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Preoperative cardiopulmonary variability assessment for predicting postoperative adverse events following thoracic surgery: A systematic review

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Research Article

Keywords: heart rate variability, respiratory rate variability, cardiopulmonary variability assessment, thoracic surgery, postoperative complications, risk stratification, autonomic nervous system

Posted Date: November 1st, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11245282/v1

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Additional Declarations: Competing interest reported. Dr. Andrew Seely is the founder and CEO of Therapeutic Monitoring Systems (TMS) which holds worldwide licensing rights to several patents related to variability-derived clinical decision support. Andrew Seely and Christophe Herry are patent authors related to this work. Dr. A. Seely discloses the conflict of interest (CoI) in all grants, publications, presentations, and other public communication, and submits a CoI management agreement to Ottawa Hospital Research Institute annually. All other authors report no relevant disclosures.

Abstract

Objectives:

Postoperative adverse events (AEs) remain a major source of morbidity and mortality following thoracic surgery. Current preoperative risk assessment tools have limited ability to predict individual postoperative complications. Cardiopulmonary variability assessment (CPVA), including heart rate variability (HRV) and respiratory rate variability (RRV), has emerged as a potential biomarker of autonomic function and physiologic reserve. This systematic review evaluated the role of preoperative CPVA in predicting postoperative AEs following thoracic surgery.

Methods:

A systematic review was conducted according to PRISMA 2020 guidelines. MEDLINE and Embase were searched from inception to identify studies evaluating preoperative HRV and/or RRV as predictors of postoperative AEs in adults undergoing thoracic surgery. Eligible study designs included randomized controlled trials, cohort studies, case-control studies, and diagnostic accuracy studies. Study characteristics, CPVA methodology, comparator assessments, postoperative outcomes, and risk of bias were extracted and evaluated using the Newcastle–Ottawa Scale and QUADAS-2.

Results:

Five cohort studies comprising 693 patients met the inclusion criteria. Four studies evaluated pulmonary resection for non-small cell lung cancer and one evaluated esophagectomy. Three studies assessed HRV directly, while two evaluated functional measures of cardiopulmonary reserve. Reduced preoperative HRV, particularly lower root mean square of successive differences (RMSSD) and high-frequency power (HFP), was associated with postoperative pneumonia, atrial fibrillation, and delirium. Lower RMSSD (OR 0.812, 95% CI 0.720–0.912) and HFP (OR 0.990, 95% CI 0.983–0.996) independently predicted postoperative pneumonia, with good discrimination (AUC 0.867). Risk of bias was low to moderate.

Conclusions:

Preoperative CPVA, particularly HRV, is a promising non-invasive biomarker for predicting postoperative AEs following thoracic surgery. Reduced HRV was consistently associated with pulmonary, cardiac, and neurologic complications. Larger prospective multicentre studies using standardized acquisition and analysis protocols are required to establish the incremental value of CPVA beyond current preoperative risk assessment tools.

INTRODUCTION

Thoracic surgery involves complex operative management of pulmonary, esophageal, mediastinal, pleural, and chest wall diseases, most commonly malignancy [1]. Such surgeries are associated with significant risk of postoperative adverse events (AEs), defined as deviation from an ideal recovery, leading to prolonged length of stay, hospital cost, diminished quality of life, readmissions and worsened oncological outcomes [2–6]. Cardiopulmonary complications are the most common drivers of morbidity and mortality in the postoperative period, with elderly patients (> 65 yrs old), smoking history, body mass index (BMI) above 30kg/m^2 and chronic obstructive pulmonary disease (COPD) as the main risk factors [7–8]. These baseline perturbations in cardiopulmonary function contribute to postoperative cardiopulmonary complications [9]. Careful preoperative cardiopulmonary assessment is necessary to predict postoperative cardiac and pulmonary complications in patients undergoing thoracic surgery.

