JAFIB
Original Research
Journal of Atrial Fibrillation

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Seasonal Variation in Paroxysmal Atrial Fibrillation: A Systematic Review

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Abstract

Introduction: A variety of cardiovascular diseases have been demonstrated to have seasonal variations with peaks in the winter and troughs in the summer. Studies regarding atrial fibrillation (AF) have had varying results and this review describes the current data regarding the seasonal variation of AF and mechanisms mediating this seasonal fluctuation.

Methods: A systematic review was conducted of PubMed, EBSCO and OVID for manuscripts describing the association between seasonal variation and the occurrence of AF. Studies meeting eligibility criteria were assessed for quality and reporting bias. Data was extracted in regards to the following associations: seasonal variation and AF paroxysms, temperature and AFparoxysms, duration of daylight and AF paroxysms, barometric pressure and AF paroxysms, alcohol and AF paroxysms, as well as seasonal variation and AF related stroke.

Results: A total of 15 studies were identified for inclusion. Of these, 11 studies assessed seasonal variation and the remaining 4 studies assessed seasonal variation in AF related stroke. AF paroxysms peaked in winter with a trough in summer. There was an inverse correlation between temperatures as well barometric pressure and the occurrence of AF paroxysms and a positive correlation with duration of daylight.

Conclusions: The rate of occurrence of paroxysmal AF varies by seasons and is greatest during winter and least in summer.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia and is responsible for a majority of arrhythmia-related hospitalizations.[1] As the prevalence of AF continues to rise so does the number of related hospitalizations, morbidity, and mortality.[2] AF mechanisms include atrial ectopy, single localized reentry circuits, or multiple microreentrant circuits, all of which can be influenced by genotype, ischemic heart disease and inflammation. Other risk factors include hyperthyroidism, obstructive sleep apnea and congenital heart disease.[3-5] As the burden of AF begins to increase it is of utmost importance to identify all potential risk factors.

Multiple studies have demonstrated an association between seasonal variation and a variety of cardiac and non-cardiac disorders such as deep venous thrombosis, pulmonary embolism, aortic dissection, stroke, hypertension, congestive heart failure, angina, ventricular arrhythmias, myocardial infarction, and sudden cardiac arrest. Many of these diseases have been found to be more frequent in winter, with inverse correlations to outdoor temperature. Similar associations have been proposed for AF as well as AF related stroke.[6]

The primary purpose of this review is to summarize data regarding the association between seasonal variation and occurrence of AF paroxysms. Secondary aims of this review were to summarize data regarding additional associations to further investigate the primary association:

1) outdoor temperature and occurrence of AF paroxysms.
2) duration of daylight and occurrence of AF paroxysms.
3) barometric pressure and occurrence of AF paroxysms.
4) alcohol consumption and occurrence of AF.
5) seasonal variation and the occurrence of AF related stroke.

Key Words:
Atrial Fibrillation, Season, Summer, Winter, Stroke, Death.

Disclosures:
None.

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Methods

A systematic review of the literature was performed to identify manuscripts studying the association between various seasons and AF. This included the occurrence of AF paroxysms, AF related stroke, and AF related mortality. The overall association of AF with the seasons, any particular month, temperature, amount of daylight, and barometric pressure were all studied. The review was conducted using the PRISMA checklist.

Manuscript Search And Identification Strategy

Electronic databases including PubMed, EMBASE, and Ovid were queried using the following search terms: "atrial fibrillation" in conjunction with one of the following "season", "summer" or "winter".

Table 1: Study characteristics

Study	Year	Design	N	Endpoint	Parameters studied
Kupari et al	1990	Cohort, unclear if retrospective or prospective	286 patients	AF	Season, temperature, alcohol
Gluszak et al	2008	Cohort, unclear if retrospective or prospective	739 patients	AF	Season, barometric pressure
Watanabe et al	2007	Cohort, unclear if retrospective or prospective	237 patients	AF	Season, temperature, daylight
Gluszak et al	2009	Cohort, unclear if retrospective or prospective	1,475 patients	AF	Season, daylight
Kountouris et al	2005	Prospective cohort	342 patients	AF	Season, daylight
Frost et al	2002	Retrospective cohort	32,992 patients	AF	Season, temperature
Deshmukh et al	2013	Retrospective cohort	2,909,423 hospitalizations	AF	Season
Kiu et al	2004	Retrospective cohort	24 patients	AF	Season
Upshur et al	2004	Retrospective cohort	90,200 hospitalizations	AF	Season
Fustinoni et al	2013	Retrospective cohort	899 patients	AF	Season, temperature
Murphy et al	2004	Retrospective cohort	68,045 hospitalizations	AF	Season, temperature
Christensen et al	2012	Retrospective cohort	39,632 patients	Stroke in AF	Season
Christensen et al	2012	Retrospective cohort	36,088 patients	Stroke in AF	Season
Frost et al	2006	Retrospective cohort	24,470 patients	Stroke in AF	Season
Spengos et al	2003	Retrospective cohort	315 patients	Stroke in AF	Season

