The association between fish consumption and risk of stroke

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Abstract

This research study reviewed literature to investigate the association between habitual fish consumption and risk of stroke. The association between fish consumption and the risk of stroke has been widely studied amongst different populations, with the subgroups of adult and gender and utilizing predominantly observational studies. However the results from these studies remain inconsistent. This research aimed to ascertain whether there is a positive association between fish consumption and lower risk of stroke. The studies of Caicoya (2002), Myint et al (2006), Mozaffarin et al. (2005) and He et al. (2002) were selected for this purpose with regard to difference in study design (prospective cohort study design and case- control study design). Research designs, sample size, sampling method, measurements, and findings as well as study bias, confounding factors and factors adjusted for will be analysed in the four studies. High fish intake can be considered as a protective factor to stroke, particularly for ischemic strokes; nevertheless, it seems that there is no relationship between fish consumption and hemorrhagic strokes. Other available studies should be scrutinised to research the factual association between fish consumption and incidence of stroke. Indeed, further studies should consider other factors that can impact the association between fish intake and strokes, such as patterns, type of fish consumed and preparation methods in different populations.

Key words: stroke, ischemic and haemorrhagic stroke, fish consumption

Introduction

Stroke is divided into two main categories; ischemic and haemorrhagic stroke. Although the direct mechanism leading to a stroke is different in each category, both types of stroke share similar risk factors, for example, history of heart disease, smoking status, alcohol consumption, diabetes and old age. In recent decades, there have been a number of studies researching the relationship between eating fish and incidence of stroke. However, findings appear to be contradictory to each other. While fish consumption was found to reduce the incidence of stroke in general (Gillum, Mussolino & Madans, 1996; Iso et al., 2001; Keli, Feskens and Kromhout, 1994), other studies have contradicted this (Caicoya, 2002; Orencia, Daviglus, Dyer, Shekelle, & Stamler, 1996). Whereas, a meta- analysis of cohort studied by He et al., (2004) suggested that there is an inverse association between fish intake and risk of stroke, especially ischemic stroke. These discrepancies are derived from research design, methodology, sampling, targeted population, temporal factors, and potential confounding, as well as bias. Consequently, four studies with two different study designs will be included in this literature review to investigate the epidemiological aspects that may lead to conflicting findings regarding to relationships between fish consumption, stroke and its subtypes.

Study design, main research question and sample size

Three cohort studies and one case-control study were conducted to determine the association between habitual fish consumption and risk of stroke. Of the cohort studies, the study by Myint et al. (2006) investigated the relationship in a sample of 24,312 men and women within the ages 40-79 years who had no history of stroke at baseline in Norfolk, the United Kingdom. The study by Mozaffarian et al. (2005) specifically targeted the elderly population. This study used a sample of 4775 adults aged 65-98 years old in four US communities, who were free from known cardiovascular disease at the baseline in 1989-1990. Similarly, He, Rimm and Merchant (2002) used a sample of 43,671 male health care professionals aged 40-75 years old and free of cardiovascular disease in 1986. Caicoya's study (2002) was the only case-control study in this group. The participants were residents of Asturias, Spain and aged 40-85 years. The 440 cases were defined following the World Health Organisation's (WHO) criteria while the 473 controls were randomly selected from the study's base population.

Measurements

In the study by Mozaffarian et al. (2005), the usual dietary intake was assessed using a food frequency questionnaire which measured the consumption in tuna and other broiled or baked fish which were correlated with plasma phospholipids long chain n-3 fatty acid levels. This was in order to ascertain incidences of stroke prospectively.

Meanwhile, in the study by Caicoya, the usual diet in a year prior to the event, (i.e. a stroke in the case group, or medical interview in the control group) was studied by a food frequency questionnaire containing 150 food items. Fish consumption was then explored by frequency, times, portion size and preparation of fish consumed, and where possible, the type of fish consumed was also asked.

Myint et al. used the fish section of the food frequency questionnaire to ask participants their average fish consumption in the previous year. This included how often fish was consumed, the portion sizes and the type of fish consumed. The baseline assessments were undertaken by trained staff using standard protocols on blood pressure, body mass index, non- fasting blood samples for serum levels of total cholesterol, high density lipoprotein cholesterol and triglycerides on fresh samples. The participants were further asked about smoking status and frequent intake of food supplements or fish oils and their level of physical activity.

In the dietary information obtained by He et al., participants were asked to indicate their average consumption of specified portions of each selected food during the previous years, with a frequency option. The nutrient intakes were calculated by multiplying the consumption frequency of each food by the nutrient content of specified portions according to composition values from US Department of Agriculture (USDA). With respect to fish consumption, the consumption of canned tuna fish, dark-meat fish such as mackerel, salmon and sardines, other fish and shrimps and lobsters were asked. Participants were further asked about the use of fish oil supplements.

