

New-Onset Atrial Fibrillation and Incident Cancer: an Integrative Review of Contemporary Population-Based Studies (2020–2024)

Marcelo Flávio Gomes Jardim Filho

Department of Cardiology, PMERJ (Polícia Militar do Estado do Rio de Janeiro), Brazil.

***Corresponding Author:** Marcelo Flávio Gomes Jardim Filho, Department of Cardiology, PMERJ (Polícia Militar do Estado do Rio de Janeiro), Brazil.

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Abstract

Background: Recent registry and cohort data suggest that new onset atrial fibrillation (AF) is temporally associated with an increased risk of occult malignancy, but contemporary estimates derived from large populations remain limited.

Objective: To quantify the short and medium term cancer risk following a first AF diagnosis using evidence published from 2020 to 2024, to characterise the spectrum of tumours detected, and to identify clinical features that may support risk adapted surveillance.

Methods: An integrative review was conducted in accordance with PRISMA 2020, searching PubMed, Embase and Web of Science for January 2020 – July 2025. Seven observational studies met eligibility criteria: five nationwide registry based cohorts (Netherlands, Norway, China, Austria, Netherlands BLITZ) comprising > 26 million AF patients, one hospital cohort (South Korea), and one meta analysis of 24 studies involving \approx 1.1 million cancer survivors. Data extraction was performed independently by two reviewers; outcomes were narratively synthesised because of methodological heterogeneity.

Results: One year cancer incidence after AF ranged from 2.5 % to 2.8 % in European cohorts and 12.6 % in a large Chinese insurance database. Short term adjusted hazard ratios or risk ratios for incident malignancy lay between 1.28 and 1.52, with the greatest excess observed during the first 90 days following AF onset. Lung, gastrointestinal, pancreatic and haematologic cancers predominated, and two studies demonstrated bidirectional associations (cancer \rightarrow AF and AF \rightarrow cancer). A meta analysis of cancer survivors reported a pooled relative risk of 1.29 for developing AF. Age \geq 65 years, male sex, metabolic comorbidity and systemic inflammation were consistent modifiers of risk across studies.

Conclusions: Contemporary data confirm that new onset AF is linked to a clinically relevant, short term increase in cancer detection, supporting the concept of AF as an early systemic signal rather than an isolated cardiac finding. Prospective research should determine the cost effectiveness and optimal scope of targeted malignancy screening in selected high risk AF populations.

Key Words: atrial fibrillation; cancer risk; occult neoplasia; standardized incidence ratio; population-based cohort; oncology screening

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia encountered in clinical practice, with an estimated global prevalence exceeding 37 million individuals and a projected continued increase due to population aging and the rising burden of chronic cardiovascular conditions [1,2]. While AF is well recognized for its association with ischemic stroke, heart failure, and increased mortality, accumulating evidence suggests a possible bidirectional relationship between AF and malignancy. Several large-scale observational studies have reported an increased incidence of cancer following a new diagnosis of AF, suggesting that AF may serve not only as a cardiovascular marker but also as a potential early indicator of occult neoplasia [3–4].

The underlying biological rationale for this association remains under investigation. It is hypothesized that systemic inflammation, prothrombotic states, neurohormonal dysregulation, and shared risk factors (such as advanced age, smoking, and metabolic syndrome) may contribute to both atrial remodeling and tumorigenesis [5]. Moreover, the increased frequency of imaging and laboratory evaluations in patients with new-onset AF may contribute to earlier detection of subclinical malignancies, raising the possibility of detection bias.

Nonetheless, the temporal pattern of cancer detection following AF diagnosis, especially the concentration of diagnoses within the first months suggests more than incidental association. Therefore, this study aimed to systematically review and synthesize data from population-

based cohort studies to (1) quantify the short- and long-term risk of incident cancer after AF diagnosis; (2) identify malignancy types most frequently detected; and (3) evaluate whether certain subgroups may benefit from enhanced cancer surveillance in the setting of new-onset AF.

Methods

Study Design

This study employed an integrative review methodology to explore the potential association between new-onset atrial fibrillation (AF) and the subsequent diagnosis of occult or incident malignancy. The review focused on observational studies with a population-based approach and was conducted in accordance with the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. These guidelines provided a standardized framework for identifying, selecting, and synthesizing the relevant literature, ensuring methodological transparency and reproducibility throughout the review process.

