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RF-EMF Exposure emitted from Mobile/Cellular Phone and Risk of Glioma, Meningioma and Acoustic Neuroma: A Systematic Review and Meta-Analysis

Yu Xin Feng[1*], Zhi Ru Zhou[1], Quan Ming Fei[1] and Ying Wang[2,3]

[1]*Department of Radiation Oncology, Xiangya Medical School, Central South University, Changsha, China*
[2]*Department of Pathology, School of Basic Medical Science, Central South University, Changsha, China*
[3]*Department of Pathology, Xiangya Hospital, Central South University, Changsha, China*

Abstract

Background: To evaluate the association between mobile/cellular phone use and risk of three intracranial tumors (glioma, meningioma and acoustic neuroma) based on case-control studies through pooling the published data.

Methods: We conducted a systematic literature search in databases including PubMed, EMBASE, and the Cochrane Library up to September 2021. The primary outcome was the risk of tumors by mobile/cellular phone use, which was measured by pooling each Odds Ratio (OR) and its 95% Confidence Interval (CI). The random- or fixed-effects model was applied to combine the results depending on the heterogeneity of the analysis. And we estimated publication bias using Begg's and Egger's test.

Results: We ultimately included 6 articles for glioma, 6 articles for meningioma and 8 for acoustic neuroma from 1999 to 2015. Totally 41478 participants including 13021 cases and 28457 controls were enrolled in the final analysis. There was no significant association between mobile/cellular phone use and risk of glioma (OR, 0.98; 95% CI, 0.81-1.17; I^2=76.9%, p=0.001) and acoustic neuroma (OR, 0.98; 95% CI, 0.76-1.25; I^2=60.7%, p=0.013). And no statistical significance was observed between any subgroup of duration of use and these two types of cancer. However, mobile phone use was associated with decrease the risk of meningioma, especially when the time since first use was between 0-5 years (OR, 0.83; 95% CI, 0.76-0.90; I^2=39.5%, p=0.142) and 5-10 years (OR, 0.83; 95% CI, 0.75-0.93; I^2=32.3%, p=0.194), while the protective effect disappeared in longer term (more than 10/11 years) (OR, 0.91; 95% CI, 0.80-1.03; I^2=0.0%, p=0.870).

Conclusion: Evidence from our study mobile/cellular phone use may decrease risk of meningioma. Further studies are needed to explore the possible influence of long-term use of mobile phone and underlying mechanism.

Key words: RF-EMF; Radiofrequency; Mobile phone; Cancer

Abbreviations: RF-EMF: Radiofrequency Electromagnetic Fields; OR: Odds Ratio; CI: Confidence Interval.

Introduction

The increasing spread of Radiofrequency Electromagnetic Fields (RF-EMF) has aroused wide concern about health care. Mobile phones are one of the most important factors that can give rise to human exposure of RF-EMF. There are some studies indicating that mobile phones or similar equipment may be factors that cause oxidative stress and even cause damage to DNA, which may lead to the development of different pathology including tumors [1,2]. But the confidence level and specific mechanism still remain unclear, which makes it necessary to evaluate the risk of cancer. In the year of 2011, the International Agency for Research on Cancer (IARC) concluded that Radiofrequency (RF) radiation from personal devices like mobile phones and other devices is classified as a Group 2B, meaning that RF-EMF is possibly carcinogenic to humans. But it is only weak mechanistic evidence that proves the relativity. As mobile phone gradually being a necessity of life, the relativity needs to be proved [3].

When it comes to mobile phone and tumors, it is true that glioma, meningioma and acoustic neuroma are more common disease. Gliomas are the most common primary intracranial tumor, representing 81% of malignant brain tumors and they cause significant mortality and morbidity. More and more factors have been speculated and confirmed as potential contributors to glioma risk including exposure to ionizing radiation and a decrease in risk by history of allergies or atopic disease(s) [4]. Meningiomas are one of the most common primary tumors of the central nervous system. They can be found arising from any intracranial or spinal dural surface. Typically, meningiomas are not fast growing or infiltrative lesions and they have an insidious symptom onset [5]. Acoustic neuromas account for 8% of all intracranial tumors and are the most common neoplasm of the cerebellopontine angle in adults. These tumors derive from myelinating Schwann cells of the vestibular division of the vestibulocochlear nerve. The term "vestibular schwannoma" is preferred over the historical misnomer "acoustic neuroma" [6]. An Odds Ratio (OR) is a statistic that quantifies the strength of the association between two events, A and B. The odds ratio is defined as the ratio of the odds of A in the presence of B and the odds of A in the absence of B. In a

***Corresponding author:** Yu Xin Feng, Department of Radiation Oncology, Xiangya Medical School, Central South University, Changsha, China, E-Mail: 1367037980@qq.com

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good number of epidemiological researches, if one of the properties (A or B) is sufficiently rare (this is called the rare disease assumption), then the OR is approximately equal to the corresponding Risk Ratio (RR).