No specific restriction on year of publication was used. Two reviewers (RL and SA) screened the resulting studies by title and abstract. Full text of the selected studies meeting eligibility criteria was then retrieved in their entirety. Further, references of these studies were hand searched for additional relevant manuscripts. Studies in a language other than English were excluded.

Published manuscripts available in full text were included in this review if they presented data from retrospective or prospective cohort studies or randomized controlled trials investigating the occurrence of AF paroxysms, AF related stroke, and AF related death and their association with season, calendar month, temperature, amount of daylight, and barometric pressure. Studies were included in this analysis if they included at least one of the factors identified above.

Authors RL and SA then reviewed these full text manuscripts for quality. Any disparities in scoring of manuscripts were then independently reviewed by another author. The Newcastle-Ottawa scale and Critical Appraisal Skills Programme (CASP) checklist were used to assess the quality of cohort studies.

Data Extraction

Data regarding baseline patient characteristics and outcomes were extracted from the manuscripts identified for inclusion. Study level data were independently collected with use of a data collection tool. The data extraction was then reviewed to ensure integrity of the resulting data. If no information was available about particular outcomes this was designated separately. Authors of included studies were not contacted for additional data.

Bias Analysis

Bias was assessed concurrently with quality assessment of studies using the Newcastle-Ottawa scale and CASP checklist for cohort studies as described above.

Data analysis

No quantitative data analysis was performed.

Results

Study Identification

Using the search terms as described above 96 unique manuscripts were identified. Of these papers, 12 focused on stroke in AF and 84 of these were not related to stroke in AF. Ultimately, quantitative data were extracted from 15 studies after inclusion of only cohort studies and randomized trials, 4 of which focused on stroke in AF and 11 of which were not related to stroke in AF (Figure 1).[7-21]

Study Characteristics

All 15 studies from which quantitative data were extracted from were cohort studies. Of these studies, 8 were retrospective and 1 was prospective. For the 6 remaining studies it was unclear whether these were retrospective or prospective. Of the 11 non-stroke related AF studies, 5 were retrospective, 1 prospective, and 5 unknown. Of the 4 stroke related studies, all were retrospective (Table 1).

The 11 non stroke related AF studies consisted of 36,994 patients. Two studies did not report patient number but rather hospitalizations, which consisted of 3,067,668 hospitalizations. Three of these studies were registry based studies while the remainder were retrospective or

