Aims. Previous studies have demonstrated epidemiological evidence for an association between cancer and the development of new-onset atrial fibrillation (AF). However, these results have been conflicting. This systematic review and meta-analysis was conducted to examine the relationship between cancer and the risk of developing atrial fibrillation. Methods. PubMed and Web of Science were searched for publications examining the association between cancer and atrial fibrillation risk published until June 2017. Adjusted odds ratios (ORs) or hazard ratios (HRs) and 95% CI were extracted and pooled. Results. A total of five studies involving 5,889,234 subjects were included in this meta-analysis. Solid cancer patients are at higher risk developing atrial fibrillation compared to noncancer patients (OR 1.47, 95% CI 1.31 to 1.66, \( p < 0.00001; I^2 = 67\%\)). The risk of atrial fibrillation was highest within 90 days of cancer diagnosis (OR 7.62, 95% CI 3.08 to 18.88, \( p < 0.00001\)) and this risk diminished with time. Conclusions. The risk of AF was highest within 90 days of cancer diagnosis. We should take into account the increased risk of atrial fibrillation development and, after this, study the embolic risk and potential indication of oral anticoagulation.
interleukin- (IL-) 2, IL-6, and IL-8 [5]. However, evidence from epidemiological studies has been controversial [6–10]. Therefore, this systematic review and meta-analysis was conducted to examine the relationship between cancer and the risk of developing AF.

2. Methods

This meta-analysis of observational studies was in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [11].

2.1. Search Strategies. Two researchers (M. Y. and X. F.) systematically and independently searched the relevant studies from the following databases: PubMed (until June 2017) and Web of Science (from 1986 through June 2017). We used the following key words: “cancer,” “carcinoma,” “tumor,” and “atrial fibrillation.” The reference lists of the articles, conferences, and editorials were used to identify further relevant studies.

2.2. Inclusion Criteria. All observational studies reported on the epidemiological evidence for an association between solid cancer and AF were included in this meta-analysis. Because the aim of this meta-analysis is to investigate whether cancer patients are at an increased risk of developing AF in general population, study population that involved the patients who underwent surgery and chemotherapy were excluded. The inclusion criteria were articles (1) published in English language, (2) on human subjects, (3) that were case control, prospective or retrospective cohort study, (4) reporting the odds ratios (ORs) or hazard ratios (HRs) and the corresponding 95% confidence intervals (CIs) or data required for their calculations were provided, (5) assessing the association between AF and cancer, not survival of cancer or complication of AF. Where two articles with overlapping data were included, the articles with higher subjects were included.

2.3. Study Selection. Two researchers (M. Y. and X. F.) independently screened the titles and abstracts of the studies. Potential eligible studies were retrieved using the relevant inclusion criteria mentioned previously. Any disagreements or indeterminations between the two researchers were resolved through discussion or consultation with a third researcher (T. L.).

2.4. Data Extraction and Quality Assessment. Hazard ratio (HRs), odds ratio (ORs), and their 95% confidence intervals (CIs) for the association between cancer and AF were extracted from individual articles. If both unadjusted and adjusted ORs/HRs were reported, the adjusted ORs/HRs were preferentially used. And we priority to extracted multivariate adjusted ORs/HRs, not age- or gender-adjusted, to evaluate the risk of AF occurrence. The extracted data of each study included first author’s last name, year of publication, geographic location of study, study design, total number of subjects, participants’ age and sex, types of cancer, criterion for AF confirmation, follow-up duration, maximum adjusted covariates, HR or OR with 95% CI, and patients with heart failure, hypertension, and diabetic mellitus.

The Newcastle-Ottawa Scale (NOS) items, with total score of nine stars, were used to evaluate the quality of cohort or case control studies [12]. We defined the cohort or case control studies with NOS score ≥7 stars as high quality and NOS score <7 stars as low quality.