There are several previous studies that have discussed the association between wireless phones and above-mentioned tumors while concluding the opposite result. Michael Carlberg found relationships between exposure of mobile phone and other similar devices while Michael H Repacholi have the contrary conclusion [7,8]. Michael Carlberg and Lennart Hardell's meta-analysis of case-control studies drew the conclusion that glioma is caused by RF radiation by using the nine Bradford Hill viewpoints [7]. Also, Elisa Carvalho de Siqueira provided evidence of relation between parotid tumor and wireless phone use though presenting mild effect. However, divergence exists [8]. Michael H Repacholi found no consistent relationship between glioma, meningioma, acoustic neuroma, or parotid gland tumors and wireless phone use in both *in vivo* and epidemiology studies, knowing that the four tumors originate in the areas of the head that most absorb the RF energy from wireless phone [9]. In a word, inconsistency remains in the study of whether cancer is associated with wireless phone use. Besides, the duration of use is also controversial. There have been few studies highlighting the fact that long-term (>10 years) wireless phone use may increase the risk of cancers like acoustic neuroma, meningioma and glioma [10,11], according to which we divide the group of the latency time in 1-5 years as short-term use, ≥ 10 years as long-term use and remaining part as medium-time use.

Above all, this meta-analysis was to evaluate the relationship of glioma, meningioma, acoustic neuroma and duration of use of mobile/cellular phones in order to find supportive results.

Materials and Methods

We searched PubMed, EMBASE, and the Cochrane Library in September 2021, using "(cordless phones OR mobile phone OR cellular phone OR electromagnetic fields OR radiofrequency electromagnetic fields) and (glioma OR meningioma OR acoustic neuroma OR vestibular schwannoma)" as the search term. Each source was last searched in September 25th. Two authors independently reviewed the articles from the search and selected articles meeting the predetermined selection criteria. Disagreements between the two authors were resolved by discussion the references of these included studies were then checked to identify additional relevant publications.

Selection criteria

The inclusion we developed and applied for data analysis are as follows:

- Studies assessing the association between mobile/cellular phone and the three kinds of cancer.
- Researches on humans.
- Diseases confirmed through professional methods such as histology, imaging, and pathology.
- Case-control design instead of cohort design.
- Detailed data of the calculated OR value and 95% Confidence Intervals (CIs) or numbers of people of case and control subjects were provided.
- If a series of studies of the same group of the same population are reported, the latest study shall be included.

Exclusion criteria:

- When including duplicate articles from previous publications, or meta-analysis, conference abstracts, letters, comments, or editorial articles, these studies are excluded.
- Researches on parental occupational exposure and offspring cancer were excluded.
- Articles not written in Chinese or English are also excluded.

Data Collection and Quality Assessment

The following information was extracted from the included studies: title, first author, year of publication, countries studied, sample size, study period, phone type, age range, sex, age, adjusted OR (95% CI) and adjustment factor. Newcastle-Ottawa Quality Assessment Scale (NOS) was used to evaluate the quality of articles from three perspectives of selection, comparability and exposure, with a score ranging from 0 to 9. We also collected time since first regular use (years) and the corresponding ORs. These Articles had similar partition criterion, so we put data of same interval length into three subgroups: Long-time use (≥ 10/11 years), Medium-time use (5-9/10 years) and Short time use (1/1.5-4/5 years).

In the subgroup analysis, if the OR value was not reported directly, the number of individuals in cases and controls were also abstracted when needed, instead of copying the adjusted OR value from the literature. If the article didn't report the number of people who never/rarely use mobile/cellular phone, we calculated it by subtracting number of regular use from total. Additionally, when an individual study reported data on wireless phone instead of mobile phone or cellular phone, the data were not selected to ensure the accuracy. We firstly used the adjusted data if the study reported it.

Main and subgroup analyses

For the main analysis, in order to find the relation between RF-EMF exposure produced by mobile/cellular phone and cancer, we collected adjusted ORs to calculate the total OR value. The studies on our topic used different research methods on the length of exposure (including especially separate time periods since first use of a mobile/cellular phone), which were put into subgroup Meta analyses.

For subgroup analysis of length of use for glioma, meningioma, acoustic neuroma, we set appropriate standard for selecting the referent and exposure group to guarantee the logical results. the groups with longer than about 10 years exposure selected as the long-time use and never/rarely groups as referent group were put together to calculate the total OR value. In the same way, the subgroup of Medium time use (5-9/10 years) and Short time use (1/1.5-4/5 years) use for each cancer type. However, the study whose divided time periods were really disparate with others, were excluded from this subgroup.