Current preoperative risk stratification tools, however, have important limitations. Conventional assessments such as pulmonary function testing (PFTs), predicted postoperative forced expiratory volume in 1 second (ppoFEV1), diffusion capacity of carbon monoxide (DLCO), stair-climbing tests, and cardiopulmonary exercise testing (CPET) provide valuable estimates of functional capacity, yet their ability to predict individual postoperative complications remains modest. These approaches are often static, threshold-based measures that may not fully capture physiologic adaptability or autonomic reserve under surgical stress [10–13]. Despite limitations, preoperative evaluation is necessary to determine survival chances, decide on an optimization regimen, and reduce the potential risk of complications.

Cardiopulmonary variability assessment (CPVA), including heart rate variability (HRV) and respiratory rate variability (RRV), has emerged as a promising physiologic biomarker of dynamic reserve. HRV reflects beat-to-beat variation in cardiac rhythm, while RRV quantifies fluctuations in respiratory timing and pattern [14–15]. Greater variability is generally considered indicative of a resilient autonomic nervous system capable of adapting to physiologic stress, whereas reduced variability has been associated with frailty, impaired recovery, and adverse clinical outcomes [16]. Unlike CPET-derived metrics such as anaerobic threshold or peak oxygen uptake, CPVA specifically evaluates autonomic regulation and may therefore provide complementary information regarding perioperative risk. However, evidence remains fragmented, with heterogeneity in patient populations, monitoring techniques, variability metrics, and reported endpoints.

Accordingly, we conducted a systematic review to evaluate the current evidence regarding preoperative CPVA as a predictor of postoperative adverse events following thoracic surgery, and to assess its potential role in future perioperative risk stratification pathways.

METHODS

This systematic review was conducted in accordance with the Preferred Reporting of Items in Systematic Reviews and Meta-Analyses (PRISMA) guidelines 2020 [17]. Ethics approval was not required for this review as no human subjects were involved. This review was not registered with PROSPERO.

Search Strategy

A comprehensive literature search was conducted in two electronic databases: MEDLINE, Embase. Keywords related to preoperative assessment, cardiopulmonary variability, risk stratification, postoperative adverse events and thoracic surgery were applied to the databases to aid in the search. The search query was: (("thoracic surgery"[MeSH] OR "lung resection" [Title/Abstract] OR lobectomy [Title/Abstract] OR pneumonectomy [Title/Abstract] OR esophagectomy [Title/Abstract]) AND ("postoperative complications"[MeSH] OR "postoperative adverse events" [Title/Abstract] OR "atrial fibrillation" [Title/Abstract] OR "pulmonary complication*" [Title/Abstract] OR "air leak" [Title/Abstract]) AND ("heart rate variability" [MeSH] OR HRV [Title/Abstract] OR "respiratory rate variability" [Title/Abstract] OR RRV [Title/Abstract] OR "cardiopulmonary variability" [Title/Abstract]) AND (preoperative [Title/Abstract] OR "pre-operative" [Title/Abstract] OR "before surgery" [Title/Abstract]) AND (predict* [Title/Abstract] OR prognosis* [Title/Abstract] OR "risk assessment" [Title/Abstract])). The search query was designed based on each database's specific syntax. A language restriction was set to studies published in English, but there was no time restriction.

Inclusion and Exclusion Criteria

This review included diagnostic accuracy studies, case control studies, prospective or retrospective cohort studies, and randomized controlled trials. Eligible studies investigated preoperative HRV and/or RRV to predict postoperative cardiac and/or pulmonary complications in patients undergoing thoracic surgery. The studies compared the predictive performance of HRV and RRV with conventional preoperative risk assessment tools (e.g., FEV1, PAL score, Passman's score) or no comparator. The studies involved adults aged 18 years and above undergoing major thoracic surgery, including lobectomy, pneumonectomy, esophagectomy, thoracotomy or mediastinal tumor resection. The studies measured postoperative AEs, including atrial fibrillation, prolonged air leak, readmission, length of stay, and mortality. Excluded studies included all studies involving pediatric populations (age < 18 years) as well as studies involving animal populations or in vitro analyses. Case reports, case series with fewer than 10 patients, editorials, letters, and narrative reviews were also excluded, as were studies involving urgent or emergent surgeries, patients with implanted pacemakers or pre-existing arrhythmias.