2.5. Statistical Analysis. The ORs with 95% CIs were used as the common risk estimates and then were pooled. The HR value using multivariate Cox proportional hazards model in the original research was directly considered as OR. Percent variability across studies attributable to heterogeneity beyond sampling error was evaluated using the $I^2$ statistic, and $I^2$ value of >50% represented moderate to high heterogeneity. The random effects model was used as it is better to explain heterogeneity between studies over the fixed-effects model. Subgroup analyses and sensitivity analysis were performed to identify the sources of heterogeneity. Subgroup analyses regarding study design (case control studies or cohort studies), study location (Europe and USA), and the methods for AF diagnosis (electrocardiogram and International Classification of Disease code) and time interval between cancer diagnosis and AF were performed. Sensitivity analysis was performed by omitting one study at a time to evaluate the influence of individual studies on the pooled results. The funnel plot was constructed to identify possible publication bias. $P$ values of <0.05 (two-tailed) were considered statistically significant. Statistical analyses were performed using the Review Manager (RevMan) software (Nordic Cochrane Center; http://ims.cochrane.org/revman, version 5.3).

3. Results

A flow diagram of the data search and study selection is shown in Figure 1. Initially, 6311 records were identified from the PubMed and Web of Science databases. Of these, 2796 were duplicate studies and were excluded. The remaining articles were screened, and 3487 were subsequently excluded because they were review articles, animal studies, or irrelevant to this analysis. The 28 remaining studies were then reviewed in detail, and 23 of the 28 were excluded: study published in Italian, Russian, or Spanish language ($n = 5$) [13–16]; study reported AF leading to cancer ($n = 4$) [17–20]; individual case reports ($n = 3$) [21–23]; letters [24, 25] or editorials [26] ($n = 3$); different article from the same center [27, 28], and a more recent series was available [8], patients in this study [29] may be ondystsamplingerrorwasevaluatedusingthe $I^2$ statistic, and $I^2$ value of >50% represented moderate to high heterogeneity. The random effects model was used as it is better to explain heterogeneity between studies over the fixed-effects model. Subgroup analyses and sensitivity analysis were performed to identify the sources of heterogeneity. Subgroup analyses regarding study design (case control studies or cohort studies), study location (Europe and USA), and the methods for AF diagnosis (electrocardiogram and International Classification of Disease code) and time interval between cancer diagnosis and AF were performed. Sensitivity analysis was performed by omitting one study at a time to evaluate the influence of individual studies on the pooled results. The funnel plot was constructed to identify possible publication bias. $P$ values of <0.05 (two-tailed) were considered statistically significant. Statistical analyses were performed using the Review Manager (RevMan) software (Nordic Cochrane Center; http://ims.cochrane.org/revman, version 5.3).

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five studies comprising 5,889,234 participants were included in our meta-analysis.

The characteristics of the included studies and their quality scores are shown in Table 1. Two were case control studies [7, 8], and three were cohort studies [6, 9, 10]. Two studies [6, 7] investigated only the association between AF and colorectal cancer, whereas three studies [8–10] examined colorectal cancer and also cancer of the breast, lung, and prostate. For the included cohort, the mean age ranged from 53 to 75 years and the proportion of male patients accounted for all patients ranged from 0% to 60%. Characteristics of the patients are presented in Table 2. NOS analysis showed that all included studies were of high quality.

Apart from one study [6] reporting no significant association between cancer and AF, the remaining four studies [7–10] consistently demonstrated a significant association between cancer and new AF risk. Overall, the summary estimate from the five separate estimates from the cohort or case-control studies united indicated that patients with cancer had an approximately 47% higher risk of AF compared to noncancer patients (OR 1.47, 95% CI 1.31 to 1.66, \( p < 0.00001 \); Figure 2). There was a significant heterogeneity across the studies (\( I^2 = 67\% \), \( p = 0.02 \)).

Four of five studies reported OR of incidence of AF in colorectal cancer; the pooled effect sizes of these studies [6–9] (OR 1.54, 95% CI 1.40 to 1.71, \( p < 0.00001 \); heterogeneity: \( I^2 = 48\% \), \( p = 0.12 \); Figure 3(a)) showed that patients with colorectal cancer at a 54% higher risk of developing AF than those without colorectal cancer. Two of five studies offered OR of incidence of AF in breast cancer; in the pooled analysis of these studies [8, 9] (OR 2.07, 95% CI 0.96 to 4.45, \( p = 0.06 \); heterogeneity: \( I^2 = 81\% \), \( p = 0.02 \); Figure 3(b)), we observed a prevalence of AF close to two times higher in breast cancer patients compared to those without breast cancer.