Statistical analysis

Microsoft Excel was used to organize the initial data, show the basic information and build a database. Adjusted ORs and numbers of individuals in every group were saved in Excel, to compute a pooled OR with its 95% CI using different methods. For the study which we collected number of individuals instead of adjusted OR, we firstly calculated OR and then calculated pooled OR with others. All statistical analyses were conducted by 2 reviewers independently.

In our meta-analysis, the random-effects method of DerSimonian and Laird was used when heterogeneity was present in some of the comparisons. DerSimonian and Laird (D-L method) is a classic model and in the Univariate setting, the non-iterative method proposed by

DerSimonian and Laird is a simple and now standard way of performing random effects meta-analyses. In other cases, we used fixed-effects method (inverse variance). Heterogeneity was assessed by Chi-square based Q-test and I squared test. If P value for Q test <0.05 or I^2>50%, heterogeneity is significant. By performing sensitivity analysis, we excluded several studies to reduce the heterogeneity as far as possible. We estimated publication bias using Begg's and Egger's test. When there is publication bias the p-value<0.05. The Stata/MP 16.0 software was used for statistical analysis (StataCorp, College Station, Texas, USA).

Results

Totally 41478 participants including 13021 cases and 28457 controls were enrolled in the final analysis (Table 1). The most common

1st author, Year of publication	Study period	Country	Type of cancer	Sex (Age)	Score	Sample size Ca/Co	Type of phones used in analysis	Adjusted OR from manuscript (95% CI)	Adjustments
E. Cardis [12]	2000-2004	Australia, Canada, Denmark, Finland, France, Germany, Israel, Italy, Japan, New Zealand, Norway, Sweden and the UK	Meningiomas	M+F (30-59)	8	2708/2972	Mobile	0.81 (0.7-0.94)	Sex, age, study centre, ethnicity in Israel and education
J. Schuz, et al. [13]	2000-2003	France	Gliomas	M+F (30-59)	8	366/732	Cellular	0.98 (0.74-1.29)	Educational level, disposable income, and marital status
			Meningiomas			381/762		0.84 (0.62-1.13)	
S. Lönn, et al. [14]	2000-2002	Sweden	Gliomas	M+F (20-69)	8	371/674	Mobile	0.8 (0.6-1.0)	Age, gender, geographic region, and education
			Meningiomas			273/674		0.7 (0.5-0.9)	
A. Lahkola, et al. [15]	2000-2004	Denmark, Finland, Norway, Sweden and the United Kingdom	Meningiomas	M+F (20-69 years in the Nordic countries and 18–59 years in Southeast England)	7	1204/2945	Mobile	0.76 (0.65-0.89)	Sex, five-year age group, region and country
G. Coureau, et al. [16]	2005-2008	France	Gliomas	M+F (≥ 16)	8	253/504	Mobile	0.90 (0.61-1.34)	Level of education and ionising radiation exposure
			Meningiomas			194/388		1.24 (0.86-1.77)	
M. Carlberg, et al. [17]	1997-2003 and 2007-2009	Sweden	Meningiomas	M+F (20-80 (1997-2003), 18-75 (2007-2009)	8	956/2148	Mobile	1.0 (0.9-1.2)	Age at diagnosis, gender, SEI-code and year of diagnosis
A. Lahkola, et al. [18]	2000-2004	Denmark, Finland, Norway, Sweden, Southeast England	Gliomas	M+F (18-69)	7	1521/3301	Mobile	0.78 (0.68-0.91)	Use of hands-free devices
L.Hardell, et al. [19]	1997-2003 and 2007-2009	Sweden	Gliomas	M+F (20-80)	8	1380/3530	Mobile	1.3 (1.1-1.6)	Age at diagnosis, gender, SEI-code, and year for diagnosis
Sarah J Hepworth, et al. [20]	2000-2004	England	Gliomas	M+F (18-69)	7	966/1716	Mobile	0.94 (0.78-1.13)	Age at reference date (in 5 year age groups), sex, region, Townsend deprivation category, and interview reference date category
L.Klaeboe, et al. [21]	2001-2002	Norway	Acoustic neuromas	M+F (16-69)	7	45/358	Mobile	0.5 (0.2-1.0)	Age, sex, residential area and attained educational level
E. Cardis [22]	2000-2004	Australia, Canada, Denmark, Finland, France, Germany, Israel,Italy, Japan, New Zealand, Norway, Sweden, and the UK	Acoustic neuromas	M+F (30-59)	8	1105/2145	Mobile	0.85 (0.69-1.04)	Sex, age, study centre, ethnicity in Israel, and education
H. C. Christensen, et al. [23]	2000-2002	Denmark	Acoustic neuromas	M+F (20-69)	9	106/212	Cellular	0.90 (0.51-1.57)	Educational level, marital status, use of hands-free devices in vehicles(ever vs. never), and region