Study Selection and Data Extraction

Two independent reviewers screened titles, abstracts and full text of retrieved studies. Duplicates and studies that did not meet the inclusion criteria were excluded from the review. Disagreements were resolved through consensus. Data was extracted using a standardized data extraction form. The extracted data related to study characteristics, including author, year, country, research design, and sample size, and population characteristics, such as age and sex of patients. Data related to surgical details, CPVA measurement methods and metrics (HRV and RRV), comparator tools or models and outcomes such as postoperative AEs, including atrial fibrillation, prolonged air leak, readmission, length of stay, and mortality, were also extracted.

Risk of Bias Assessment

The methodological quality of the included studies was assessed using the Cochrane Risk of Bias (RoB) tool for evaluating risk of bias in randomized trials [18]. The Newcastle–Ottawa Scale (NOS) was used to evaluate the risk of bias in observational studies [19]. The Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool was used to assess the risk of bias in diagnostic studies [20]. The results were interpreted descriptively, and overall risk was described as either low, moderate or high.

Data Synthesis

Extracted data were analyzed using descriptive and narrative analyses. IA manually coded the data and clustered codes into thematic categories, allowing for recurring themes on preoperative cardiopulmonary variability assessment for predicting postoperative complications in patients undergoing thoracic surgery to emerge. A narrative analysis of the emerging themes was conducted, and a thematic matrix was provided comparing the expression of themes and sub-themes across the included studies.

RESULTS

Initial literature search in MEDLINE and EMBASE databases yielded 1,308,113 articles, where 1,308,041 duplicates or irrelevant articles were excluded before screening (Fig. 1). Among the remaining 72 articles whose titles and abstracts were screened, 59 studies were excluded. The full texts of the remaining 13 studies were scrutinized and assessed for eligibility, and 8 additional studies were excluded. Five studies met the eligibility criteria and were included in the review.

Summary of Study Characteristics

A total of five [21–25] prospective and retrospective cohort studies with a combined 693 patients were included in this review. Four of the five studies (80%) were single-centre studies, while one study was a multi-centre study. Two studies were conducted in China, while Poland, Japan and France accounted for one study each. The sample ranged between 30 and 257 patients, with a mean age ranging between 58.7 and 72.9 years. Male patients dominated the

sample. Patient BMI was reported in three studies (60%), with mean values ranging from 23.8 to 24.5 kg/m², while one study reported BMI categories. Patients in four studies (80%) were diagnosed with lung cancer and were treated using wedge, segmentectomy, bilobectomy, lobectomy or pneumonectomy. Patients in one study presented with esophageal cancer during diagnosis and were treated with esophagectomy.

Three out of five studies (60%) assessed heart rate variability (HRV), while two studies used functional testing to quantify patient exercise capacity and autonomic resilience. More specifically, Holter testing was used to measure CPVA performance in three studies, one study used a stair climbing test, and one study used a pulse oximeter and heart rate monitor. HRV recordings were derived from short-term electrocardiographic recordings in most studies, typically using 5-minute segments obtained within 24 hours prior to surgery [19, 21, 22]. One study utilized 24-hour Holter monitoring with analysis of selected 5-minute segments from different time periods [19], while another obtained 10-minute recordings with extraction of the most stable 5-minute segment for analysis [21]. Four of the five studies (80%) compared CPVA performance to conventional preoperative assessment tools, including pulmonary function testing (e.g., FEV1, DLCO) and ASA classification [20, 23]. The timing of assessment in three studies (60%) was between 1 and 24 hours before the surgery.

