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Mobile phone use and risk of glioma: a case-control study in Korea for 2002-2007

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Objectives There has been a growing concern about the possible carcinogenic effects of the electromagnetic radiofrequency fields emitted from mobile phones. The purpose of this study was to investigate the association between mobile phone use and the development of gliomas in Korea.

Methods Our study methods were based on the International Interphone study that aimed to evaluate possible adverse effects of mobile phone use. This study included 285 histologically-confirmed Korean patients 15 to 69 years of age, with gliomas diagnosed between 2002 and 2007 in 9 hospitals. The 285 individually matched controls were healthy individuals that had their medical check-up in the same hospitals. Unconditional logistic regression was used to calculate the adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for use of mobile phones.

Results For the entire group, no significant relationship was investigated between gliomas and regular use of mobile phones, types of mobile phones, lifetime years of use, monthly service fee, and the other exposure indices. Analyses restricted to self-respondents showed similar results. For ipsilateral users, whose the body side for usual mobile phone use match the location of glioma, the aORs (95% CIs) for lifetime years of use and cumulative hours of use were 1.25 (0.55 to 2.88) and 1.77 (0.32 to 1.84), respectively. However, the contralateral users showed slightly lower risk than ipsilateral users.

Conclusions Our results do not support the hypothesis that the use of mobile phones increases the risk of glioma; however, we found a non-significant increase in risk among ipsilateral users. These findings suggest further evaluation for glioma risk among long-term mobile phone users.

Keywords Electromagnetic field, Glioma, Brain tumor, Mobile phone

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Introduction

Glioma, the most common primary brain tumor that comprises morphologically distinct cancers such as astrocytoma, ependymoma, and oligodendro glioma [1], is a malignant tumor in the central nervous system with a corresponding high fatality rate. According to the data of the Statistics Korea, 1703 persons with brain or central nervous system tumors accounted for 0.7% of 244177 new cancer cases in 2012 [2]. There are several factors that may have increased the risk of gliomas, including exposure to radiation, genetic drift, and electromagnetic field [3], but the exact causes of gliomas are yet to be determined.

From a health-prospective, concerns have been raised regarding microwaves transmitted from the antenna of a mobile phone could cause brain tumors or increase the risk of the development of potential tumors [4-7] albeit its low-power. In particular, exposure to radiofrequency-electromagnetic field (RF-EMF) has been receiving attention due to its negative effect on health, amidst the rapid spread of the use of wireless information service systems.

Most epidemiologic research studies conducted so far on the use of mobile phones and gliomas have failed to show any increase in danger caused by the long-term use of mobile phones [8-13].

However, some studies have reported findings on the relationship between gliomas or brain tumors and the use of mobile phones as follows: the odds ratios (OR) and 95% confidence intervals (CI), i.e., the risk of gliomas when using an analog mobile phone is 1.8 (1.1 to 3.2) [14], the OR (95% CI) for brain tumors based on the use of mobile phones in rural areas is 1.4 (0.98 to 2.0) [15] and 1.12 (0.79 to 1.61) [16], the OR (95% CI) for brain tumors based on the use of analog mobile phones is 2.3(1.2 to 4.1) [14], and the OR (95% CI) associated with use of an analog mobile phone and gliomas is 2.1 (1.3 to 3.4) [17].

In this regard, the International Agency for Research on Cancer (IARC), an international organization for cancer research under the World Health Organization (WHO), examined the validity of epidemiologic research in 1997 in order to investigate the association between the generation of electromagnetic waves from mobile phones and cancer. Subsequently, they started a set of international case-control studies on the link between the use of mobile phones and the development of brain tumors (Interphone study), in which a total of 13 countries participated [18].

The results of recent international epidemiologic studies have increased popular interest in possible health problems and gliomas and other brain tumors owing to the use of mobile phones [4,19-23]. However, little has been known as to their potential mechanisms. Furthermore, there is not enough evidence, either epidemiological or experimental, to support whether RF-EMF has detrimental effect on organisms [24]. Nevertheless, electromagnetic waves from mobile phones may have had a comparatively high effect on the nerves and meningeal tissues close to the surface of the head, thus gliomas and meningiomas become our main concerns.

In 2013, the leading cause of death in Korea was cancer: 144.4 in every a hundred thousand people died of cancer, and 2.4 in every a hundred thousandpeople died of brain tumors.

