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# ASSOCIATION OF MIGRAINE AND ATRIAL FIBRILLATION : A TEN YEARS SYSTEMATIC REVIEW

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## ABSTRACT

***Background:*** *Migraine is a primary headache that can present with several neurological and autonomic symptoms, which generally occurs in young to middle-aged women. When accompanied by aura, migraines have a major impact on quality of life due to the severity of the symptoms.*

***The aim:*** *This study aims to show association of migraine and atrial fibrillation.*

***Methods:*** *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

***Result:*** *In the PubMed database, the results of our search brought up 41 articles, whereas the results of our search on SagePub brought up 135 articles. The results of the search conducted for the last year of 2013 yielded a total 26 articles for PubMed and 50 articles for SagePub. The result from title screening, a total 2 articles for PubMed and 19 articles for SagePub. In the end, we compiled a total of 10 papers. We included five research that met the criteria.*

***Conclusion:*** *Migraine is associated with an increased risk of myocardial infarction, ischemic stroke, hemorrhagic stroke, venous thromboembolism, and atrial fibrillation and atrial flutter. Migraine is an important risk factor for most cardiovascular diseases.*

**Keyword:** *Migrain, aura, atrial fibrillation, cardiovascular disease.*

## INTRODUCTION

Migraine is a chronic primary headache characterized by moderate to severe pain and associated specific symptoms, including nausea/vomiting, photophobia, and phonophobia. About a third of migraine sufferers also experience aura symptoms, which are temporary neurological symptoms (most often visual disturbances) before the onset of the headache caused by changes in brain activity. Migraine, particularly migraine with aura, is consistently associated with increased risk of overall and specific cardiovascular disease (CVD) events on a relative scale, and migraine has been included in CVD risk scores.[1]

Migraine is a neurological disease that affects approximately one billion people worldwide and is considered the 6th most disabling disease in the world. This disease occurs more often in women than men and affects more than 30% of women aged between 25 and 55 years. Due to the throbbing nature of the disease, we often assume migraines have vascular causes, when in fact there are three different theories including the vascular theory, neurovascular theory, and cortical spreading depolarization (CSD). Migraine is an inherited disease that has a genetic link of around 42%. Certain environmental factors can cause migraine attacks including diet, stress, alcohol, smoking, sleep disorders, hormonal changes, sensory stimulation (light smells or sounds), weather changes and certain foods.[2]

Migraine is associated with an increased risk of cardiovascular disorders, including stroke and coronary artery disease. Potential mechanisms of increased risk of cardiovascular disease in migraine patients include endothelial dysfunction, inflammatory processes, genetic predisposition to migraine, and vascular risk factors. In addition, migraines are also known to be associated with cardiovascular risk factors, including type 2 diabetes mellitus, hypertension, and obesity. Although many previous epidemiological studies have revealed that migraine with or without aura is a risk factor for cardiovascular disease.[3]

The incidence of AF is significantly increased in women with severe migraine with aura compared with those without migraine. Positive effects on migraine symptoms have been observed following AF catheter ablation. Chronic use of non-aspirin NSAIDs may be a cause of increased risk of AF or flutter. Another explanation may be the autonomic dysfunction that occurs during a migraine attack that causes AF. In addition, various electrographic changes, e.g. bradycardia, increased P dispersion, or non-specific ST-T changes, have been reported in people experiencing migraine attacks and may contribute to the onset of AF. Conversely, AF can cause thrombo-embolic events, which in turn can lead to CSD, leading to migraine aura.[4]

## METHODS

### Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

### Criteria for Eligibility

For the purpose of this literature review, we compare and contrast association of migraine and atrial fibrillation. It is possible to accomplish this by researching or investigating association of migraine and atrial fibrillation. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine about association of migraine and atrial fibrillation. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2013, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

### Search Strategy

We used "association of migraine and atrial fibrillation." as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: *((*"Migraine*"[MeSH Subheading] OR* "Atrial fibrillation*"[All Fields] OR* "Mechanism of migraine*" [All Fields]) AND (*"Risk factor of atrial fibrillation*"[All Fields] OR "* Effects of migraine for cardiovascular system *"[All Fields]) AND (*"atrial fibrillation in migraine condition*"[All Fields]) OR (*"migraine and atrial fibrillation" *[All Fields]))* used in searching the literature.

### Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

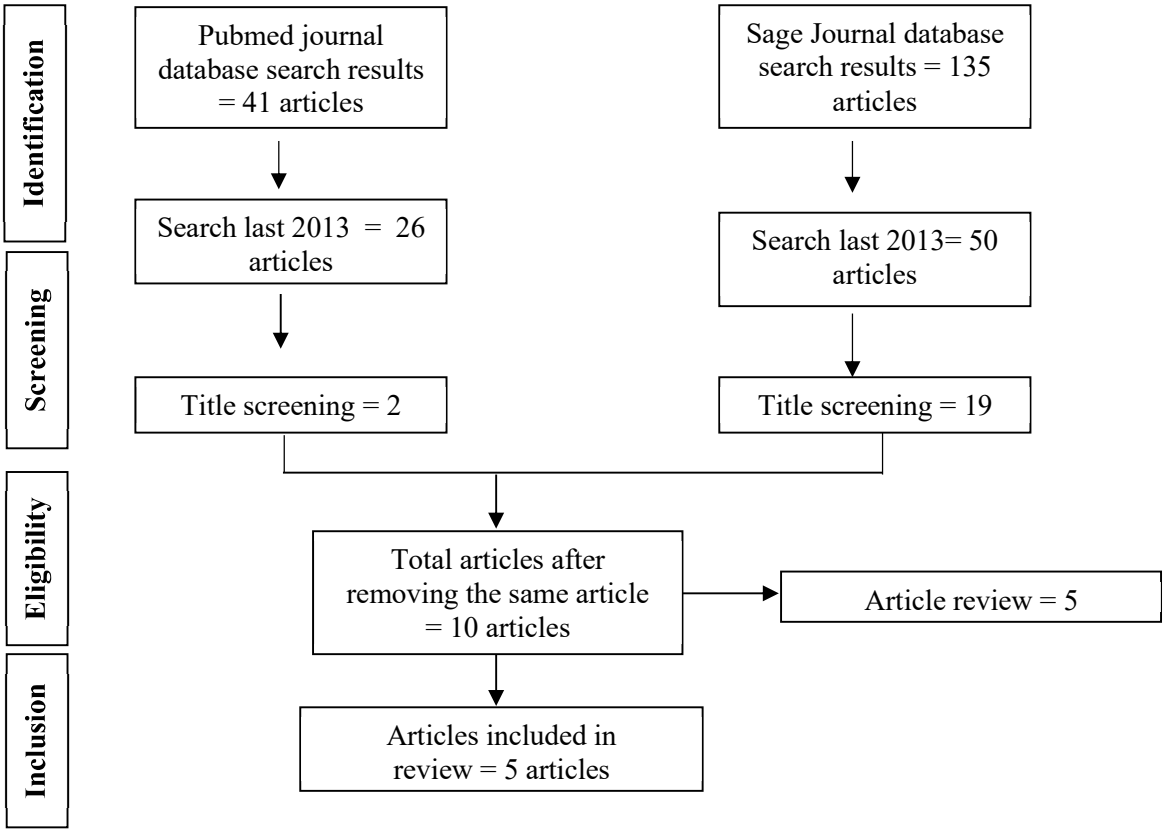


**Figure 1. Article search flowchart**

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

## Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

## RESULT

In the PubMed database, the results of our search brought up 41 articles, whereas the results of our search on SagePub brought up 135 articles. The results of the search conducted for the last year of 2013 yielded a total 26 articles for PubMed and 50 articles for SagePub. The result from title screening, a total 2 articles for PubMed and 19 articles for SagePub. In the end, we compiled a total of 10 papers. We included five research that met the criteria.