Incidence of Postoperative Complications

Three studies [21, 23, 24] directly assessed preoperative heart rate variability (HRV), but the recording protocols differed. Ciszewski et al. used 24-hour Holter monitoring on the day before surgery and analyzed three separate 5-minute ECG strips obtained in the afternoon, at night, and on the morning of surgery [21]. Echizen et al. recorded a single 10-minute 3-lead ECG 6–12 hours before surgery and analyzed the 5-minute segment with the least noise [23]. Lai et al. performed short-term 5-minute ECG recordings on the day before surgery, with preoperative samples obtained in the early morning and late evening [24]. Thus, the included HRV studies relied predominantly on short-term preoperative recordings, although one study incorporated these within a 24-hour Holter protocol [21]. In this same study, hypotension during the first 3 postoperative days occurred in 15% (18/117) [21]. Postoperative atrial fibrillation occurred in 16% (19/117) of patients, with peak incidence of onset being 2–3 days after operation. Cough and obstructive atelectasis occurred in 26% (31/117) of patients that presented with postoperative atrial fibrillation, with more than 55% requiring forced diuresis after operation [21]. Furthermore, postoperative delirium occurred in 23% (7/30) of patients [23], while postoperative pneumonia occurred in 13% (33/257) of patients [24].

Two studies used conventional methods, specifically the functional stair climbing test [22] and the functional test (6-minute walk test and sit-to-stand test) [25], to predict postoperative complications in patients undergoing thoracic surgery. In the study using functional stair climbing test (SCT), symptomatic cardiac arrhythmia occurred in 19% (32/170), prolonged mechanical ventilation in 4.7% (8/170), lobular atelectasis in 3.5% (6/170), acute carbon dioxide retention in 2.4% (4/170), pneumonia in 1.8% (3/170) and mortality in 1.8% (3/170) of non-small cell lung cancer patients [22]. In the study using functional tests, infectious complications such as pneumonia, pleurisy, and parietal abscess occurred in 7.6% (9/118) of patients, pleuro-pulmonary complications including air leaks, atelectasis, respiratory distress, pneumothorax, pleural effusion and pulmonary embolism in 26.3% (31/118), cardiac rhythm disorder in 3.4% (4/118), and nerve paralysis in 2.5% (3/118).

Prediction of Postoperative Complications using CPVA

Preoperative heart rate variability (HRV) was assessed using electrocardiographic (ECG)-derived R–R interval analysis, with variation in acquisition protocols across studies. In Ciszewski et al., HRV was derived from 24-hour Holter monitoring performed the day before surgery, with analysis based on three separate 5-minute ECG segments obtained in the afternoon, at night, and on the morning of surgery. In Echizen et al., HRV was measured using a 3-lead ECG recorded for 10 minutes 6–12 hours prior to surgery, with the 5-minute segment demonstrating the least noise selected for analysis. In Lai et al., HRV was assessed using standardized 5-minute ECG recordings obtained on the day before surgery under controlled conditions, including supine positioning, a resting period prior to acquisition, controlled ambient temperature, and avoidance of stimulants such as caffeine.

Across studies, HRV metrics included time-domain and non-linear measures such as root mean square of successive differences (RMSSD; short-term variability reflecting parasympathetic activity), short-interval variations (SD1; reflecting parasympathetic control and equivalent to RMSSD) and long-interval variations (SD2; reflecting combined parasympathetic and sympathetic tone), both derived from Poincaré plots, as well as frequency-domain measures such as high-frequency power (HFP), reflecting parasympathetic modulation. However, methodological details were inconsistently reported across studies. While Lai et al. described controlled acquisition conditions, other studies did not clearly specify patient positioning, activity during recording, or environmental conditions. Additionally, although some analyses incorporated clinical variables such as ASA classification and BMI, adjustment for potential confounders including medications, comorbidities, and age was not consistently reported, which may influence HRV measurements and interpretation.