The use of mobile phones is increasing not only in overseas countries but also in Korea. Statistics showed that subscribers to mobile phones in Korea alone were 47944 thousand in 2009, 50767 thousand in 2010, 52507 thousand in 2011, and 53625 thousand in 2012 [25]. Korea is characterized by relatively high levels in terms of mobile penetration, cumulative hours of use, and lifetime years of use.

Given such an abrupt increase in mobile phone usage, it is important in terms of public health to determine whether electromagnetic waves transmitted by mobile phones are harmful and to carry out the epidemiologic study. Although considerable researches on the effect of electromagnetic waves from mobile phones have been carried out in many countries, there have been few studies that examine the possible link between electromagnetic waves and gliomas in Korea.

Therefore, this study aimed to investigate a possible association between mobile phone use and glioma using a case-control design in nine Korean hospitals based on the protocol of Interphone study [26].

Materials and Methods

Study Subjects

In its final analysis, this study examined 285 patients among 897 patients with gliomas, who were recruited from five areas including Seoul (Seoul, Gyeonggi-do, Gyeongsang-do, Jeolla-do, Chungcheong-do, Gangwon-do, and Jeju-do) and were checked at department of neurosurgery in nine hospitals (Korea University Hospitals (Anam, Guro, Ansan), Inje University Sanggye Paik Hospital, Samsung Medical Center in Seoul, Seoul National University Hospital, Asan Medical Center, Korea Cancer Center Hospital, and Hallym University Sacred Heart Hospital) from 2002 to 2007. The other 612 patients were excluded due to refusal of participation, excessive pain, and impossibility of individual matching (Table S1). The patient group consisted of those who were pathologically diagnosed with gliomas aged between 15 years and 69 years (International Classification of Diseases for Oncology-3 codes 9380-9384, 8391-9460, and 9480) (Table 1) [27].

The control group subjected to the final analysis consisted of 285 healthy persons out of a total of 1051 who randomly re-

Table 1. Histologic type of glioma cases

Type	ICD-O-3 code	n (%)
All cases of glioma	9380-9384, 9391-9460, 9480	285 (100)
Histologic type of tumor		12 (4.2)
Astrocytoma (all grades): grade II	9384, 9400-9421, 9424, 9440-9442	56 (19.6)
Anaplastic astrocytoma: grade III	9384, 9400-9421, 9424, 9440-9442	32 (11.2)
Glioblastoma and gliosarcoma: grade IV	9384, 9400-9421, 9424, 9440-9442	47 (16.5)
Other type	9383, 9391-9394	82 (28.8)
Oligodendroglioma and mixed glioma	9382, 9450-9451	44 (15.4)
Other and unspecified types of glioma	9430-9381, 9422, 9423, 9430, 9460, 9480	12 (4.2)

ICD-O-3, International Classification of Diseases for Oncology-3.

ceived health screenings at the same hospitals as the patient group and were individually matched according to the method for selecting patient-control groups as proposed by the IARC Interphone study team, excluding 766 for the reasons of refusal of participation, excessive pain, and insincere responses (Table S1). The nine hospitals that participated in the study reported patient groups of the diseases to our research team within one week after diagnosis. A questionnaire survey was performed in the individual interview to obtain information for general characteristics and potential confounders. The informed consent was obtained from each subject before enrollment and institutional review board of Korea University approved the study.

Mobile Phone Use Information

Information related with mobile phone use was obtained by a self-administered questionnaire. The types of mobile phone use