L. Hardell, et al. [24]	Uppsala-Orebro region (1994-1996) and Stockholm region (1995-1996)		Acoustic neuromas	M+F (mean age:50)	7	209/425	Cellular	0.98 (0.69-1.41)	Not reported
L. Hardell, et al. [25]	1997-2003 and 2007-2009	Sweden	Acoustic neuromas	M+F (Ca:23-80/ Co:19-80)	7	316/3530	Mobile	1.6 (1.2-2.2)	Age at diagnosis, gender, SEI-code and year of diagnosis
B. Schlehofer, et al. [26]	2000-2003	Germany	Acoustic neuromas	M+F	8	97/194	Mobile	0.67 (0.38 -1.19)	SES, living area urban/ rural, age at diagnosis and study centre
D. Pettersson, et al. [27]	2002-2007	Sweden	Acoustic neuromas	M+F (≥ 20)	7	422/643	Mobile	1.18 (0.88-1.59)	Unadjusted
S. Lonn, et al. [28]	1999-2002	Sweden	Acoustic neuromas	M+F (20-69)	8	148/604	Mobile	1.0 (0.6-1.5)	Age, sex, residential area, and educational level

Table 1: General characteristics of studies included in the meta-analysis.

Study	SECTION				Compar-ability	EXPOSURE			Score
	Adequate Definition of Patient Cases	Representativeness Patient Cases	Selection of Controls	Definition of Controls		Ascertain-ment	Same Method of Ascertainment	Non-Response Rate	
Acoustic neuroma									
L. Klaeboe, et al. [21]	1	1	1	1	1	1	1	0	7
E. Cardis [22]	1	1	1	1	2	1	1	0	8
HC. Christensen, et al. [23]	1	1	1	1	2	1	1	1	9
L. Hardell, et al. [24]	1	1	1	0	2	1	1	0	7
L. Hardell, et al. [25]	1	1	1	1	1	1	1	0	7
B. Schlehofer, et al. [26]	1	1	1	1	2	1	1	0	8
D. Pettersson, et al. [27]	1	1	1	0	2	1	1	0	7
S. Lonn, et al. [28]	1	1	1	1	2	1	1	0	8
Giloma									
S. Lonn, et al. [14]	1	1	1	1	2	1	1	0	8
A. Lahkola, et al. [18]	1	1	0	1	2	1	1	0	7
G. Coureau, et al. [16]	1	1	1	1	1	1	1	1	8
L. Hardell, et al. [19]	1	1	1	1	2	1	1	0	8
Sarah J Hepworth, et al. [20]	1	1	0	1	2	1	1	0	7
J.Schuz, et al. [13]	1	1	1	1	2	1	1	0	8
Meningioma									
E.Cardis [12]	1	1	1	1	2	1	1	0	8
J.Schuz, et al. [13]	1	1	1	1	2	1	1	0	8
S. Lönn, et al. [14]	1	1	1	1	2	1	1	0	8
A.Lahkola, et al. [15]	1	1	0	1	2	1	1	0	7
G.Coureau, et al. [16]	1	1	1	1	1	1	1	1	8
M.Carlberg, et al. [17]	1	1	1	1	2	1	1	0	8

Table 2: Patients quality assessment at different stages.

type discussed is acoustic neuromas (8 out of 17 studies, 47%), followed by meningiomas (6/17, 35%), salivary gland tumors (6/17, 37%), as some of the articles discussed more than one type of cancer. The types of phones classified in the studies are mobile phones (14/17, 82%) and cellular phones (3/17, 18%).

Quality assessment

Table 2 shows the methodological quality assessment of the included articles using NOS. The included articles scored between 7 and 9, with an average score of 8. Among them, there are 7 with a score of 7, 9 with a score of 8 and 1 with a score of 9. Articles with scores less than 9 are mainly due to their poor control selection or lower comparability between the experimental group and the control group or lower response rate.

Main analysis

Compared with never or none, the overall use of Mobile/Cellular phones was not associated with risk of glioma in a random-effects meta-analysis of all 6 studies (OR, 0.98; 95% CI, 0.81-1.17; I^2=76.9%, p=0.001). For acoustic neuroma, there's no statistical significance between them (OR, 0.98; 95% CI, 0.76-1.25; I^2=60.7%, p=0.013) either. However, decreased risk of meningioma was observed: OR, 0.84; 95% CI, 0.78-0.91; I^2=47.3%, p=0.091, which calculated with fixed effect model (Figures 1,2).

Subgroup analysis

Due to the heterogeneity and publication bias between studies, subgroup analyses were performed to evaluate the association between length of mobile/cellular phone use and specific type of cancer.