In one study, ASA grade III was associated with a > 4-fold increased risk of atrial fibrillation post-operation (OR = 4.1) and 3-fold increased risk of left pneumonectomy (OR = 2.9) in patients undergoing major pulmonary resection [21]. In another study, reduced preoperative RMSSD (OR = 0.812, 95% CI: 0.720–0.912, p = 0.001) and lower preoperative HFP (OR = 0.990, 95% CI: 0.983–0.996, p = 0.002) were associated with postoperative pneumonia in patients undergoing lung cancer surgery. Similarly, BMI and preoperative RMSSD and HFP showed positive diagnostic accuracy for postoperative pneumonia (AUC = 0.867, p < 0.001) [22]. In another study, lower preoperative HFP (mean = 57.4 ± 93.9, p < 0.05) was associated with postoperative delirium in patients undergoing elective surgery for esophageal cancer [23].

In conventional methods, one study using pulmonary function testing showed positive diagnostic accuracy of postoperative cardiopulmonary complications using FEV1 (AUC = 0.750, 95% CI: 0.668–0.831) in patients undergoing surgery for non-small cell lung cancer [22]. Another study using functional exercise testing with the 6-minute walk test (6MST) and sit-to-stand test (STST) demonstrated that the number of steps during the 6MST (AUC = 0.82, 95% CI: 0.75–0.90) and the number of lifts during the STST (AUC = 0.85, 95% CI: 0.77–0.93) strongly predicted severe cardiopulmonary complications and mortality due to organ failure [25].

Risk of Bias Assessment

Risk of bias was assessed using the NOS and QUADAS-2 tools. All five studies were assessed using the NOS tool, with results showing that three studies [21–23] demonstrated moderate risk while two studies [24–25] demonstrated low risk of bias. Most of the studies demonstrated good quality in selection and representativeness of the cohort, poor to fair quality in comparability of cohorts on the basis of design or confounders, and fair quality in outcomes assessment. QUADAS-2 assessment of HRV-based studies [21, 23–24] showed predominantly low risk across domains except for one study that demonstrated high risk in the patient selection domain, most likely due to the small sample size [22]. Overall, the evidence base is felt to be robust, but the small cohorts and limited external validity may affect the generalizability of findings.

DISCUSSION

This systematic review suggests that preoperative cardiopulmonary variability assessment (CPVA), particularly heart rate variability (HRV), may provide clinically meaningful prognostic information for patients undergoing thoracic surgery. Across included studies, HRV parameters such as root mean square of successive differences (RMSSD) and high-frequency power (HFP) were associated with important postoperative complications including pneumonia, atrial fibrillation, and delirium. Collectively, these findings support the concept that autonomic dysfunction or reduced physiologic adaptability before surgery may identify patients at increased risk of adverse postoperative outcomes. Several studies demonstrated that HRV captures risk beyond conventional heart rate measurements alone. For example, Ciszewski et al. reported that altered preoperative HRV profiles, rather than absolute heart rate, were associated with postoperative atrial fibrillation following pulmonary resection [21]. Patients who developed atrial fibrillation exhibited distinct variability patterns and altered circadian autonomic fluctuation. Similarly, Echizen et al. found lower preoperative HFP to be associated with postoperative delirium after esophagectomy [23], while Lai et al. demonstrated that reduced RMSSD and lower HFP were independently associated with postoperative pneumonia after lung cancer surgery [24]. These findings suggest that HRV may function as a non-invasive marker of autonomic reserve and perioperative resilience.

Conventional preoperative functional assessments remain valuable and, in many centres, more immediately practical. Functional tests such as the stair-climbing test, 6-minute walk test (6MST), and sit-to-stand test (STST) are inexpensive, accessible, and easy to incorporate into routine pathways. Included studies demonstrated strong predictive performance of these tools for severe cardiopulmonary complications and mortality [22, 25]. Prior literature has similarly established the value of stair-climbing tests, pulmonary function testing, radionuclide perfusion scanning, and cardiopulmonary exercise testing (CPET) in assessing operative fitness. Accordingly, CPVA should currently be viewed as complementary rather than competitive with established risk stratification tools.