Table 2. Distribution of selected characteristics by study group

Characteristics		Cases (n=285)	Controls (n=285)	*p*-value[a]
Sex	Male	159 (55.8)	159 (55.8)	0.86
	Female	126 (44.2)	126 (44.2)	
Age at interview[b]	<20	10 (3.5)	8 (2.8)	0.89
	20-29	53 (18.6)	48 (16.8)	
	30-39	68 (23.9)	73 (25.6)	
	40-49	57 (20.0)	65 (22.8)	
	50-59	55 (19.3)	55 (19.3)	
	≥60	42 (14.7)	36 (12.6)	
Area[c]	Seoul-Gyeonggi	182 (63.9)	183 (64.2)	<0.01
	Gyeongsang	43 (15.1)	20 (7.0)	
	Jeolla	20 (7.0)	34 (11.9)	
	Chungcheong	29 (10.2)	45 (15.8)	
	Gangwon-Jeju	11 (3.9)	3 (1.1)	
Marital status	Married	210 (73.7)	205 (71.9)	0.26
	Unmarried	72 (25.3)	70 (24.6)	
	Others[d]	3 (1.1)	10 (3.5)	
Education	≤ Primary school	27 (9.5)	27 (9.7)	<0.01
	Middle school	29 (10.2)	25 (9.0)	
	High school	131 (46.0)	90 (32.5)	
	≥ University	98 (34.4)	135 (48.7)	
Self-reported annual income (10^4 Korean won)	<100	44 (15.9)	40 (14.2)	0.41
	100 - 299	137 (49.5)	125 (44.3)	
	300 - 499	68 (24.5)	81 (28.7)	
	≥500	28 (10.1)	36 (12.8)	
Respondents[e]	Self	219 (76.8)	273 (95.8)	<0.01
	Proxy	66 (23.2)	12 (4.2)	
Hair coloring	No	145 (51.4)	118 (41.5)	0.01
	Yes	137 (48.6)	116 (58.5)	
Alcohol drinking	No	156 (54.7)	128 (45.3)	0.02
	Yes	129 (45.3)	155 (54.8)	
Cigarette smoking	No	229 (80.6)	243 (85.2)	0.14
	Yes	55 (19.3)	42 (14.7)	
Computer use	No	115 (40.4)	91 (32.0)	0.03
	Yes	170 (59.6)	193 (68.0)	
Watching TV	No	16 (5.6)	13 (4.6)	0.57
	Yes	269 (94.4)	271 (95.4)	
Radio listening	No	179 (62.8)	173 (60.9)	0.64
	Yes	106 (37.2)	111 (39.1)	
Electro-blanket use	No	171 (60.0)	202 (71.1)	<0.01
	Yes	114 (40.0)	82 (28.9)	
Transmission tower[f]	No	219 (77.4)	208 (73.2)	0.25
	Yes	64 (22.6)	76 (26.8)	

[a]*p*-value tested by the Fisher's exact test.
[b]The age of patients at the time of the interview was nearly identical to the age at the time of the diagnosis of the tumor (for patients with tumors) and the age at the time of hospital admission.
[c]The area category comprises Seoul Metropolitan City and all the provinces of South Korea.
[d]The others category comprises the widowed and the divorced.
[e]The proxy respondent is the patient's spouse or other family member.
[f]If the transmission tower is located within less than 300 meters from a patient's residence, it is considered yes.

(analog, analog+digital, and digital mobile phones), the lifetime years of use before one year from diagnosis (non-user, < 48 months, 48-84 months, and > 84 months) the cumulative hours of use (non-user, < 300 hours, 300-900 hours, and > 900 hours) were obtained. The total amount of mobile phone use was calculated with cumulative hours and lifetime years of use. The monthly service fee was divided into < 30, 30-49, 50-80, and > 80 (unit: 10^3 Korean won, KRW). Moreover, the average daily receiving call and the average daily sending call were divided into ≤ 2 times, 3-5 times, 6-9 times, and ≥ 10 times; and the average call duration time was divided into ≤ 2 minutes, 3-4 minutes, and ≥ 5 minutes. The types of mobile phones were classified into flip-type, slide-type, and folder-type; and the regions for carrying a mobile phone during travel were divided into bag, neck, shoulder, pants, and hands. Finally, the usual use of a mobile phone has two categories, rural and urban area.

Confounders or Covariates

Independent variables in the analysis of case-control groups for this study include sex, age (20s, 30s, 40s, 50s, and 60s or older), residential region (Seoul, Gyeonggi, Gyeongsang, Jeolla, Chungcheong, Gangwon, and Jeju), marital status (married, unmarried, others), educational achievement (primary school or lower, middle school or lower, high school or lower, and university or above), income level (< 100, 100-299, 300-499, and ≥ 500, unit: 10^4 KRW), respondent (patient in person and proxy: spouse or other family member), and the existence of a transmission tower within 300 m from the residential area. The alcohol drinking (non-drinking, one drink or more a month on average for last one year) and smoking (non-smoking, current smoking) were considered.