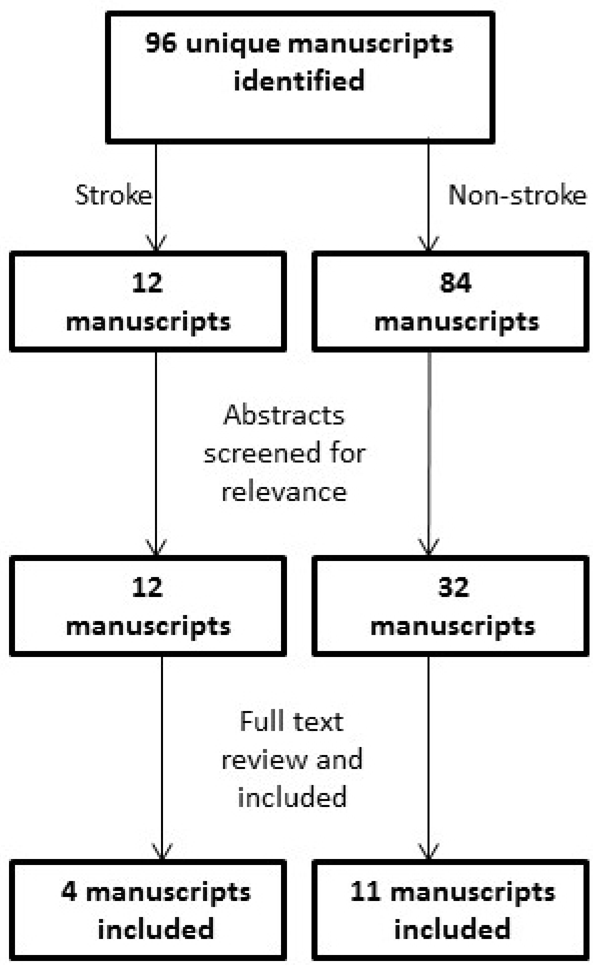

Figure 1: Study results

prospective cohort studies. Two of these studies reported incidence rate only, 1 study reported prevalence rate only and 8 studies reported both incidence and prevalence rates.[7-17]

The 4 stroke related AF studies consisted of 100,505 patients. All 4 of these studies were registry based studies. All 4 of these studies reported incidence rates.[18-21]

Association Data

Data regarding particular associations were extracted from the following number of studies: seasonal variation and occurrence of AF paroxysms from 11 studies, outdoor temperature and occurrence of AF paroxysms from 6 studies, duration of daylight and occurrence of AF paroxysms from 2 studies, barometric pressure and occurrence of AF paroxysms from 1 study, duration of alcohol and occurrence of AF paroxysms from 1 study, and seasonal variation and occurrence of AF related stroke from 4 studies.

Bias and Quality

Subjective analysis of bias with respect to patient selection, patient allocation, blinding, and outcome reporting showed minimal overall bias amongst the included studies. Quality assessment is outlined in Table 2.

Seasonal Variation And The Occurrence Of AF Paroxysms

Of the studies that analyzed the association between seasonal variation and the occurrence of AF paroxysms, 10 (91%) demonstrated an association between the seasons and AF paroxysms. All 10 of these studies demonstrated peak occurrence of AF paroxysms in winter with a nadir in summer with a 20% to 300% increase in the rate of AF paroxysms during the winter peak when compared to the summer nadir. February and April were both identified by 33% of studies as the peak months while July was identified by 42% of studies as the nadir month.[7-15, 17] Murphy et al. also demonstrated a 15% to 26% increased risk of AF related mortality during winter[13] (Table 3).

Outdoor Temperature And The Occurrence Of AF Paroxysms

Of the studies that analyzed the association between outdoor temperature and the occurrence of AF, 3 (50%) of these studies demonstrated an association between outdoor temperature and AF paroxysms.[8,11-13,15,16] The studies that demonstrated an association found an inverse correlation between temperature and AF paroxysms.[8, 12, 15] Again, the study by Murphy et al. demonstrated a 5% increased risk of inpatient mortality but no increase in outpatient mortality[13] (Table 3).

Duration Of Daylight And The Occurrence Of AF Paroxysms

Two studies investigated the association between duration of daylight and the occurrence of AF paroxysms. Watanabe et al. demonstrated a strong inverse correlation while Gluszak et al. noted such an inverse correlation in women but not in men[11, 17] (Table 3).

Barometric Pressure and the Occurrence of AF Paroxysms

A single study investigated the association between barometric pressure and the occurrence of AF paroxysms and noted that the risk of AF paroxysms was greatest 24 to 48 hours before the arrival of a low pressure front[7] (Table 3). Further details were not provided.

Alcohol And The Occurrence Of AF Paroxysms

Kupari et al. demonstrated a positive correlation between alcohol sales and the occurrence of AF paroxysms, with both being highest in April[12] (Table 3). Further details were not provided.

Seasonal Variation And AF Related Stroke

All the studies that investigated the association between seasonal variation and AF related stroke demonstrated highest risk in winter with the lowest risk in winter. There was a 22% to 200% increase in the risk of AF related stroke in the winter compared to summer.[18-21] There was no association between seasonal variation and mortality after AF related stroke[20] (Table 3).