Results, conclusions and recommendations

Myint et al. reported a total of 421 incidences of strokes out of the total person-years of 20,923 within the 8.5 year follow-up period. The authors indicated no significant relationships between total fish consumption and risk of stroke in men and women. Moreover, oily fish consumption was significantly lower in women who subsequently had a stroke among the consumers verses the non-consumers with an Odds Ratio (OR) = 0.69 (95% Confident interval (CI) = 0.51 - 0.94, p value (p) =0.02). The trend in men was similar, however, there was not a significant difference among the consumers verses the non-consumers with an OR= 0.88 (95% CI= 0.65 – 1.19, p =0.41). No consistent relationship was found between fish consumption and stroke in the British population, this inconsistency was attributed to different patterns and type of fish consumed and the preparation methods.

Results from the study by Caicoya indicated the risk of stroke increased with the consumption of fish (χ^2 = 4.12, p= 0.04). The author indicated that those in the highest quintile of consumption, who consumed 46g of fish/day compared to the lowest quintile, who consumed 11g/day had a multivariate adjusted OR = 1.95 (95% CI: 1.14-3.33). In addition, the risk of stroke and cerebral infarction increased with the consumption of fish, with an OR = 1.98 (95% CI: 1.08-3.47). The consumption of n-3 fatty acids in fish was also compared between those in the highest quintile of n-3 fatty acids consumption (660mg/day) and those in the lower quintile (115mg/day). This showed the risk of stroke with an OR = 1.76 (95% CI: 0.95-3.26) and the risk of cerebral infarction with OR = 1.89 (95% CI: 0.95-3.75). The author concluded that high fish consumption was associated with an increased risk of stroke and cerebral infarction, although misclassification and residual confounding of exposure could not be ruled out.

He et al. reported 608 strokes in the 12- year follow up period with 377 ischemic, 106 haemorrhagic and 125 unclassified strokes. Of ischemic stroke sufferers, the Multivariate Relative Risk (RR) was 0.57 (95% CI: 0.31-0.94) among those who ate fish 1- 3 times/month versus those eating fish less than 1 time/month. Among those eating fish equal or greater than 1 time/month compared to those eating fish less than 1 time/month, the multivariate RR (ischemic stroke) was 0.56 (95% CI, 0.38-0.83) while the multivariate RR of haemorrhage stroke was 1.36 (95% CI, 0.48-3.82). The authors drew a conclusion that eating fish once per month or more can reduce the risk of ischemic stroke in men. However, there were no significant associations between fish or long chain Omega-3 PUFA intake and risk of haemorrhagic stroke.

Finally, Mazaffarin et al. also described 626 incidents of strokes, including 529 ischemic strokes, 65 haemorrhagic strokes and 32 unclassified strokes. Tuna, or other fish in multivariate analyses, compared with an intake of equal or less than 1 times/month were inversely associated with total stroke (p =0.4) and ischemic stroke (p= 0.2) There was a 27% lower risk of ischemic stroke with an intake of 1-4 times/week with the hazard ratio (HR) = 0.73 (95% CI: 0.55-0.98). There was a 30% lower risk with intake of equal or greater than 5times/week (HR = 0.70; 95% CI: 0.50-0.99). Fried fish/fish sandwiches were positively associated with total stroke (p = 0.006) and ischemic stroke (p = 0.003). The authors suggested that the consumption of tuna/other broiled or baked fish is associated with lower risk of ischemic stroke; whereas, the intake of fried fish or fish sandwiches is associated with higher risk among the elderly.

Discussion

All the four studies showed different conclusions from each other about the main topic. The difference of these conclusions potentially stems from variation in study design, study populations, sample size, assessment of fish intake, and stroke endpoint, as well as adjustment for covariates, coupled with the fact that most studies did not separate ischemic from hemorrhagic stroke (meta analysis). Each of these studies has more than one research questions; however, within the scope of this literature review, critiques will concentrated on the topic of the relationship between consuming fish and stroke incidence. Therefore, secondary questions of the studies will only be covered briefly. There will be two main discussions so as to cover strengths and limitations of each study in two types of observational study design which were conducted. The first one will critique Caicoya's Case- control research in the year 2002. Then, the second part will discuss the Prospective cohort studies of Myint et al, (2006), He et al. (2002) and Mozaffarin et al., (2005).

Case-control study

In terms of the research design, Caicoya clearly concentrated on the relationship between fish consumption, stroke and stroke subtype in the defined population. In this study, eating fish was identified as an exposure to measure the affect on stroke- the first cause of mortality in Asturias, Spain. Although the case control design has a number of disadvantages, in this situation, it was appropriately used.