Statistical Analysis

To compare characteristics between cases and controls, χ^2 test or Fisher's exact test was performed. The unconditional logistic regression adjusted for sex, age, type of respondent, five residential regions, educational achievement, the use of dye, alcohol drinking, the use of computer, and the use of electric blanket was used to estimate the risk of the brain tumor in relation with usage of mobile phone. Adjusted odds ratios (aORs) and 95% CIs were calculated. As for whether tumor location corresponds to the hand and the body region primarily used during mobile phone call, statistical significance was assessed with relative risk (RR) and *p*-value the method proposed by Inskip et al. [9], ($RR = [\sqrt{OR+1}] \div 2$). All the statistical analyses of this study were conducted with SPSS version 12.0 (SPSS Inc., Chicago, IL, USA) and the significance level was 0.05.

Results

The general characteristics of the subjects are as shown in Table 2. Among 285 in the cases, 159 (55.8%) were male and 126 (44.2%) were female. The average ages of the cases and the controls were 42.3 (± 14.1) and 42.5 (± 14.0), respectively. As for the residential region, 182 resided in Seoul and Gyeonggi, accounting for 63.9% of the overall patients. For the marital status, married (73.7%, 2 in the patient group) were more than the unmarried and others. High school graduates were the most (46%, 131 in the patient group) and for the annual income level, 100-299 10^4 KRW was the highest (49.5%, 137 in the patient group). Furthermore, there were significant differences between cases and controls, in residential region, educational achievement, respondent type, the use of dye, alcohol drinking, the use of computer, and the use of electric blanket.

As for the mobile phone non-users, 9 were male and 37 were female, and the average ages of the cases and controls were 47.3 (± 16.0) and 50.4 (± 16.4), respectively. There was no significant difference between the mobile phone non-user group and the mobile phone user group in residential region, marital status, and the type of respondent (data not shown).

While the aOR (95% CI) for those who used the mobile phone regularly was 1.17 (0.63 to 2.14), the aOR (95% CI) for the self-respondents was found to be 0.94 (0.46 to 1.89) compared with those who seldom or occasionally used the mobile phone. No significant relationship was found in the regular mobile phone use, the type of mobile phone, the lifetime years of use, the monthly average service fee, and the carriage during travel. However, aOR (95% CI) was 1.92 (0.83 to 4.44) in case the self-respondents used analog and digital simultaneously, 1.35 (0.63 to 2.89) in case the model of mobile phone was folder-type, and 1.42 (0.66 to 3.07) for urban residential region, which was found to be higher than 0.50 (0.22 to 1.13) for rural residential region at a non-significant level (Table 3).

As a result of analyzing the relation between the body side of usual mobile phone use and the location of glioma using the Inskipet et al.'s method [9], the RR was found to be 1.26 ($p = 0.05$) for the overall respondents with the glioma, and 1.43 ($p = 0.01$) for self-respondents (Table 4).

The relationship was adjusted for sex, age, residential region, educational achievement, the use of dye, alcohol drinking, the use of computer, and the use of electric blanket. The risks of glioma for different levels of mobile phone use by ipsilateral and contralateral body side were shown in the Table 5 (total respondents) and Table S2 (self-respondents). In the case of ipsilateral users for total respondents, aORs (95% CI) for the lifetime years of use, cumulative hours of use, the average daily frequency of receiving a call, and the average daily frequency of sending a call were 1.25 (0.55 to 2.88), 1.77 (0.32 to 1.84), 1.52 (0.56 to 4.10), and 3.13

(0.83 to 11.31), respectively, which were found to be high at a non-significant level. On the other hand, contralateral users showed slightly lower aORs (95% CI) than ipsilateral users (Table 5).

Discussion

After adjusting for sex, age, residential region, and other variables, this study found no significant relationship between glio-

Table 3. Adjusted Odds ratio (aORs) and 95% confidence intervals (CIs) for risk of glioma in relation to mobile phone exposure[a]