Discussion

In our analysis, a majority of studies demonstrated an association between seasonal variation and the occurrence of AF paroxysms. AF paroxysms were most frequent during winter and early spring and least frequent in the summer with peak months being February and April. The nadir of AF paroxysms was observed to be in the month of July. It is reasonable to imagine that stroke, a complication of AF,

Table 2: Study quality and bias evaluation

Study	Baseline patient characteristics described*	Patient selection	Allocation Concealment	Blinding	Incomplete Outcome Data	Free of Selective Outcome Reporting	Other Bias	Newcastle-Ottawa Score
Kupari et al	yes	moderate	n/a	n/a	low	low	low	8
Gluszak et al (2008)	yes	moderate	n/a	n/a	low	low	low	9
Watanabe et al	yes	low	n/a	n/a	low	low	low	9
Gluszak et al (2009)	yes	moderate	n/a	n/a	low	low	low	8
Kountouris et al	yes	moderate	n/a	n/a	low	low	low	9
Frost et al (2002)	yes	moderate	n/a	n/a	low	low	low	8
Deshmukh et al	no	moderate	n/a	n/a	low	low	low	7
Kiu et al	yes	moderate	n/a	n/a	low	low	low	8
Upshur et al	yes	moderate	n/a	n/a	low	low	low	8
Fustinoni et al	no	moderate	n/a	n/a	low	low	low	8
Murphy et al	no	moderate	n/a	n/a	low	low	low	9
Christensen et al (2012)	yes	moderate	n/a	n/a	low	low	low	8
Christensen et al (2012)	yes	moderate	n/a	n/a	low	low	low	8
Frost et al (2006)	yes	moderate	n/a	n/a	low	low	low	8
Spengos et al	no	moderate	n/a	n/a	low	low	low	8

*Must have described at least gender and age would be more frequent at times of greatest AF burden and thus studies investigating seasonal variation and AF related stroke were also reviewed which demonstrated highest frequency of AF related stroke during the winter and the lowest during summer. Mortality during AF hospitalizations also appears to be greatest in winter while inpatient mortality during AF related stroke hospitalizations does not appear to be affected by seasonal variation.[7-15,17,20]

Several mechanisms have been proposed to explain the increased risk of AF paroxysms in winter with lower temperatures being the common denominator. Lower temperatures have been demonstrated to enhance sympathetic function by activation of central angiotensin or hypothalamic mineralocorticoid receptors, which can increase the risk of AF.[22-25] Blood pressure can also increase due to lower temperatures, which can ultimately lead to increased atrial pressure with subsequent atrial dilatation and pulmonary vein stretch leading to initiation and propagation of AF.[26-28] Endothelin I, renin, and angiotensin II levels may increase due to lower temperatures, which can also enhance arrhythmogenesis.[29-32] Cold temperatures may worsen atrial ischemia and promote glucose intolerance, both of which may increase the risk of AF paroxysms.[15] Our review demonstrates equivocal results regarding the association between temperature and the occurrence of AF paroxysms.

Duration of daylight has also been proposed as a mechanism to explain the increased risk of AF paroxysms in winter. Yamashita et al. have demonstrated circadian variation in the expression of potassium channels, particularly that decreased exposure to sunlight can lead to alterations in cardiac ion channels such that action potentials shorten, increasing the risk of reentrant arrhythmias such as AF.[33] The role of Vitamin D, a vitamin whose synthesis is dependent upon exposure to sunlight, in the setting of this particular association has also been investigated and it appears that Vitamin D does not mediate this phenomenon. Vitamin D does not appear to have a role in this interaction.[17]

Barometric pressure may be another factor mediating the effects of seasonal variation on the occurrence of AF paroxysms. Gluszak et al. demonstrated that barometric pressure, specifically low pressure fronts, increases the risk of AF paroxysms. Interestingly, risk was greatest 24 to 48 hours before the actual change in barometric pressure.[7] This temporal finding was consistent with previously reported findings from a study by Delyukov et al. that demonstrated negative effects of changes in barometric pressure on cardiovascular function preceding arrival of the atmospheric front by 3 to 24 hours.[34] The timing of the effects of low pressure fronts on physiologic changes may be due to alterations in the electrical field that occur before arrival of the atmospheric front.

Alcohol consumption may also play a part in the increased occurrence of AF paroxysms in the winter. Kupari et al. investigated and found a positive correlation between alcohol sales and the occurrence of AF paroxysms. Actual alcohol consumption, however, was not directly assessed in this study and alcohol sales were used a surrogate.[12] This association remains unclear.