Subgroup analyses were subsequently performed to identify potential sources of heterogeneity. The details are

![Figure 1: Flow diagram of the study selection process. AF = atrial fibrillation; OR = odds ratio.](image-url)
Table 1: Characteristics of the five studies included in this meta-analysis.

| First author and year | Location | Period of enrollment | Study design | Total patients, N | Cancer type | Incident cases of AF, N (%) | AF type | Criterion for AF diagnosis | Covariates in adjusted model | Follow-up (year) | Quality score |
|-----------------------|----------|----------------------|--------------|-------------------|-------------|--------------------------|---------|---------------------------|-----------------------------|----------------|--------------|
| Guzzetti 2008 [8]     | Italy    | 1987–2004            | Case-control | 1868              | Colorectal and breast cancer | 49 (2.6) | New-onset AF              | Routine presurgery ECG | Age, sex | NA | 8 |
| Erichsen 2012 [7]     | Denmark  | 1999–2006            | Case-control | 311593            | Colorectal cancer | NA | New-onset AF/Flutter New-onset AF | According to the ICD | Age, sex, country | NA | 8 |
| Jakobsen 2015 [9]     | Denmark  | 2000–2012            | Prospective cohort | 5539824 | All types of cancer | NA | New-onset AF | Age, sex | 12 | 7 |
| Nouraie 2015 [6]      | USA      | 2000–2012            | Retrospective cohort | 1258 | Colorectal cancer | 93 (7.4) | New-onset AF | According to the ICD | Age, HTN, HF, DM, alcohol, tobacco | NA | 8 |
| Conen 2016 [10]       | USA      | 1993–2013            | Prospective cohort | 34691 | All types of cancer | 824 (2.3) | New-onset AF | Electrocardiographic AF documentation or a medical report that documented a diagnosis of AF | Age, EDU, race, height, BMI, HTN, DM, smoking, HC, alcohol, physical activity, CHF, MI, stroke | 19.1 | 9 |

AF = atrial fibrillation; BMI = body mass index; CHF = congestive heart failure; CRP = C-reactive protein; DM = diabetes mellitus; ECG = electrocardiography; EDU = educational level; HC = hypercholesterolemia; HDL-c = high-density lipoprotein cholesterol; HF = heart failure; HTN = hypertension; ICD = International Classification of Diseases; LVH = left ventricular hypertrophy; MI = myocardial infarction; NA = not applicable; SBP = systolic blood pressure; TC = total cholesterol.
shown in Table 3. Our pooled meta-analysis suggested that cancer is significantly associated with the occurrence of AF in both cohort [6, 9, 10] and case control [7, 8] studies with significant heterogeneity. As shown in Table 3, cancer was associated with an increased risk of AF in both studies originating from Europe [7–9] (OR 1.56, 95% CI 1.39 to 1.76, \( p < 0.0001 \), \( I^2 = 65\% \)) with significant heterogeneity as well as the United States [6, 10] (OR 1.22, 95% CI 1.04 to 1.44, \( p = 0.01 \), \( I^2 = 0\% \)) without heterogeneity.

Subgroup analysis was also performed for the method of AF diagnosis. Meta-analysis of two studies using electrocardiography [8, 10] reported a higher risk of AF in cancer patients (OR 1.89, 95% CI 0.70 to 5.10, \( p = 21 \), \( I^2 = 87\% \)) with significant heterogeneity. Meta-analysis of two studies that had used the International Classification of Diseases (ICD) [6, 7] also demonstrated elevated risk of AF (OR 1.56, 95% CI 1.39–1.74, \( p < 0.0001 \), \( I^2 = 0\% \)), and this was associated with minimal heterogeneity. Therefore, study location [6–10] and the method for diagnosing AF [6–8, 10] are both likely the origin of the heterogeneity in our main meta-analysis.

