest a re-

evaluation of clinical guidelines, in the sense of adapting them to the needs of the patient with cardiovascular risk undergoing non-cardiac surgery [27].

Chapter 6. Study II - Prospective Analysis of the Influence of Preoperative Beta-Blockers on Cardiovascular Events after Non-Cardiac Surgery

Beta-blockers represent one of the cornerstones of cardiovascular therapy; however, their prophylactic value in non-cardiac surgery remains disputed, owing to conflicting evidence concerning peri-operative benefits and risks.

To assess objectively the cardiovascular impact of pre-operative beta-blocker administration, we designed a prospective observational study. The study cohort comprised 100 adult patients admitted for non-cardiac surgical interventions, of whom 30 were receiving chronic beta-blocker therapy. The cohort was divided into G1 (70 patients without beta-blockers) and G2 (30 patients on chronic beta-blockers). The principal indications for beta-blockade were atrial fibrillation (46.7 %), arterial hypertension (36.7 %), extrasystoles (10 %), and chronic coronary syndrome (6.6 %). Patients with recent severe cardiac pathology or those unable to undergo continuous monitoring were excluded.

A key methodological element was 24-hour Holter ECG monitoring, initiated at least one hour before surgery, which enabled continuous recording of cardiac rhythm during the pre, intra-, and postoperative periods. This type of monitoring, rarely used in the setting of noncardiac surgery, provided a detailed, real-time view of cardiac events such as bradycardia,
atrial-fibrillation episodes, ST-segment changes, and ventricular tachyarrhythmias. In addition
to electrocardiographic data, the study incorporated relevant clinical and biochemical
parameters—blood-pressure values, haemoglobin, troponin, and C-reactive protein—allowing
extensive correlation between clinical status, biomarkers, and the cardiac events detected.

The results revealed marked differences between the two groups. Patients receiving beta-blockers exhibited a higher incidence of peri-operative bradycardia, including cases of severe bradycardia (< 40 bpm) requiring therapeutic intervention—an effect consistent with the negative chronotropic action of beta-blockers, accentuated under anaesthesia. Chronic beta-blocker users also experienced more episodes of hypotension and consequent haemodynamic instability.

Another notable finding was that de-novo atrial fibrillation—a frequent and potentially severe postoperative arrhythmia—was not significantly influenced by beta-blocker use. Instead, its occurrence correlated chiefly with prolonged surgical duration and low

postoperative haemoglobin values, underscoring the multifactorial nature of this complication. Transient ST-segment changes and episodes of non-sustained ventricular tachycardia occurred in both groups, without a clear association with beta-blocker therapy.

In summary, chronic beta-blocker therapy correlates with bradycardia and, to a lesser extent, peri-operative hypotension, without increasing the incidence of malignant ventricular arrhythmias. Continuous Holter monitoring optimises the detection of transient events and can guide a personalised peri-operative strategy [28].

Conclusions

The present work, entitled "Impact of Abdominal Surgical Procedures on Cardiovascular Functional Dynamics," seeks to identify the factors that influence haemodynamic changes—blood-pressure values, heart rate, tachy- and bradyarrhythmias, and terminal-phase electrocardiographic alterations—detected by 24-hour Holter ECG monitoring during the peri-operative period in patients undergoing non-cardiac surgery. The presence of such asymptomatic cardiovascular changes may herald cardiac complications associated with the heightened morbidity of non-cardiac surgical procedures. Although risk-scoring systems can facilitate better pre-operative assessment, including cardiovascular risk, they must be tailored to each patient in order to anticipate potential complications. Detailed analysis of cardiovascular events by 24-hour Holter ECG can supply additional information on asymptomatic arrhythmias and silent ischaemia.

Our study identified several cardiovascular events associated with multiple perioperative factors. One of the most important findings was the occurrence of postoperative atrial fibrillation, which correlated with longer operative times. Low haemoglobin levels were linked to a higher frequency of atrial fibrillation, while elevated day-2 postoperative troponin values were likewise associated with new-onset atrial fibrillation. A pro-inflammatory status, reflected by increased pre- and postoperative CRP values, was also related to postoperative atrial fibrillation. Asymptomatic, non-sustained ventricular tachycardia detected on Holter ECG was uncommon and correlated with elevated intra-operative blood pressures and increased day-1 postoperative troponin levels.