Other factors that may contribute to the association between seasonal variation and the occurrence of AF paroxysms include the increased burden of respiratory infections and chronic obstructive pulmonary disease in the winter, which can trigger AF. These factors, although possible AF triggers, may also confound the association between seasonal variation and occurrence of AF paroxysms as asymptomatic AF may be detected more frequently in the winter due to an increased number of hospitalizations for these other reasons. Additionally, heart failure and sepsis, which are also more frequent in winter, may attribute to the greater risk of AF in winter.[6]

The risk of AF-related stroke peaks during winter season and nadirs in summer. This is likely due to previously documented seasonal variations in fibrin, fibrinogen, and factor VII.[35, 36] Additionally, cold temperatures increase erythrocyte and platelet count, increasing blood viscosity and subsequent risk of thrombus formation.[37] Whether prescription of therapy or compliance rates with treatment have any role remains unclear. This association is important to note as care providers should stress the importance of monitoring and controlling blood pressure, activity level, and avoiding infections

Table 3: Study results

Study	Seasonal association	Peak season	Trough season	Peak month	Trough month	Temperature association	Daylight association	Pressure association	Alcohol association
Kupari et al	Yes	Winter and early spring	Late spring and summer	April	July	Yes	–	–	Yes
Gluszak et al (2008)	Yes	Winter	Summer	February	July	No	–	Yes	–
Watanabe et al	Yes	Fall	Summer	September	June	No	Yes	–	–
Gluszak et al (2009)	Yes	Winter	Summer	–	–	–	Yes	–	–
Kountouris et al	No	–	–	–	–	No	–	–	–
Frost et al (2002)	Yes	Winter	Summer	February	July	Yes	–	–	–
Deshmukh et al	Yes	Winter	Summer	February	July	–	–	–	–
Kiu et al	Yes	Winter	Summer	–	–	–	–	–	–
Upshur et al	Yes	Spring	Summer	April	August	–	–	–	–
Fustinoni et al	Yes	Fall and winter	Spring and summer	–	–	Yes	–	–	–
Murphy et al	Yes	Winter	Summer	December	July	No	–	–	–
Christensen et al (2012)	Yes	Winter	Summer	February	–	–	–	–	–
Christensen et al (2012)	Yes	Winter	Summer	–	–	–	–	–	–
Frost et al (2006)	Yes	Winter	Summer	January	July	–	–	–	–
Spengos et al	Yes	Winter	Summer	December and january	August	–	–	–	–

in those with already known AF as the winter season approaches. Those with hypertension should be advised to ensure compliance with current therapy and blood pressure should be closely monitored. All patients should be encouraged to maintain appropriate activity levels and exercise during the winter, a season often associated with decrease in activity. Those with AF should be particularly encouraged to obtain the influenza vaccination during winter as this has been demonstrated to reduce cardiovascular and all-cause mortality and may help prevent infection induced AF.[38] Notwithstanding, patients with AF need to be counseled on the fore-mentioned things all-round the year but especially in winter season.

The strengths of reviewed studies include the large sample size of some of these studies, particularly those based on registry data. Some of the included studies also studied not only the seasonal variation and occurrence of AF paroxysms but also investigated potential factors mediating this association such as temperature, duration of daylight, and barometric pressure. Limitations of reviewed studies include that all but 1 study captured only those hospitalized for AF or those who had AF while hospitalized for other reasons. This allows for missing “milder” or asymptomatic cases. Additionally, some studies were not able to distinguish between incident and prevalent cases. Some reviewed studies also only included AF that was coded as the primary diagnosis and may have ignored cases with AF coded as the secondary or tertiary diagnosis. The use of discharge records also brings into question the reliability of discharge diagnosis, which may not always be accurate. Caution should also be exercised in determining causality due to the retrospective nature of majority of these studies.

Our study has the inherent limitations of a systematic review. We did not have access to patient level data, hence some important endpoints like medication adherence and other comorbidities could not be assessed. Due to lack of similar definitions across studies, quantitative analysis could not be performed. We are unable to make firm conclusions on most endpoints due to very low number of studies for those endpoints. Large prospective studies are needed to further clarify this potential association.

Conclusions:

There is an association between seasonal variation and the occurrence of AF paroxysms with the greatest risk being during winter and early spring and the nadir being in summer.

Temperature, duration of daylight, and barometric pressure are thought to mediate this seasonal fluctuation in AF occurrence.

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