Glioma

All the included references (6 articles including 18 studies about length of exposure and risk of glioma) had similar basis for grouping reported time since first use of wireless phone. Two studies, from S. Lönn and L. Hardell were excluded because they demonstrated significant heterogeneity. Then we calculated OR and CI values of L. Hardell's research (2015), and put this result (OR, 1.05; CI: 1.05-1.47) into meta-analysis. Therefore, 6 articles including 16 studies were analysed by selecting the three groups (Short, Medium and Long) as the exposure and people never/rarely use mobile/cellular phone as referent group to calculate the pooled OR value. In the random effect models, no association between duration of use mobile/cellular phones and gliomas was found (Figure 3).

Meningioma

Subgroup analyses were performed to identify the association between duration and cancer risk. We calculated the OR and CI values of two studies from E. Cardis (OR: 0.846; CI: 0.745-0.961) and M. Carlberg (OR: 0.909; CI: 0.778-0.963) and put them into meta-analysis. As shown in Figure 4, there were 6 articles was put into subgroup of short, medium and long time use respectively. The result from fixed effect models indicated that using mobile/cellular phones for a short or

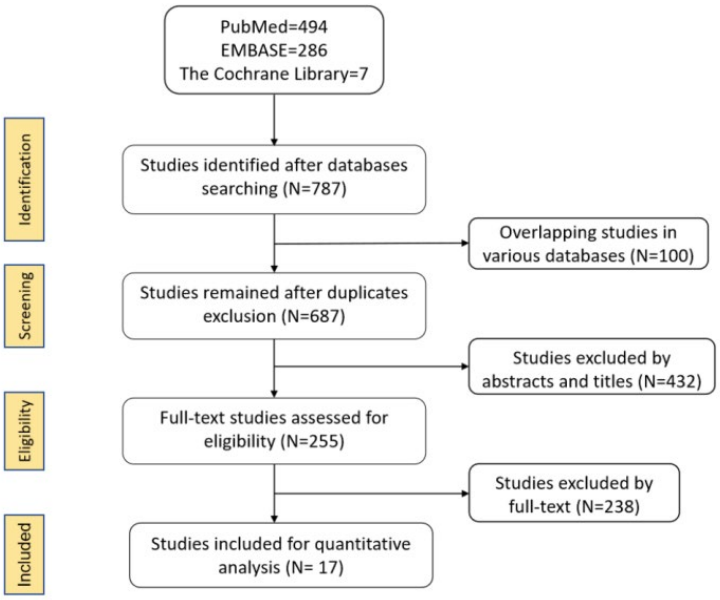


Figure 1: Study selection fom the database Pubmed, EMBASE, The Cochrane library.

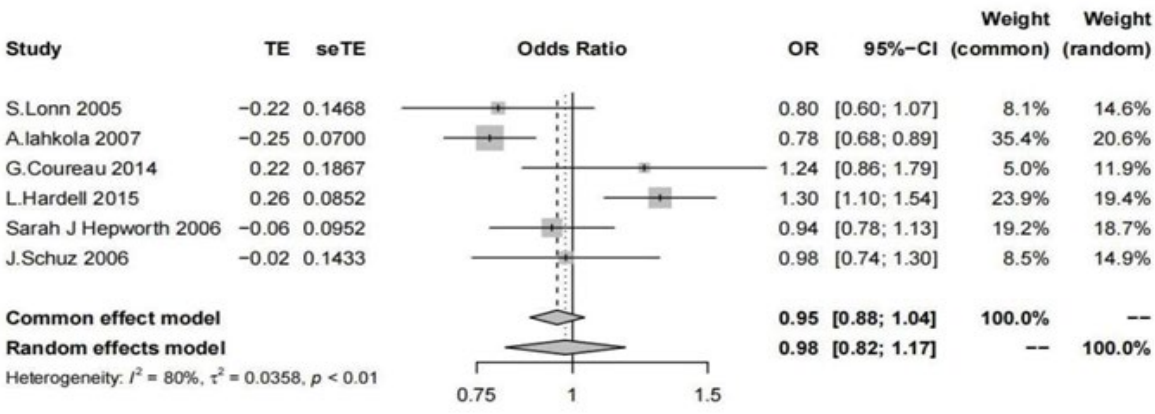
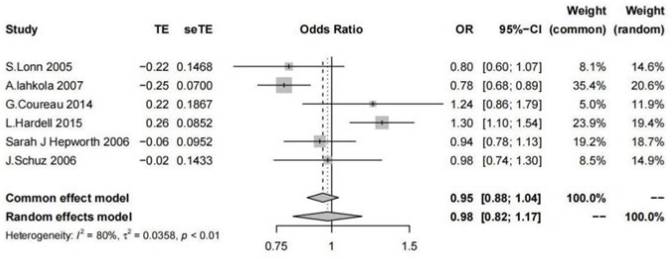
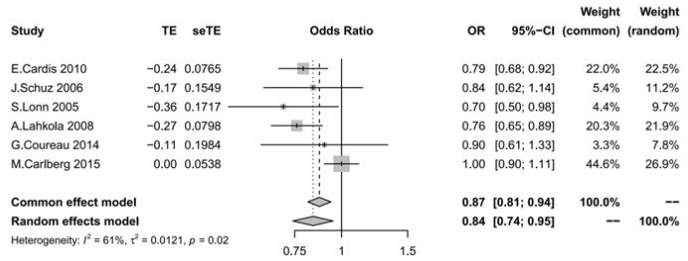