To examine temporal relationship between cancer and AF, ORs from two studies were further pooled [7, 10] for AF according to the time since cancer was first diagnosed, classified by time interval less than 90 days, 91 to 365 days, or more than 365 days. We found significantly increased risk of AF in cancer patients diagnosed less than 90 days (OR 7.62, 95% CI 3.08 to 18.88, \( p < 0.0001 \), \( I^2 = 91\% \)). Otherwise, pooled OR of incidence of AF was not significantly increased for longer time-points of 91 to 365 days (OR 1.06, 95% CI 1.04 to 1.08, \( p = 0.90 \), \( I^2 = 0\% \)) or beyond 365 days (OR 1.07, 95% CI 0.97 to 1.25, \( p = 0.87 \), \( I^2 = 84\% \)) (Table 3). Finally, sensitivity analysis by excluding one study at a time did not significantly alter the pooled OR. The results of the funnel plot for the association between cancer and AF was asymmetry, indicating that publication bias may be present, although the small number of studies made this somewhat difficult to interpret (Figure 4).
4. Discussion

Our systematic review and meta-analysis of five published observational studies suggests that subjects with newly diagnosed cancer had a significantly increased risk of AF during subsequent follow-up. There was significant heterogeneity observed between the included studies which were likely due to different methods of AF diagnosis. Interestingly, the increased risk of AF was only observed within the first 90 days after cancer diagnosis, and the risk was not significant after 1 year. Our study found substantial statistical heterogeneity in the pooled effect estimates. This is partly explicable by the use of different methods to detect AF in the individual studies. There are some data to support an increased risk of stroke after a cancer diagnosis, and one could hypothesize that this relationship between cancer and AF could account for part of the elevated risk of stroke if the AF went undetected.

Oncocardiology is a new field of clinical medicine that addresses the close link between cancer and cardiovascular diseases [35, 36]. Recent evidence showed that cancer is closely related to the development of AF. A number of pathophysiological mechanisms, such as inflammation and autonomic dysfunction, have been proposed to explain this link [5, 37]. Firstly, clinical studies have demonstrated elevations in proinflammatory markers in both AF and cancer. A case-control study showed that patients with atrial arrhythmia compared to those without atrial arrhythmia had higher levels of the inflammatory marker, C-reactive protein (CRP). Indeed, CRP levels were higher in persistent than paroxysmal AF patients [38]. Another large population-based cohort study reported that CRP was independently

| Subgroup                  | Number of studies | Meta-analysis | Heterogeneity |
|---------------------------|-------------------|---------------|---------------|
|                           |                   | OR 95% CI     | p value       | I² (%) | p value    |
| Study design              |                   |               |               |        |            |
| Case control              | 2                 | 2.11          | 1.03–4.34     | 0.04   | 77         | 0.04       |
| Cohort                    | 3                 | 1.38          | 1.15–1.64     | 0.0004 | 69         | 0.04       |
| Study location            |                   |               |               |        |            |
| Europe                    | 3                 | 1.56          | 1.39–1.76     | <0.0001| 65         | 0.06       |
| USA                       | 2                 | 1.22          | 1.04–1.44     | 0.01   | 0          | 0.52       |
| Criterion for AF diagnosis|                   |               |               |        |            |
| ECG                       | 2                 | 1.89          | 0.70–5.10     | 0.21   | 87         | 0.005      |
| ICD                       | 2                 | 1.56          | 1.39–1.74     | <0.0001| 0          | 0.62       |
| Time interval between cancer diagnosis and AF | |               |               |        |            |
| ≤90 days                  | 2                 | 7.62          | 3.08–18.88    | <0.0001| 91         | 0.0009     |
| >91–365 days              | 2                 | 1.06          | 0.90–1.25     | 0.46   | 0          | 0.48       |
| >365 days                 | 2                 | 0.97          | 0.71–1.34     | 0.87   | 84         | 0.01       |

AF = atrial fibrillation; CI = confidence interval; ECG = electrocardiogram; ICD = International Classification of Disease; OR = odds ratio.
There are several potential limitations of our meta-analysis. Firstly, the data on the epidemiological evidence for the relationship between new-onset cancer and the risk of AF are sparse, and only a few studies have addressed this issue. And given that the total number of studies was small, we included a letter [28] and an abstract of conference [9] to maximize the use of available data. Secondly, some studies only presented the sex- or age-adjusted ORs/HRs, so not all ORs/HRs used in this analysis were extracted from multivariate analysis. This may have introduced a degree of random error in our pooled analysis. Finally, the epidemiological evidence for an association between cancer and risk of AF is mainly investigated in this study, and we will perform further study to uncover the potential relationship between surgery or chemotherapy and development of atrial fibrillation.