Variable and level of exposure		Total respondents		aOR (95% CI)[b]	Self-respondents		aOR (95% CI)[c]
		Cases (n=285)	Controls (n=285)		Cases (n=219)	Controls (n=273)	
Use of mobile phone	Non-user[a]	46	41	1.00 (reference)	28	38	1.00 (reference)
	User	239	244	1.17 (0.63, 2.14)	191	235	0.94 (0.46, 1.89)
Type of mobile phone use	Non-user[a]	46	41	1.00 (reference)	25	38	1.00 (reference)
	Analogue	22	15	1.83 (0.63, 5.26)	12	15	1.51 (0.45, 5.03)
	Analogue+digital	132	119	1.89 (0.96, 3.81)	114	113	1.92 (0.83, 4.44)
	Digital	83	109	0.83 (0.43, 1.60)	63	106	0.61 (0.28, 1.33)
Lifetime years of use (mo)	Non-user[a]	46	41	1.00 (reference)	28	38	1.00 (reference)
	<48	49	43	1.28 (0.62, 2.64)	37	41	0.94 (0.42, 2.13)
	48-84	88	92	1.27 (0.63, 2.56)	76	89	1.01 (0.45, 2.23)
	>84	100	108	1.04 (0.52, 2.09)	76	104	0.90 (0.40, 2.02)
Cumulative hours of use (hr)[d]	Non-user[a]	46	41	1.00 (reference)	28	38	1.00 (reference)
	<300	97	79	1.25 (0.64, 2.45)	73	77	0.99 (0.46, 2.12)
	300-900	70	68	1.59 (0.72, 3.21)	61	67	1.17 (0.53, 2.57)
	>900	70	96	0.64 (0.30, 1.34)	55	90	0.62 (0.27, 1.43)
Monthly service fee (10^3 Korean won)	Non-user[a]	46	41	1.00 (reference)	28	38	1.00 (reference)
	<30	73	57	1.48 (0.73, 3.02)	53	55	1.09 (0.45, 2.47)
	30-49	96	111	1.11 (0.57, 2.16)	77	107	0.92 (0.45, 1.98)
	50-80	47	55	1.10 (0.52, 2.29)	42	53	0.99 (0.42, 2.29)
	>80	22	17	1.12 (0.42, 2.98)	18	16	0.81 (0.28, 2.38)
Average daily receiving call	Non-user[a]	46	41	1.00 (reference)	28	38	1.00 (reference)
	≤2	51	46	1.40 (0.68, 2.88)	43	44	0.95 (0.42, 2.15)
	3-5	80	97	1.16 (0.58, 2.31)	64	95	1.00 (0.45, 2.23)
	6-9	46	51	1.95 (0.45, 1.99)	38	47	0.89 (0.39, 2.03)
	≥10	61	49	1.41 (0.64, 3.09)	46	48	1.20 (0.49, 2.90)
Average daily sending call	Non-user[a]	46	41	1.00 (reference)	28	38	1.00 (reference)
	≤2	73	72	1.44 (0.72, 2.86)	61	69	1.08 (0.49, 2.38)
	3-5	82	100	0.97 (0.49, 1.90)	65	96	0.76 (0.34, 1.67)
	6-9	30	37	1.15 (0.52, 2.56)	25	36	1.09 (0.45, 2.66)
	≥10	53	34	1.65 (0.73, 3.76)	40	33	1.29 (0.51, 3.27)
Average duration time (min)	Non-user[a]	46	41	1.00 (reference)	28	38	1.00 (reference)
	≤2	113	116	1.18 (0.62, 2.24)	85	110	0.93 (0.44, 1.96)
	3-4	80	81	1.31 (0.65, 2.63)	67	79	1.14 (0.51, 2.54)
	≥5	45	46	1.00 (0.45, 2.24)	39	45	0.81 (0.33, 1.99)
Shape	Non-user[a]	46	41	1.00 (reference)	28	38	1.00 (reference)
	Flip	19	26	1.51 (0.59, 3.85)	15	26	1.19 (0.41, 3.42)
	Folder	187	139	1.72 (0.87, 3.38)	148	131	1.35 (0.63, 2.89)
	Sliding	30	76	0.55 (0.26, 1.19)	25	75	0.42 (0.10, 1.02)
Carriage	Non-user[a]	46	41	1.00 (reference)	28	38	1.00 (reference)
	In bag	75	74	1.24 (0.61, 2.48)	58	72	1.00 (0.45, 2.24)
	Hung by neck	12	10	0.76 (0.21, 2.77)	7	7	0.82 (0.20, 3.38)
	In shirt	56	51	1.48 (0.68, 3.21)	43	49	1.26 (0.52, 3.06)
	In pants	87	95	0.96 (0.47, 1.95)	74	93	0.75 (0.34, 1.66)
	At hand	9	14	0.74 (0.24, 2.29)	9	14	0.65 (0.18, 2.25)
Proportion urban/rural at first use	Non-user[a]	46	41	1.00 (reference)	28	38	1.00 (reference)
	Urban	174	154	1.66 (0.86, 3.22)	139	147	1.42 (0.66, 3.07)
	Rural	65	90	0.63 (0.31, 1.30)	52	88	0.50 (0.22, 1.13)