Search Strategy and Data Sources

A comprehensive literature search was conducted using three major electronic databases: PubMed, Embase, and Web of Science. The search encompassed articles published from January 2020 to March 2025 and employed a combination of controlled vocabulary and free-text terms. The Boolean search string applied was: (“atrial fibrillation” OR “atrial flutter”) AND (“occult cancer” OR “incident cancer” OR “neoplasm”) AND (“cohort” OR “population-based”). This strategy was designed to maximize the sensitivity of the search across multiple databases. In addition, the reference lists of all included articles were manually screened to identify further relevant studies that may not have been retrieved through the primary search. The database search and article selection were conducted independently by two reviewers, with discrepancies resolved through consensus or consultation with a third reviewer.

Eligibility Criteria

To be included in this review, studies had to meet the following conditions: they investigated adult individuals (aged 18 years or older) diagnosed with new-onset atrial fibrillation and reported cancer incidence as a primary or secondary outcome. Studies were required to include a general population or comparator group and to report quantitative estimates of association, such as standardized incidence ratios (SIRs),

hazard ratios (HRs), or relative risks. Eligible study designs included cohort studies (retrospective or prospective), case-control studies, and population-based studies. Studies were excluded if they were case reports, editorials, opinion articles, systematic reviews, narrative reviews, or if they did not include original data or a comparator group. Non-peer-reviewed literature and studies conducted in pediatric populations were also excluded.

Outcomes and Statistical Measures

The primary outcome of interest was the incidence of cancer following the diagnosis of atrial fibrillation, expressed primarily through standardized incidence ratios (SIRs) comparing observed cancer rates in AF patients to those expected in the general population. Secondary outcomes included site-specific cancer incidence, staging at diagnosis, and temporal distribution of cancer diagnoses after AF onset (e.g., within 3 months, 12 months, or longer). Additionally, the analysis explored potential modifying effects of demographic and clinical variables such as age, sex, hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), and cirrhosis. Due to the heterogeneity in study designs, patient populations, outcome definitions, and analytical methods, meta-analysis was not performed. Instead, findings were synthesized narratively and supported by comparative tables to highlight trends and differences across the included studies.

Ethical Considerations

All studies included in this review utilized de-identified, secondary data obtained from administrative health databases or registries and were conducted in accordance with national ethical and regulatory standards. Each study reported appropriate approval from institutional review boards or national ethics committees. As this integrative review did not involve the collection of new, individual-level data or any direct contact with human subjects, further ethical approval was not required for the present analysis.

Results

Following completion of study selection and application of eligibility criteria, seven peer-reviewed observational investigations published between 2020 and 2025 were retained for the integrative review. Together, these studies describe cancer incidence after new-onset atrial fibrillation (AF) and provide complementary insights into risk magnitude, temporal distribution, tumour spectrum and underlying pathophysiological hypotheses.

S NO	Reference (first author, year)	Country / Data source	n (AF patients)	Key oncological findings
1	Chen Q. et al., 2024 – <i>European Heart Journal</i>	Netherlands – linked national registries	320 139	1-year cancer risk = 2.5 %; adjusted HR 1.52 for cancer diagnosis; AF + cancer associated with higher 1-year mortality
2	Ay C. et al., 2022 – <i>Research & Practice in Thrombosis & Haemostasis</i>	Austria- nationwide health-insurance claims	100 026	Cancer patients: AF prevalence 4.2 %; adjusted risk ratio 1.37 for incident AF
3	Bao Y. et al., 2023 – <i>Cardio-Oncology</i>	Meta-analysis (24 studies; \approx 1.1 M cancer survivors)	—	Pooled RR 1.29 for AF among survivors; moderate heterogeneity; low risk of bias
4	Chen M. et al., 2022 – <i>JMIR Public Health & Surveillance</i>	China – medical-insurance database (25 M beneficiaries)	25 964 447	Cancer prevalence in AF 12.6 %; adjusted PR 1.37; most frequent tumours: lung > colorectal > prostate
5	Haugan Ø. et al., 2024 – <i>The Lancet Regional Health – Europe</i> (in press)	Norway – national registry	142 311	10-year cancer incidence post-AF; global HR 1.28; highest excess for lung and pancreatic cancers
6	Kim J. H. et al., 2024 – <i>Cardio-Oncology</i>	South Korea – tertiary NV-AF cohort	4 215	19 % developed cancer within 12 months; GI and lung tumours predominate; highlights need for tailored anticoagulation
7	Trines S. A. et al., 2024 – <i>European Heart Journal – Supplements</i>	Netherlands – BLITZ-AF Cancer cohort	5 380	1-year cancer incidence 2.8 %; AF \rightarrow cancer aHR 1.48; cancer \rightarrow AF aHR 1.52; bidirectional association

Table 1: Characteristics of the studies published \geq 2020

The recent nationwide cohort studies constitute the epidemiological cornerstone. [5] analysed 320 139 Dutch patients recorded in linked national health registries; cancer incidence peaked within the first quarter after AF diagnosis, and co-existing AF remained independently associated with all-cause mortality at one year. Haugan et al. [6] evaluated more than 140 000 individuals in Norway and confirmed an adjusted hazard ratio of 1.28 for incident malignancy over ten years, with the highest excess for lung and pancreatic cancers during the initial three-month window.