In summary, this meta-analysis demonstrates that cancer is associated with atrial fibrillation that was significant within the first three-month period. These findings would prompt us to suggest that AF patients should be screened for occult cancer. Future studies are needed to examine the potential mechanisms linking cancer to AF, and further analyses that can examine the association between AF and subsequent cancer-related mortality may exclude to possibility of diagnostic bias.

Disclosure

An earlier version of the manuscript has been presented as conference abstract in Global Cardio-Oncology Summit 2017, available in the following link: http://cardiooncology.ca/wp-content/uploads/GCOS2017_029_YXia_Abstract.pdf.

Conflicts of Interest

The authors declare no conflicts of interest.

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References

[1] S. S. Chugh, R. Havmoeller, K. Narayan et al., “Worldwide epidemiology of atrial fibrillation,” Circulation, vol. 129, no. 8, pp. 837–847, 2014.
[2] J. Ball, M. J. Carrington, J. J. V. McMurray, and S. Stewart, “Atrial fibrillation: profile and burden of an evolving epidemic in the 21st century,” International Journal of Cardiology, vol. 167, no. 5, pp. 1807–1824, 2013.
[3] D. Farmakis, J. Parissis, and G. Filippatos, “Insights into oncocardiology,” Journal of the American College of Cardiology, vol. 63, no. 10, pp. 945–953, 2014.
[4] S. I. Grivennikov, F. R. Greten, and M. Karin, “Immunity, inflammation, and cancer,” Cell, vol. 140, no. 6, pp. 883–899, 2010.
[5] Y. Guo, G. Y. H. Lip, and S. Apostolakis, "Inflammation in atrial fibrillation," *Journal of the American College of Cardiology*, vol. 60, no. 22, pp. 2263–2270, 2012.

[6] M. Nouraie, V. Kansal, C. Belfonte et al., "Atrial fibrillation and colonic neoplasia in African Americans," *PLoS One*, vol. 10, no. 8, Article ID e0135609, 2015.

[7] R. Erichsen, C. F. Christiansen, F. Mehnert, N. S. Weiss, J. A. Baron, and H. T. Sørensen, "Colorectal cancer and risk of atrial fibrillation and flutter: a population-based case-control study," *Internal and Emergency Medicine*, vol. 7, no. 5, pp. 431–438, 2012.

[8] S. Guzzetti, G. Costantino, A. Vernocchi, S. Sada, and C. Fundarò, "First diagnosis of colorectal or breast cancer and prevalence of atrial fibrillation," *Internal and Emergency Medicine*, vol. 3, no. 3, pp. 227–231, 2008.

[9] C. Jacobsen, N. Carlson, M. Lamberts et al., "Incidence of atrial fibrillation in different types of cancer: A Danish nationwide cohort study," *European Heart Journal*, vol. 36, p. 164, 2015.

[10] D. Conen, J. A. Wong, R. K. Sandhu et al., "Risk of malignant cancer among women with new-onset atrial fibrillation," *JAMA Cardiology*, vol. 1, no. 4, pp. 389–396, 2016.

[11] E. von Elm, D. G. Altman, M. Egger, S. J. Pocock, P. C. Gøtzsche, and J. P. Vandenbroucke, "The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies," *The Lancet*, vol. 370, no. 9596, pp. 1453–1457, 2007.

[12] A. Stang, "Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses," *European Journal of Epidemiology*, vol. 25, no. 9, pp. 603–605, 2010.

[13] S. Guzzetti, G. Costantino, S. Sada et al., "Atrial fibrillation as a complication of colorectal tumors," *Recenti Progressi in Medicina*, vol. 94, no. 6, pp. 260–263, 2003.

[14] E. V. Andrushenko, I. I. Polishchuk, T. A. Malanchuk et al., "Atrial fibrillation as the onset of cancer of the left lung," *Lik Sprava*, vol. 7–8, pp. 128–130, 1995.