Adelborg, K *et al* (2018)[5] showed Outcomes of incident myocardial infarction, ischemic and hemorrhagic stroke, peripheral arterial disease, venous thromboembolism, atrial fibrillation or atrial flutter, and heart failure were ascertained using all recorded inpatient and outpatient diagnoses. To determine the underlying mechanisms, the risks of deep vein thrombosis, pulmonary embolism, induced venous thromboembolism, and unprovoked venous thromboembolism were separately analyzed.

Sen, S *et al* (2018)[6] showed Migraine with aura was associated with higher incidence of AF (crude HR 1.44, 95% CI 1.10–1.88) compared with migraine without aura. After adjustment for age and sex, migraine with aura was associated with incident AF (HR 1.46, 95% CI 1.11-1.91). After adjusting for age, sex, race, hypertension, diabetes, hypercholesterolemia, smoking, coronary artery disease, and congestive heart failure, migraine with aura was associated with incident AF (HR 1.39, 95% CI 1.05-1.83).

**Table 1. The litelature include in this study**

| Author | Origin | Method | Sample Size | Result |
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| **Adelborg, K *et al*., 2018**[5] | Denmark | Cohort study | 51 032 patients with migraine and 510 320 people from the general population | The absolute risk is higher in patients with migraine than the general population. The cumulative incidence per 1000 persons for the migraine cohort compared with the general population was 25:17 for myocardial infarction, 45:25 for ischemic stroke, 11:6 for hemorrhagic stroke, 13:11 for peripheral stroke, arterial disease, 27:18 for venous thromboembolism, 47:34 for atrial fibrillation or atrial flutter, and 19:18 for heart failure. Migraine was associated with myocardial infarction (adjusted hazard ratio 1.49, 95% confidence interval 1.36 to 1.64), ischemic stroke (2.26, 2.11 to 2.41), and hemorrhagic stroke (1, 94, 1.68 to 2.23), as well as venous thromboembolism (1.59, 1.45 to 1.74) and atrial fibrillation or atrial flutter (1.25, 1.16 to 1.36). There was no significant association between peripheral arterial disease (adjusted hazard ratio 1.12, 0.96 to 1.30) or heart failure (1.04, 0.93 to 1.16). |
| **Sen, S *et al*., 2018**[6] | USA | Cohort study | 11939 participats | Of the 11,939 participants who had headaches and no prior AF or stroke, 426 reported migraines with visual aura, 1,090 migraines without visual aura, 1,018 nonmigraine headaches, and 9,405 no headaches. Over 20 years, incident AF was noted in 232 (15%) of 1,516 with migraine and 1,623 (17%) of 9,405 without headache. After adjusting for confounders, migraine with visual aura was |

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| | | | | associated with an increased risk of AF compared with no headache (hazard ratio 1.30, 95% confidence interval 1.03–1.62) as well as when compared with migraine without visual aura (hazard ratio 1.39, 95 % confidence interval 1.05–1.83). Data suggest that AF is a potential mediator of migraine with visual aura-stroke risk. |
| **Rhee, TM *et al*., 2022**[7] | South Korea | Cohort study | 4020488 participants | A total of 4,020,488 participants were enrolled from January 1 to December 31, 2009 and followed up until December 31, 2018; 4,986 subjects experienced migraine with aura (age 50.6 ± 14.0 years, male 29.3%); and 105,029 people experienced migraine without aura (age 51.6 ± 14.3 years, men 30.9%). The risk of AF in mild migraine was similar to the control group, regardless of gender or presence of aura. Severe migraine without aura slightly but significantly increased the risk of AF in both men and women compared with the control group, with the increased risk of AF being most predominant in women suffering from severe migraine with aura [incidence rate (IR) = 3.39, hazard ratio (HR)) adjusted = 1.48, 95% confidence interval (CI) = 1.18–1.85]. No significant association according to aura was observed in men with severe migraine (p interaction 0.011). |
| **Gollion, C *et al*., 2020**[8] | France | Single-centre study | 339 patients | A total of 339 patients (mean/SD age 43.8/8.8 years, 62.83% men) participated in this study. Migraine with aura was diagnosed in 58 patients, and migraine without aura in 54 patients. Migraine with aura was strongly associated with atrial fibrillation (odds ratio, 5.08; 95% confidence interval, 1.24–21.92; p = 0.011) and negatively associated with atherosclerosis (odds ratio, 0.29; 95% confidence interval , 0.05–0.97; p = 0.033) and small vessel disease (odds ratio, 0.13; 95% confidence interval, 0.00–0.87; p = 0.022). No other causes of stroke were significantly associated with |