Also, the sampling and sample size could be acceptable. The cases were recruited properly when the case definition was based on the World health organisation's criteria and met the demand temporally and geographically. They were defined based on the CT- Scan results and/or with diagnosis of the physician, therefore, the incidence reported was reliable. Similarly, the control selection was representative to the geographically defined population during the specific time of the study. The sample size was sufficient and almost matched with the required size as explained by the author based on α, β, and minimum odds ratio.

However, there was potential for bias in this study. Both groups were asked about the diet in the year before the event. For the cases, interviews (53%) were undertaken after the stroke had occurred, and proxies (47%) were employed when the participants had a communication problem. Apart from the inaccurate answers that might arise from the participants' impaired health status after the stroke, the information from proxies could well fail to reflect true dietary facts. This source of information bias, particularly, recall bias can also apply to the controls when they were asked about the past. Also, an interviewer bias could well occur when the same medical interviewers examined both categories of participants (Caicoya, 2002, p. 108). According to Oklecno (2008, p. 274), when an in-person interview is conducted, the interviewers can learn to recognise the cases and controls as well exposure to the research.

Furthermore, confounding was likely to happen in this research when other health factors such as alcohol consumption, hypertension and history of cardiovascular diseases, were not excluded at the baseline. These factors include a high risk of stroke due to a history of heart disease. Consequently, it could distort the results.

Meanwhile, the exposure failed to be exactly measured to minimise potential bias. Although the fish consumption was clearly defined to be asked on the frequency, times, portion size, type of fish and preparation of dishes; the categories for fish consumption were divided objectively rather than scientifically. Indeed, the measurement methods which have been discussed in the above part were not free of problem. Furthermore, blinding was not undertaken in this case - control study when it was conducted, even though it was possible, for example, through blinding interviewers.

In fact, Caicoya was aware of the confounding factors and limitations of the study when interpreting the results. A discrepancy in age (cases were almost 3 years older than controls) (p. 109) and a possible source of confounding related to information collection were acknowledged. Moreover, the validity and reliability of the dietary questionnaires were also noticed and Caicoya took into account the non-differential misclassification that then led to underestimation or overestimation of fish consumption. Therefore, differential misclassification was likely to occur (p. 112). With regard to other possible confounders, the author employed multivariate analysis to adjust them.

The main results of the study are represented below through the tables. From these, the author concluded that after adjustments, the risk of stroke increased with the consumption of fish and the risk of cerebral infarction also followed this trend.

Table 1: OR of stroke with increasing consumption of fish

Fish, g/day	Cases	Controls	Crude OR	95% CI	Adjusted OR	95% CI
0, reference	18	10	1		1	
1-22.5	99	145	0.38	0.17-0.86	0.30	0.12-0.78
23-45	128	145	0.49	0.22-1.10	0.44	0.18-1.41
46-90	155	144	0.60	0.27-1.34	0.59	0.24-1.47
91-250	42	29	0.80	0.33-1.99	0.76	0.27-2.1
Adjusted for hypertension, alcohol, atrial fibrillation and peripheral artery disease						

Table 2: OR of cerebral infarction with increasing consumption of fish

Fish, g/day	Cases	Controls	Crude OR	95% CI	Adjusted OR	95% CI
0, reference	18	10	1		1	
Adjusted for age, sex, hypertension, alcohol, coronary artery disease, atrial fibrillation and peripheral artery disease and energy intake. X2 of trend: 3.00, p = 0.08						

Although assuming that the results from this community case- control study were accurately analysed, the associations between fish consumption, stroke and stroke subtype are unreliable due to a number of gaps. Recall bias, interviewer bias, confounding factors and other limitations with regard to validity and reliability of the questionnaire are likely to significantly distort the results. Although the research design was appropriate for the research focus, the methods incorporated a number of flaws, and consequently, the reliability of the results should be considered carefully.

Cohort study design

In terms of study design, these three cohort studies are quite good quality with relatively large sample sizes, standard methodology, clearly definition for measurements and outcomes, and implementation for adjusting of covariates. This study designs also minimized selection bias and recall bias. Additionally, the long-term follow-up periods also increased the statistical power to examine the overall associations of fish intake and incidence of stroke (Gordis, 2009). Particularly, the studies of He and Mozaffarin lasted for 12 years whilst Myint study's follow- up time was about 8.5 year. This difference in follow-up time might affect the results obtained. It is likely that a period longer than 10 years' exposure is required for the observed beneficial effect of fish consumption on risk of stroke (Myint et al., 2006).