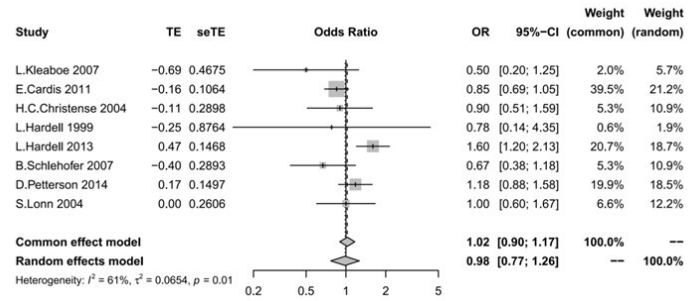
Figure 2: Mobile/Cellular phone use and risk of (A) Gliomas (B) Meningiomas and (C) Acoustic neuromas in meta-analysis of case-control studies.
Note: ES-Effect Size (odds ratio), CI-Confidence Interval.



(A) Glioma



(B) Meningioma



(C) Acoustic neuroma

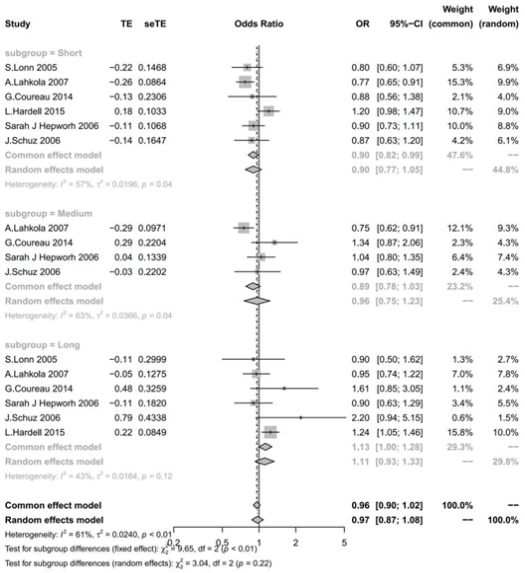


Figure 3: Mobile/cellular phone use duration and risk of glioma in subgroup meta-analysis of case-control studies.
Note: OR-Odds Ratio, CI-Confidence Interval.

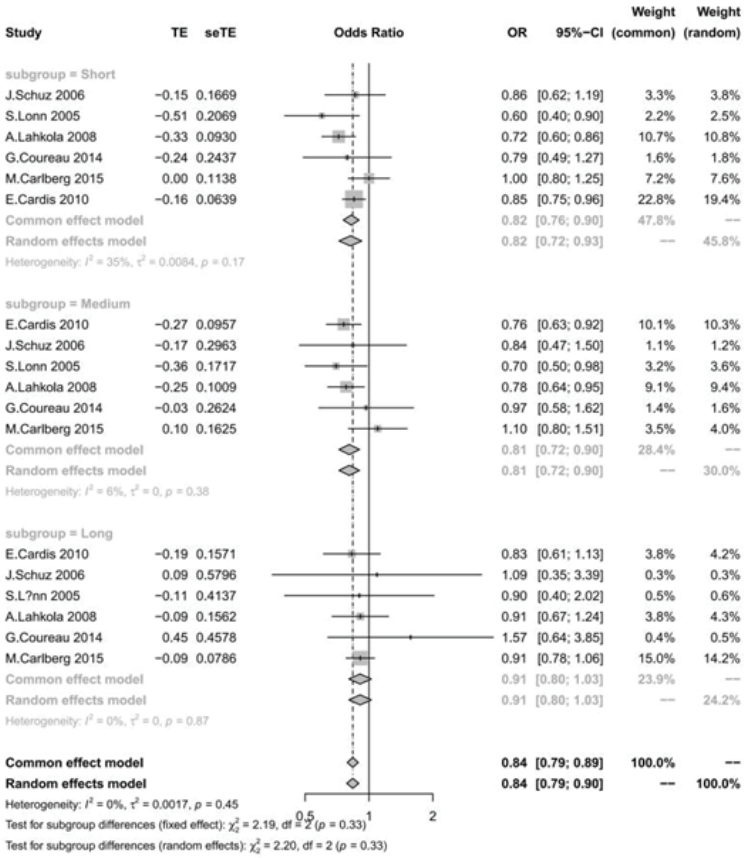


Figure 4: Mobile/cellular phone use duration and risk of meningioma in subgroup meta-analysis of case-control studies.
Note: OR-Odds Ratio, CI-Confidence Interval.