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| | | | | migraine. The most common causes of stroke are atherosclerosis in patients without migraine, dissection in migraine patients without aura, and patent foramen ovale in migraine patients with aura. |
| **Wang, K *et al*., 2022**[9] | China | Cross-sectional study | 5692 participants | 5,692 subjects participated in this study, with a CVD prevalence of 13.3%. Participants with CVD tended to be older, male, non-Hispanic white, more educated, former smokers, and alcohol drinkers, and had larger waist circumferences, less physical activity, higher triglyceride and creatinine levels, and lower triglycerides and creatinine. high-density lipoprotein cholesterol (HDL-C) and estimated glomerular filtration rate (eGFR) (all P < 0.05). Migraine was associated with a higher risk of CVD [odds ratio (OR) 2.77; 95% confidence interval (CI): 1.56–4.90]. Subgroup analysis showed a higher risk of CVD in women, namely those aged more than 60 years, with lower levels of body mass index (BMI) (≤ 30 kg/m2), higher levels of eGFR (> 90 mL/min/1 .73 m2), hypertension and hyperlipidemia and no diabetes. |

Rhee, TM *et al* (2022)[7] showed Severe migraine with aura increases the risk of AF in women significantly, but not in men. Monitoring the incidence of AF and prompt lifestyle changes may be beneficial, especially for young women suffering from severe migraine with aura.

Gollion, C *et al* (2020)[8] showed atrial fibrillation was a common cause of ischemic stroke in young adults with migraine with aura.

Wang, K *et al* (2022)[9] showed The positive association between migraine and CVD in the US adult population is nationally representative. These findings highlight that migraine should be prioritized as an important risk factor for CVD.

## DISCUSSION

Migraine is a common primary headache, affecting up to 20% of the general population. The incidence of migraine increases after puberty with earlier age in women. About 90% of all patients experience their first attack before the age of 50 years. In the end, migraine sufferers experience aura before or during an attack, which is characterized by neurological symptoms that can be cured, most often in the form of visual disturbances, as well as sensory, language, brain stem or motor symptoms.[10]

In the Atherosclerosis in Communities study, migraine with aura was associated with cardioembolic mechanisms in stroke patients and the incidence of atrial fibrillation in a stroke-free population. Similar results were observed in a cohort study based on the Danish Medical Registry. A more recent study found a strong association between MA and atrial fibrillation in a group of young stroke patients (18–54 years). However, no association between MA or MO and atrial fibrillation was found in a large cohort of the Brescia Stroke Registry cohort, including 1,738 patients with a mean age of 70 years. Although the exact mechanism linking migraine and AF is unknown, potential causes include arrhythmias caused by autonomic dysfunction or AF-related microembolism.[11]

Migraine is a risk factor for ischemic stroke, and is associated with cardiac arrhythmias and atrial fibrillation which provides a clearer picture. People who experience migraines with aura have a higher risk of atrial fibrillation than those who do not have aura. Although a significant association has been demonstrated, the underlying mechanisms remain unclear. Recently, the predictor QRISK3 named migraine as an overall risk factor for cardiovascular disease; however, the United States has not yet adopted this new risk factor. It is important to remain vigilant and actively screen for atrial fibrillation in patients suffering from chronic migraine, as this can significantly reduce the burden of thromboembolic stroke and reduce the incidence of cerebrovascular events and death. Formal guidelines and protocols are needed to achieve this, and more research is needed to determine the exact mechanisms by which migraines cause atrial fibrillation.[12]

## CONCLUSION

Migraine is associated with an increased risk of myocardial infarction, ischemic stroke, hemorrhagic stroke, venous thromboembolism, and atrial fibrillation and atrial flutter. Migraine is an important risk factor for most cardiovascular diseases.

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