[a]Reference category is never or non-regular use of any type of mobile phone.
[b]aORs and 95% CIs were derived from unconditional logistic regression for 1:1-matched pairs, with results adjusted for area, education, respondent type, hair coloring, alcohol drinking, computer use and electro-blanket use.
[c]aORs and 95% CIs were derived from unconditional logistic regression for 1:1-matched pairs, with results adjusted for area, education, hair coloring, alcohol drinking, computer use and electro-blanket use.
[d]For cumulative number and duration of calls category cut-off points were median and 75th percentile.

Table 4. Laterality of tumor with respect to laterality of telephone use among glioma patients with regular use of mobile phone[a]

Tumor type	Tumor site	Total respondents			RR[b]	*p*-value	Self-respondents			RR[b]	*p*-value[c]
		Total					Laterality of mobile phone use				
		Right	Left	Total			Right	Left	Total		
Glioma	Right	37	15	52	1.26	0.05	32	13	45	1.43	0.01
	Left	22	21	43			14	20	34		
Total		59	36	95			46	33	79		

RR, relative risk; OR, odds ratio.
[a]Patients with tumors whose tumor or telephone use was not exclusively attributed to one side or the other were excluded from the analysis. Laterality was examined by the method proposed by Inskip et al. [9].
[b]The RR of a brain tumor associated with mobile phone use was estimated as $[(\sqrt{OR}+1)\div 2]$, where OR denotes the unadjusted OR.
[c]*p*-value tested by the Fisher's exact test.

Table 5. Risk of glioma for different levels of mobile phone use by ipsilateral and contralateral among total respondents[a]

Variable and level of exposure		Ipsilateral		aOR (95% CI)[b]	*p* for trend	Contralateral		aOR (95% CI)[b]	*p* for trend
		Cases (n=104)	Controls (n=93)			Cases (n=83)	Controls (n=85)		
Use of mobile phones	Non-user[a]	46	41	1.00 (reference)	0.98	46	41	1.00 (reference)	0.35
	User	58	52	0.95 (0.50, 1.83)		37	44	0.90 (0.43, 1.89)	
Type of mobile phone use	Non-user[a]	46	41	1.00 (reference)	0.96	46	41	1.00 (reference)	0.14
	Analogue	2	3	0.42 (0.55, 3.34)		6	2	3.26 (0.52, 20.3)	
	Analogue+digital	34	29	1.13 (0.52, 2.45)		19	22	0.97 (0.40, 2.33)	
	Digital	21	20	0.74 (0.32, 1.68)		12	20	0.64 (0.24, 1.70)	
Lifetime years of use (mo)	Non-user[a]	46	41	1.00 (reference)	0.98	46	41	1.00 (reference)	0.29
	<48	8	4	1.25 (0.29, 5.32)		6	7	0.75 (0.17, 3.17)	
	48-84	15	22	0.61 (0.25, 1.44)		13	12	1.29 (0.48, 3.46)	
	>84	34	26	1.25 (0.55, 2.88)		18	25	0.72 (0.29, 1.78)	
Cumulative hours of use (hr)[c]	Non-user[a]	46	41	1.00 (reference)	0.94	46	41	1.00 (reference)	0.25
	<300	14	14	0.96 (0.37, 2.47)		14	13	1.20 (0.43, 3.29)	
	300-900	21	19	1.04 (0.45, 2.40)		9	12	1.09 (0.36, 3.28)	
	>900	22	19	1.77 (0.32, 1.84)		14	19	0.63 (0.24, 1.65)	
Monthly service fee (10^3 KRW)	Non-user[a]	46	41	1.00 (reference)	0.40	46	41	1.00 (reference)	0.37
	<30	15	16	0.86 (0.35, 2.08)		14	13	1.12 (0.39, 3.21)	
	30-49	29	26	1.04 (0.48, 2.25)		13	16	1.05 (0.40, 2.74)	
	50-80	8	7	0.72 (0.20, 2.61)		6	12	0.46 (0.12, 1.65)	
	>80	6	1	4.37 (0.45, 41.9)		4	2	2.26 (0.33, 15.5)	
Average daily receiving call	Non-user[a]	46	41	1.00 (reference)	0.43	46	41	1.00 (reference)	0.26
	≤2	9	11	0.83 (0.29, 2.41)		9	8	1.05 (0.32, 3.45)	
	3-5	19	21	0.81 (0.35, 1.91)		12	17	0.97 (0.37, 2.56)	
	6-9	12	10	0.85 (0.30, 2.42)		6	6	1.18 (0.30, 4.62)	
	≥10	18	10	1.52 (0.56, 4.10)		9	13	0.57 (0.18, 1.80)	
Average daily sending call	Non-user[a]	46	41	1.00 (reference)	0.34	46	41	1.00 (reference)	0.40
	≤2	11	14	0.73 (0.28, 1.91)		13	11	1.16 (0.41, 3.23)	
	3-5	26	23	0.97 (0.43, 2.14)		9	19	0.61 (0.22, 1.70)	
	6-9	6	11	0.44 (0.12, 1.56)		6	6	1.38 (0.36, 5.32)	
	≥10	15	4	3.13 (0.83, 11.3)		8	8	0.75 (0.21, 2.72)	
Average duration time (min)	Non-user[a]	46	41	1.00 (reference)	0.88	46	41	1.00 (reference)	0.25
	≤2	26	27	2.50 (0.57, 10.9)		18	24	2.65 (0.39, 17.8)	
	3-4	21	18	1.03 (0.44, 2.42)		12	11	0.84 (0.28, 2.49)	
	≥5	11	7	0.94 (0.28, 3.09)		6	9	0.65 (0.18, 2.26)	