A major finding of this review was the substantial methodological heterogeneity across studies. HRV recordings ranged from short resting 5-minute tracings to 24-hour Holter monitoring, with variation in timing, patient positioning, environmental controls, and analytic metrics. Time-domain, frequency-domain, and non-linear HRV measures were inconsistently reported, limiting direct comparison and precluding pooled meta-analysis. Similar limitations exist with conventional functional tests, where thresholds for unacceptable operative risk remain inconsistent.

Several barriers likely explain the limited adoption of CPVA in thoracic surgical practice. Although international standards for HRV analysis have been published, these methods have not been consistently translated to perioperative populations. Reliable signal acquisition, artifact correction, and advanced time-series analysis require technical expertise and infrastructure that may not be universally available. In addition, most included studies were single-centre with modest sample sizes, limiting external validity.

These findings have important implications for future research. First, standardized acquisition protocols, predefined HRV/RRV metrics, and multicentre prospective validation studies are needed to determine whether CPVA adds incremental predictive value beyond existing models such as frailty indices, pulmonary function tests, and CPET. Additionally, a notable finding of this review is the limited amount of published evidence evaluating CPVA in thoracic surgery despite the widespread adoption of consumer wearable devices capable of measuring HRV. Millions of patients now routinely generate longitudinal physiologic data through smartwatches and smart rings, yet these data remain largely unexplored for perioperative risk prediction [26]. This represents a substantial opportunity for future research, particularly as wearable technologies become increasingly accurate and integrated with electronic health records and machine learning approaches. Continuous, non-invasive assessment of autonomic function may ultimately enable more personalized perioperative risk stratification and targeted prehabilitation strategies.

CONCLUSION

Despite a paucity of studies to date, cardiopulmonary variability assessment (CPVA) represents a promising emerging biomarker of physiologic reserve in thoracic surgery. Evidence from this review suggests that impaired baseline parasympathetic cardiac modulation, reflected by reduced HRV, is associated with an increased risk of postoperative cardiopulmonary and neurologic complications. While current evidence remains limited and heterogeneous, CPVA offers a unique physiologic perspective that is not captured by traditional measures of pulmonary function or exercise capacity. Future research should focus on large-scale prospective validation, standardization of acquisition and analytic methodologies, and integration with existing clinical risk prediction models. Given the widespread adoption of consumer wearable devices capable of measuring HRV, the paucity of evidence identified in this review is notable. Future studies should leverage these increasingly accessible technologies to determine whether continuous preoperative physiologic monitoring can improve individualized perioperative risk stratification and guide targeted optimization strategies.

Declarations

Conflicts of Interest:

Dr. Andrew Seely is the founder and CEO of Therapeutic Monitoring Systems (TMS) which holds worldwide licensing rights to several patents related to variability-derived clinical decision support. Andrew Seely and Christophe Herry are patent authors related to this work. Dr. A. Seely discloses the conflict of interest (CoI) in all grants, publications, presentations, and other public communication, and submits a CoI management agreement to Ottawa Hospital Research Institute annually. All other authors report no relevant disclosures.

Competing Interests

Dr. Andrew Seely is the founder and CEO of Therapeutic Monitoring Systems (TMS) which holds worldwide licensing rights to several patents related to variability-derived clinical decision support. Andrew Seely and Christophe Herry are patent authors related to this work. Dr. A. Seely discloses the conflict of interest (CoI) in all grants, publications, presentations, and other public communication, and submits a CoI management agreement to Ottawa Hospital Research Institute annually. All other authors report no relevant disclosures.

Funding Statement:

No funding was received for this study.

Author Contribution

Authors' contributions: AS and DJ conceived the design and concept for this paper. IA and RS performed the systematic review. All authors contributed to the preparation, writing and review of this manuscript. All authors read and approved the final manuscript.

Data Availability:

The data underlying this article will be shared on reasonable request to the corresponding author.