To derive a conference for general population, sample selection for these studies were not well representative (selection bias). The participants in He et al.'s study were male health professionals while Mozaffarian et al. targeted to British elderly people. Moreover, it is generally acknowledged that, in the United Kingdom, fish is usually eaten after heavy processing (Myint et al., 2006). Therefore Myint et al.'s study might fail to calibrate the variability of fish consumption compared to other nations (Myint et al., 2006; Welch et al., 2002). In regards to sampling, the study by He et al. has a largest sample size which is almost double that of in Myint et al.'s research, and about ten times higher than in the study of Mozaffarian.

With respect to measurements, there are a number of differences in these three studies. Firstly, although all the three studies used the questionnaires to evaluate typical fish intake at the previous year prior to the baseline. These food frequency questionnaires had derived from different standard sources from which the variation in the obtained information could distort the analysis's results. Moreover, the definition of 'fish types' and 'fish consumption scales' also varied within the studies. As for the result of these studies, whilst the Ka He study used the relative risk of stroke to assess the association between fish consumption and strokes, the two other studies used the odds ratio and hazard ratio. Thus, this leads to difficulties when comparing results between studies.

Relating to the information bias and confounding adjustment, He et al.'s study seems to be the most effective one to control these factors. To reduce the affect of possible dietary changes over the follow-up time which might impact the incidence of stroke, the information about the fish consumption was collected through a semi quantitative food frequency questionnaire in the beginning of each four- year period, which was 1986, 1990 and 1994. Whereas, the similar attempts were applied in the Mozaffarian et al.'s study; however, the follow-up was divided into two roughly equal halves, which was approximately six years, then, the associations were researched separately based on the separate diet assessments in the two different periods. This adjustment was not implemented in the study of Myint et al.

Furthermore, the authors did identify potential confounders in their study and adjustments were applied to analyse the data. Myint et al. acknowledged a number of confounding factors in their study. An illustration is that the participants, who subsequently had a stroke, had higher mean systolic blood pressure, serum cholesterol, also a higher proportion of people with diabetes, and were physically inactive at the baseline. Also, psychosocial factors which differ between sexes and play a role in cardiovascular health were unadjusted although several variables including smoking, physical activity and total energy intake were controlled.

Similarly, Mozaffarian et al. adjusted the results for confounding including; systolic blood pressure and low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglyceride, and C-reactive protein levels. However, in the study by He et al., the authors acknowledged that hypercholesterolemia was the only confounder that could significantly distort the association. Then, it was adjusted for the precise conclusion.

In terms of attrition bias, the study of He et al. had highest follow- up rate (about 94%), which was effective to reduce the potential for this kind of bias. The response rate in Myint et al.'s study was only 40–45% at the baseline and during the follow-up. Meanwhile, this rate was unclearly mentioned in the study of Mozaffarian.

Regarding the findings, although there were substantial differences in the findings between the three studies due to the discrepancies in the methods as well as potential confounding and bias, there are some similarities shared. The studies of He et al. and Mozaffarian et al. showed evidence of reverse relationship between fish consumption and stroke. Although the Myint et al.'s study concluded that there was no consistent association, there appeared to be an inverse association between oily fish consumption and the relative risk of stroke in women.

Each of these four studies has their own strengths and limitations. Overall, the methodology in the study of He et al. seems to be most appropriate when it could control potential confounding and bias although its sample (male health professionals) was less representative for the general population. Whereas, Myint study is the best designed of these studies in terms of a population-based recruitment strategy then enhances generalizability. But, it did not separate ischemic from hemorrhagic stroke, and hence its capacity to examine fish intake in relation to stroke subtypes was limited, and it could not explore the association between fish consumption and stroke. Meanwhile, Mozaffarian et al.'s study appeared to have the smallest sample size compared to that of Myint et al. and He et al. Moreover, it targeted to the elderly population, which could not represent for the general population. With regards to the case - control study of Caicoya, it comprised a number of bias and confounding factors and other limitations which were addressed in the first discussion, therefore, its conclusion could be doubted.

Conclusion

In conclusion, the studies of Caicoya (2002), Myint et al (2006), Mozaffarin et al. (2005) and He et al. (2002) yielded inconsistent results of the relationship between fish consumption and risk of stroke. After analysing the research designs, sample size, sampling method, measurements, findings as well as their bias, confounds and how they were adjusted, the association found from the study by He et al. (2002) appeared to be most reliable due to its better research design, large sample size, fewer chances of bias and confounds compared to the three others. As a result, high fish intake can be considered as a protective factor to stroke, particularly for ischemic strokes; nevertheless, it seems that there is no relationship between fish consumption and hemorrhagic strokes. However, more scrutiny on epidemiological aspects in other available studies should be made to investigate the factual association between eating fish and stroke incidence. Also, further studies should be conducted to explore the impact of other factors that can affect the association between fish consumption and strokes, such as type of fish consumed, and fish preparation methods in different populations.

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