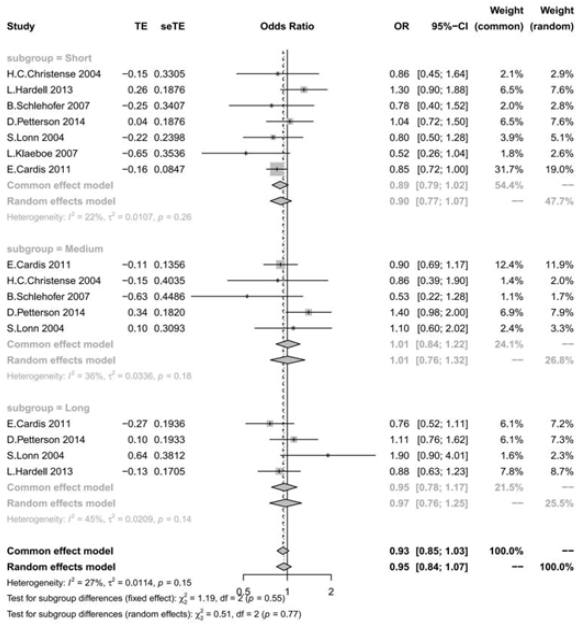


Figure 5: Mobile/cellular phone use duration and risk of acoustic neuroma in subgroup meta-analysis of case-control studies.
Note: OR-Odds Ratio, CI-Confidence Interval.

medium time (≤ 10 years) could reduce the risk of meningioma (OR, 0.83; 95% CI, 0.76-0.90; I^2=39.5%, p=0.142; OR, 0.83; 95% CI, 0.75-0.93; I^2=32.3%, p=0.194). However, the protective effect lost in the subgroup of long time use (OR, 0.91; 95% CI, 0.80-1.03; I^2=0.0%, p=0.870).

Acoustic neuroma

After excluding H. C. Christensen and L. Hardell's studies in the subgroup of long time and medium time use respectively through sensitivity analysis. B. Schlehofer's study was also excluding because of the small-sample size which led to statistical limitation. ORs and CIs of three studies including L. Klaeboe (OR, 0.52; CI: 0.26-1.05), E. Cardis (OR: 0.85; CI: 0.72-1.01) and L. Hardell (OR, 0.88; CI: 0.63-1.22) were calculated using numbers of individuals before pooled them into meta-analysis. Similar to glioma, no association between duration of use mobile/cellular phones and acoustic neuroma were observed in the final fixed effect model (Figure 5).

Publication bias

Publication bias was not observed in the main and subgroup meta-analysis according to the results of Begg's test and Egger's test.

Discussion

In this meta-analysis, we found no association between mobile/cellular phone use and risk of glioma and acoustic neuroma no matter in main or subgroup analyses. For meningioma, decreased risk was observed mobile phone use was associated, especially when the time since first use was less than 10 years, while the protective effect disappeared in longer term (more than 10/11 years).

As for glioma, our result showed no association correlation between mobile phone use of any duration and glioma risk when pooled data of time since first use from 6 articles into meta-analysis, which was consistent with the previous study [29-32]. However, several research showed long-term mobile phone use may be associated with an increased risk of glioma: Yang, M reported the significant positive association between long-term mobile phone use (minimum, 10 years) and glioma (OR=1.44; 95% CI=1.08-1.91) [32], Y. Wang, also found an association between mobile phone use more than 5 years and glioma risk (OR=1.35; 95% CI=1.09-1.62; I^2=91.9%; P < 0.05) [31], and Prasad, M. found that for mobile phone use of 10 years or longer (or >1640 h), the overall result of the meta-analysis showed a 1.33 times increase in risk [30]. Nevertheless, the INTERPHONE Study Group found no significant association between long-term mobile use and the risk of glioma (OR: 1.49; 95% CI: 0.80-2.78; I^2=91.5%) [12]. But their result showed significant heterogeneity, so whether the result was credible enough should be considered. Study quality and source of funding could also influence the research outcomes [30]. Thus, larger and longer studies are required to better characterize this possible link: the dose-response relationship exist between mobile/cellular phone uses. It is known that there are biological differences between low-grade glioma and high grade-glioma. Low-grade glioma, with a long latency period, is potentially more vulnerable to radiation from mobile phones, while high-grade disease has a short latency period [32]. As the knowledge of key molecular alterations that provided superior prognostication related to glioma developed fast [33], the linkage between mobile phone usage and glioma risk should be further investigated and discussed.