Meeting Presentation: none

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Tables

Table 1: Summary of study characteristics

Study	Country	Research Design	Sample (n)	Age (mean)	Sex (M/F) %	BMI	Main Diagnosis	History of smoking	Thoracic Procedure	HRV/RRV Assessed
Ciszewski et al. (2013)	Poland	Single-centre prospective observational study	117	58.7	78.6% / 21.4%	NR	NSCLC	NR	Pneumonectomy (n=60), Bilobectomy (n=6), Lobectomy (n=51)	Yes (HRV 24 h Holter day before surgery)
Dong et al. (2017)	China	Single-centre retrospective-prospective cohort	170	65	76% / 24%	24.5	Hypertension, coronary heart disease, chronic obstructive pulmonary disease	Yes	Pneumonectomy (22), Lobectomy (122), Wedge resection (27)	No (functional SCT-Preoperative stair-climbing test)
Echizen et al. (2021)	Japan	Single-centre prospective cohort	30	73	70% / 30%	NR	Esophageal cancer	NR	Esophageal cancer surgery	Yes (HRV6–12 hours before surgery)
Lai et al. (2025)	China	Single-centre prospective observational study	257	62.5	48.2%/ 51.8%	23.8	COPD, diabetes, cardiac and vascular comorbidity	8.60%	Lobectomy or segmentectomy	Yes (HRV-1 day preoperative and postoperative day 30)
Boujibar et al. (2022)	France	Multi-centre prospective cohort	118	65	58% / 42%	<18.5 (4%); 18.5-24.9 (51%); 25-29.9 (26%); ≥30 (19%)	Adenocarcinoma, squamous cell carcinoma, typical carcinoid, neuroendocrine carcinoma	Yes: Current smoker (29%); former smoker (20%)	Segmentectomy (22%), Lobectomy (73%), Bilobectomy (3%), Pneumonectomy (3%)	No (functional tests-Preoperative consultation)

Figures

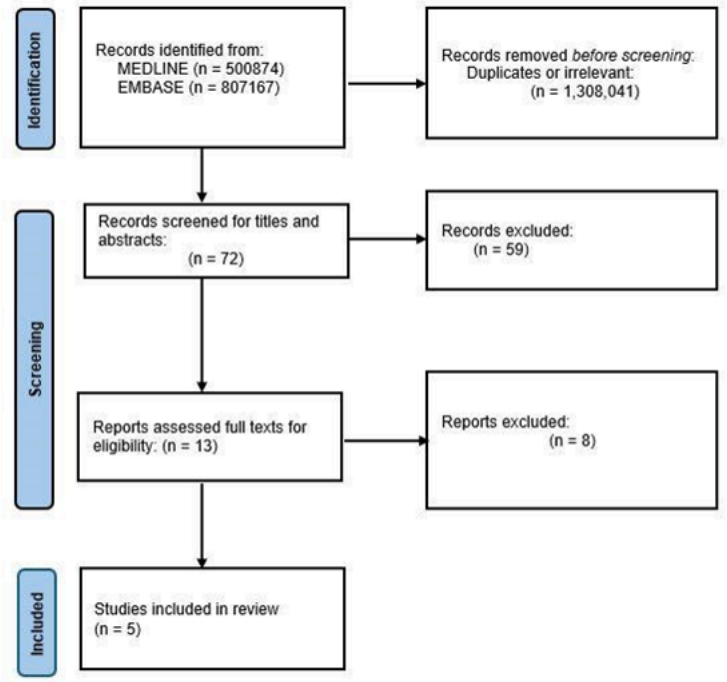


Figure 1

PRISMA flow chart illustrating the selection of included studies

Supplementary Files

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- PRISMAChecklistICVTSJuly2026.docx
- CentralFigureGraphicalAbstractICVTS.docx
- APPENDICESAppendix1ICVTS.docx
- Appendix2ROBICVTS.docx
- Appendix3ROBICVTS.docx