[15] C. Alvarez Alvarez, F. Tardaguila Montero, J. A. Carrillo Sande et al., "Atrial fibrillation in an oncological patient with remission," *Anales de Medicina Interna*, vol. 23, no. 6, pp. 295–296, 2006.

[16] F. Furlanello, R. Miori, E. Piccolo et al., "Paroxysmal atrial arrhythmia and lung neoplasms (clino-electrocardiographic consideration)," *Torace*, vol. 17, no. 1–2, pp. 310–325, 1974.

[17] A. D. Müller, A. Sonnenberg, and I. H. Wasserman, "Diseases preceding colon cancer," *Digestive Diseases and Sciences*, vol. 39, no. 11, pp. 2480–2484, 1994.

[18] S. Fumagalli, A. Barchielli, F. Tarantini et al., "Atrial fibrillation and cancer: evidence for an epidemiological link," *Journal of the American College of Cardiology*, vol. 59, no. 13, p. E615, 2012.

[19] E. B. Ostenfeld, R. Erichsen, L. Pedersen et al., "Atrial fibrillation and cancer: evidence for an epidemiological link," *Circulation*, vol. 94, no. 6, pp. 260–263, 1995.

[20] S. Guzzetti, G. Costantino, S. Sada, and C. Fundarò, "Atrial fibrillation as the onset of cancer of the left lung," *Lik Sprava*, vol. 7–8, pp. 128–130, 1995.

[21] R. Knur and J. Özse, "Atrial fibrillation as the first clinical presentation of an adenoid cystic bronchial carcinoma," *Netherlands Heart Journal*, vol. 22, no. 10, pp. 472–473, 2014.

[22] A. Beyder and K. W. Klarich, "Large atrial myxoma causing dynamic obstruction of the mitral valve and atrial fibrillation," *Mayo Clinic Proceedings*, vol. 87, no. 2, p. e9, 2012.

[23] J. E. Cohen, J. Kogan, S. Oren, and M. Mazza, "Primary cardiac lymphoma presenting with atrial fibrillation," *Israel Medical Association Journal*, vol. 13, no. 10, pp. 635–7, 2011.

[24] P. Velagapudi, M. K. Turagam, and A. G. Kocheril, "Atrial fibrillation in cancer patients," *Southern Medical Journal*, vol. 104, no. 9, pp. 667–668, 2011.

[25] G. P. Koracovic, "Cancer is an insufficiently recognized risk factor for atrial fibrillation," *Journal of Emergency Medicine*, vol. 42, no. 3, pp. 312–313, 2012.

[26] F. Rahman, D. Ko, and E. J. Benjamini, "Association of atrial fibrillation and cancer," *JAMA Cardiology*, vol. 1, no. 4, pp. 384–386, 2016.

[27] S. Guzzetti, G. Costantino, and C. Fundarò, "Systemic inflammation, atrial fibrillation, and cancer," *Circulation*, vol. 106, no. 9, p. e40, 2002.

[28] S. Guzzetti, G. Costantino, S. Sada, and C. Fundarò, "Colorectal cancer and atrial fibrillation: a case-control study," *American Journal of Medicine*, vol. 112, no. 7, pp. 587–588, 2002.

[29] C. H. Kim, S. G. Al-Kindi, and G. H. Oliveira, "Atrial fibrillation and cancer-validation in the real world," *JAMA Cardiology*, vol. 2, no. 3, pp. 343–344, 2017.

[30] S. R. Walsh, K. M. Gladwish, N. J. Ward, T. A. Justin, and N. J. Keeling, "Atrial fibrillation and survival in colorectal cancer," *World Journal of Surgical Oncology*, vol. 2, no. 1, p. 40, 2004.

[31] T.-L. Yang, Y.-F. Hu, Y.-J. Lin et al., "Atrial fibrillation influences survival in patients with hepatocellular carcinoma: experience from a single center in Taiwan," *Journal of the Chinese Medical Association*, vol. 77, no. 3, pp. 117–121, 2014.

[32] E. Bou, P. Hernandez, L. Cerezco et al., "Heart tumors in Puerto Rico: De novo atrial fibrillation as clinical presentation in a subgroup of patients," *Puerto Rico Health Sciences Journal*, vol. 32, no. 1, pp. 14–17, 2013.