With respect to bradyarrhythmias, asymptomatic sinus pauses revealed by Holter monitoring were associated with higher intra-operative systolic blood pressure and with atrial fibrillation, especially in patients receiving chronic β -blocker therapy. Sinus pauses were more frequent in elderly patients.

Silent, transient ST-segment depression detected on Holter ECG was associated with prolonged operative time, pre-existing arterial hypertension, diabetes mellitus, elevated intra-operative blood pressure, and a history of atrial fibrillation. Biochemically, silent ischaemia was more common in patients with elevated pre- and postoperative serum creatinine. The frequency of ST-segment depression increased directly with age and was associated with higher troponin levels during the first two postoperative days.

The second part of the study evaluated correlations between chronic β -blocker therapy and postoperative cardiovascular adverse effects. This prospective Holter-based analysis demonstrates that chronic β -blockade in patients undergoing non-cardiac surgery is significantly associated with an increased incidence of peri-operative bradycardia and hypotension, yet confers protective effects by preventing peri-operative atrial fibrillation and ventricular arrhythmias.

These findings underscore the ambivalent nature of β -blockers in the peri-operative setting: while they offer cardioprotective benefits, they also entail quantifiable haemodynamic risks, particularly blood-pressure instability and bradyarrhythmic disturbances. For this reason, pre-operative initiation of β -blockers in patients scheduled for non-cardiac surgery is generally not recommended. Optimal peri-operative use of β -blockers therefore requires careful patient selection, individualized risk-benefit assessment, and rigorous monitoring both intra- and post-operatively. Continuous Holter monitoring proved extremely valuable in detecting transient, asymptomatic yet clinically relevant cardiac events, highlighting its important role in perioperative surveillance.

To validate and extend these results, large multicentre studies involving greater patient numbers and longer follow-up periods are necessary. Such investigations could optimise existing clinical guidelines and improve peri-operative management protocols, promoting safer and more effective β -blocker use in surgical populations.

Study limitations

The study aimed to identify cardiovascular events that may arise during the perioperative period—through clinical and electrocardiographic monitoring—that could lead to subsequent cardiac complications in patients with non-cardiac surgical diseases, with a view to optimising management and preventive strategies. Nonetheless, methodological limitations included the relatively small sample size, the restricted 24-hour Holter monitoring window (which might miss events occurring beyond 24 h post-surgery), and the single-centre design, which may limit generalisability. These constraints highlight the need for future randomised studies with larger cohorts and extended monitoring periods.

Future Research Directions

Our investigation reveals a notable gap in the current literature concerning early, non-fatal cardiac complications in non-cardiac surgery. Despite their high prevalence and potential

clinical significance, concrete data on this topic remain scarce. Most existing studies focus either on fatal outcomes or fail to analyse separately early, transient, asymptomatic cardiac events that may precede more severe complications. This underscores the novelty and clinical relevance of the present study.

Given the preliminary nature of our findings, we plan to expand both the sample size and the assessment of anaesthetic implications for postoperative cardiovascular events. A larger, multicentre cohort would enhance statistical power, improve generalisability, and allow more nuanced stratification of risk factors. Extending cardiac monitoring beyond the 24-hour window—potentially up to 72 h post-operatively—may yield further insight into the temporal evolution and delayed emergence of arrhythmias or ischaemic changes.

Moreover, based on our statistical analyses, we aim to formulate hypotheses rigorously aligned with the data observed in this study and with the statistical robustness of our models. Our goal is to generate hypotheses that are not only clinically and biologically plausible but also methodologically sound, thereby contributing to the development of evidence-based tools for peri-operative risk stratification. Future studies should seek to validate our preliminary observations in larger populations and across diverse surgical contexts. We consider that a systematic investigation of early, non-fatal cardiac events has the potential to improve targeted monitoring strategies, optimise peri-operative care, and ultimately reduce postoperative and long-term morbidity in patients with cardiovascular disease or risk factors who require general-surgical interventions.

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