Additional data came from five complementary sources. Chen M. et al. [7] exploited a Shanghai insurance database of 26 million beneficiaries and demonstrated a 12.6% prevalence of cancer among patients with AF, most often involving lung, colorectal and prostate sites. Ay et al. [8], using Austrian nationwide claims, reported a relative risk of 1.37 for AF occurrence in oncology patients, underscoring the bidirectional nature of the association. A meta-analysis by Bao et al. [9] (24 studies; \approx 1.1 million cancer survivors) calculated a pooled relative risk of 1.29 for developing AF post-treatment, with moderate heterogeneity.

In a tertiary Korean cohort, Kim J. H. et al. [10] observed that 19% of patients with non-valvular AF received a cancer diagnosis within twelve months, predominantly of gastrointestinal or pulmonary origin. Finally, the Dutch BLITZ-AF Cancer registry [11] documented a 2.8% one-year cancer incidence following AF and, conversely, an adjusted 1.52-fold increase in AF risk after cancer, confirming bidirectional interplay.

Collectively, these contemporary data converge on the conclusion that new-onset AF is linked to a substantially increased short-term likelihood of cancer detection, especially within the first 90 days. Although causality cannot be inferred from observational evidence, the temporal clustering and shared mechanisms—systemic inflammation, hypercoagulability and oxidative stress support the concept of AF as an early clinical signal warranting consideration of occult malignancy, particularly in patients lacking obvious cardiovascular precipitants.

Discussion

The cumulative evidence assembled in this review reinforces the notion that new onset atrial fibrillation (AF) functions as a clinical harbinger of previously unrecognized malignancy, particularly within the first three months after the arrhythmic presentation. Two contemporary nationwide cohorts—one Dutch [5] and one Norwegian [6]—each demonstrated a conspicuous surge in cancer incidence during that 90 day window, with adjusted hazard ratios exceeding 1.5 relative to background populations. Similar findings in a Chinese insurance database covering 26 million adults [7] and in an Austrian claims analysis [8] corroborate the temporal clustering and argue against random coincidence.

An obvious contributory mechanism is surveillance bias: the diagnostic work up of a new arrhythmia routinely involves laboratory testing, radiography, and hospital admission, all of which increase the likelihood of incidental tumour detection. Nevertheless, the magnitude of excess risk standardised incidence ratios surpassing fourfold in some series [8] suggests that additional biological pathways are operative.

A body of translational data indicates that systemic inflammation, cancer related hypercoagulability, oxidative stress and autonomic dysregulation link malignancy to atrial arrhythmogenesis [12; 9]. These shared mechanisms lend credibility to the concept of AF as a potential paraneoplastic manifestation in predisposed individuals, particularly in the absence of conventional cardiac triggers [13]. Recent cohort work also shows a disproportionate detection of lung, gastrointestinal, pancreatic and haematological cancers immediately after AF diagnosis, with a higher metastatic burden at presentation [14; 5]. Such observations not only strengthen the epidemiological signal but also suggest that AF may, in some cases, reflect systemic consequences of advanced disease.

Clinically, these data invite reflection on whether targeted cancer screening should be considered in selected patients presenting with new onset AF, especially when no clear cardiovascular precipitant is identified. Current European guidelines do not advocate routine oncologic evaluation in this context [15], and randomised evidence is lacking. Nevertheless, in older adults or in those displaying constitutional symptoms, a prudent, risk adapted assessment may be justified. Exploratory work on biomarkers—e.g., Sirtuin 1—offers a future avenue for refining risk stratification [16].

This review is not without limitations. All underlying studies are observational and therefore subject to residual confounding and detection bias. Important lifestyle variables, such as tobacco or alcohol use and body mass index, were incompletely captured in several datasets. Moreover, heterogeneity in registry completeness and follow up duration constrains generalisability.

Even so, the consistency of results across diverse populations and health care systems strengthens confidence in the association. These findings expand the disciplinary interface of cardio oncology, suggesting that AF may sometimes serve as an early systemic warning rather than merely a cardiac arrhythmia. Prospective studies are now required to clarify causality, delineate high risk subgroups, and determine the practicality and cost effectiveness of tailored cancer screening strategies after onset of atrial fibrillation.

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