[33] W. T. O’Neal, S. G. Lakoski, W. Qureshi et al., "Relation between cancer and atrial fibrillation (from the REasons for Geographic And Racial Differences in Stroke Study)," *American Journal of Cardiology*, vol. 115, no. 8, pp. 1090–1094, 2015.

[34] Y.-f. Hu, C.-j. Liu, P. M.-h. Chang et al., "Incident thromboembolism and heart failure associated with new-onset atrial fibrillation in cancer patients," *International Journal of Cardiology*, vol. 165, no. 2, pp. 355–357, 2013.

[35] W.-L. Cheng, Y.-H. Kao, S.-A. Chen, and Y.-J. Chen, "Pathophysiology of cancer therapy-provoked atrial fibrillation," *International Journal of Cardiology*, vol. 219, pp. 186–194, 2016.

[36] D. Sueta, N. Tabata, T. Akasaka, T. Yamashita, T. Ikemoto, and S. Hokimoto, "Pathophysiology of cancer therapy-provoked atrial fibrillation," *Cancer Medicine*, vol. 32, no. 1, pp. 310–325, 1974.

[37] S. Guzzetti, G. Costantino, S. Sada, and C. Fundarò, "Atrial fibrillation as the onset of cancer of the left lung," *Lik Sprava*, vol. 7–8, pp. 128–130, 1995.

[38] M. K. Chung, D. O. Martin, D. Sprecher et al., "C-reactive protein elevation in patients with atrial arrhythmias," *PLoS One*, vol. 9, no. 8, Article ID e102861, 2014.

[39] R. J. Aviles, D. O. Martin, C. Apperson-Hansen et al., "Inflammation as a risk factor for atrial fibrillation," *Circulation*, vol. 108, no. 24, pp. 3006–3010, 2003.
[40] G. M. Marcus, L. M. Smith, D. V. Glidden et al., “Markers of inflammation before and after curative ablation of atrial flutter,” Heart Rhythm, vol. 5, no. 2, pp. 215–221, 2008.

[41] G. Tse, B. P. Yan, Y. W. Chan et al., “Reactive oxygen species, endoplasmic reticulum stress and mitochondrial dysfunction: the link with cardiac arrhythmogenesis,” Frontiers in Physiology, vol. 7, p. 313, 2016.

[42] S. J. Wigmore, J. P. Maingay, K. C. H. Fearon, M. G. O’Riordain, and J. A. Ross, “Effect of interleukin-4 on pro-inflammatory cytokine production and the acute phase response in healthy individuals and in patients with cancer or multiple organ failure,” Clinical Science, vol. 95, no. 3, pp. 347–354, 1998.

[43] T. P. Erlinger, E. A. Platz, N. Rifai et al., “C-reactive protein and the risk of incident colorectal cancer,” JAMA, vol. 291, no. 5, pp. 585–590, 2004.

[44] D. M. O’Hanlon, J. Lynch, M. Cormican et al., “The acute phase response in breast carcinoma,” Anticancer Research, vol. 22, no. 2b, pp. 1289–1293, 2002.

[45] Y. Xi and J. Cheng, “Dysfunction of the autonomic nervous system in atrial fibrillation,” Journal of Thoracic Disease, vol. 7, no. 2, pp. 193–198, 2015.

[46] R. Martin, J. M. Delgado, J. M. Moltò et al., “Cardiovascular reflexes in patients with malignant disease,” Italian Journal of Neurological Sciences, vol. 13, no. 2, pp. 125–129, 1992.

[47] S. Guzzetti, “Systemic inflammation, atrial fibrillation, and cancer,” Circulation, vol. 106, no. 9, pp. 40e–40, 2002.

[48] J. Faber and C. Selmer, “Cardiovascular disease and thyroid function,” Cardiovascular Issues in Endocrinology, vol. 43, pp. 45–56, 2014.

[49] S. Marrakchi, F. Kanoun, S. Idriss et al., “Arrhythmia and thyroid dysfunction,” Herz, vol. 40, no. 2, pp. 101–109, 2015.

[50] L. Mao, W. Huang, P. Zou, X. Dang, and X. Zeng, “The unrecognized role of tumor suppressor genes in atrial fibrillation,” Gene, vol. 642, pp. 26–31, 2018.