Our results also showed that regular use of mobile phones is associated with the risk of meningioma (OR: 0.84, 95%CI: 0.78-0.91, I^2=47.3%, p=0.091). When the subgroup analysis of the duration of mobile/cellular phone use was performed, it was found that the impact of short-term and medium-term mobile/cellular phone use on the risk of meningioma was statistically significant (OR: 0.83, 95%CI: 0.76-0.90, I^2=39.5%, p=0.142 and OR: 0.83, 95%CI: 0.75-0.93, I^2=32.3%, p=0.194, respectively), but not for long-term mobile/cellular phone use (OR: 0.91, 95% CI: 0.80-1.03, I^2=0.0%, p=0.870). Hardell L conducted a meat-analysis on the regular use and long-term use of mobile/cellular phone, results of which are consistent with ours (OR: 0.8, 95% CI: 0.7-0.99 and OR: 1.3, 95%CI: 0.9-1.8, respectively), but there is no relevant analyses on short-term and median-term [34]. Lahkola A meta-analysed the longest use of mobile phones of included articles, but found no statistically significant correlation (OR: 0.87, 95% CI: 0.72-1.05) [35].

Meningioma can cause epilepsy and neurological deficits caused by compression of adjacent nerve tissues through progressive enlargement, which is the most common tumor originating in the meninges [36]. The contribution of mobile/cellular phone use to the risk of meningioma may need to consider the synergistic effect of metal and RF-EMF. The correlation between radiation exposure and meningioma risk may be more affected by the age at the time of radiation exposure than the amount of exposure [37]. Considering that the latency period from radiation exposure to meningioma occurrence can be as long as 36 years [38], the definition of long-time exposure for meningiomas in the current researches is still not appropriate. Moreover, RF-EMF based on occupational exposure has not been shown to be associated with an increased risk of meningioma [39,40]. The current evidence concerning the risk of meningioma and the use of mobile/cellular phones is relatively limited, and more long-term studies with large samples are still urgently needed.

In this meta-analysis, there was no statistically significant association between regular use of mobile/cellular phone and acoustic neuroma (OR, 0.98; 95% CI, 0.76-1.25; I^2=60.7%, p=0.013). When it comes to subgroup analysis, the impact of duration of use still has no statistical significance. There are also a few of meta-analysis studied acoustic neuroma. In 2008, L Hardell published meta-analysis of nine studies on acoustic neuroma and yield (OR, 0.9; 95% CI, 0.7-1.1). But when it comes to use > or =10 years, the result showed positive effect on using mobile phone to the risk of acoustic neuroma (OR, 1.3; 05% CI, 0.6-2.8) [35]. However, they did not analysis the risk for all tumors. A. Bortkiewicz's meta-analysis in 2017 showed similar result as ours (OR: 0.96; 95% CI: 0.87-1.06), but they did not study the duration of using mobile phone and the risk of acoustic neuroma [41].

The followings are several limitations that may contribute to the result. Selection bias is a concern that the cases and controls may not be representative. For example, cases may be under ascertainment for the reason that they were diagnosed and treated outside study area or in some not-participating clinics. Also, people who use mobile phone regularly may have higher potential to participate, especially when the questionnaire is computer-assisted. Thus if mobile/cellular phone users in the control groups were more likely to participate than non-users, the risk may be underestimated. And few of the studies did not use blinding at interview. What should be noticed is that the dead who died of serious conditions were excluded and only survivals participated, which may also affect the result. What's more, the number of studies in the meta-analysis is small, especially when it comes to subgroup analysis.

Conclusion

In conclusion, our study performed a meta-analysis on the association between mobile/cellular phone use and risk of glioma,

meningioma and acoustic neuroma based on the duration of use. We found use of mobile phone can decrease the risk of meningioma, especially when the time since first use was between 0-5 years and 5-10 years, while the protective effect disappeared in longer term (more than 10/11 years). For glioma and acoustic neuroma, there was no statistical significance in our meta-analysis. More studies and more cases are needed to explore the possible influence of long-term use of mobile phone, and one standard protocol is also needed for large scale research.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

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Author Contributions

All authors contributed to the study conception and design.

(I) Conception and design: YF

(II) Administrative support: YW

(III) Provision of study materials or patients: YW

(IV) Collection and assembly of data: YF, ZZ, QF

(V) Data analysis and interpretation: YF, ZZ, QF

(VI) Manuscript writing: All authors

(VII) Final approval of manuscript: All authors.

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