aOR, adjusted odds ratio; odds ratio; CI, confidence interval; KRW, Korean won.
[a]Reference category is never or non-regular use of any type of mobile phone.
[b]aORs (95% CIs) were derived from unconditional logistic regression for 1:1-matched pairs, with results adjusted for area, education, respondent type, hair coloring, alcohol drinking, computer use and electro-blanket use.

mas and mobile phone use, i.e., hours since the initial use of a mobile phone, the period of use, the average daily frequency of receiving a call, the average daily frequency of sending a call, and the monthly average service fee. However, some findings, showed that the risk of gliomas increased at a non-significant level with the folder-type mobile phone and the urban region. It

also increased with the simultaneous use of analog and digital phones, the lifetime years of use, the cumulative hours of use, the monthly average service fee, and the average daily frequency of sending a call, for the case of ipsilateral users.

It has been reported that data on the deposition of wireless frequency energy resulting from the form of a car phone or a mobile phone, or the mode of carrying a mobile phone during travel, can be used for an anatomic division of tumorigenesis [28]. The results of this research showed an increased risk, although not statistically significant, when the phone was placed in a shirt pocket among the body regions for carrying a mobile phone during travel. The same results were found for self-respondents. Thus, it is deemed that the location of a mobile phone or the body region has no effect on the development of gliomas. In addition, as a result of this study, it was found that the risk had no particular relationship with a mobile phone service company. The aOR (95% CI) for the folder type mobile phones was 1.35 (0.63 to 2.89) among the self-respondents, which seems to reflect its more users than those of the sliding type, and social and economic status and educational achievement.

In addition to the frequency and duration of mobile phone use, factors that can affect the degree of exposure to micro-electromagnetic waves include the distance from a base transceiver station, localized topography, vegetation, the indoor or outdoor use of a mobile phone, a particular mobile-phone model, the position of an antenna, and the relation between the head and a phone [29,30]. It is difficult to divide and explain these variables with respect to the degree of exposure, and it seemed that these factors were unable to artificially change the frequency of mobile phone use and the time of its use. Therefore, in this study, it was actually possible to investigate the frequency of mobile phone use and the length of its use alone. Some studies revealed that the electromagnetic effect is affected by the use of the electric blanket [31,32].

In this study, the ratio of self-respondents in the patient group and the control group was 86.3% (n=492) higher than that of proxy respondents. This seems to be resulting from the fact that patients with gliomas do not have the symptoms of disease with hearing loss that can shift the position of using the mobile phone onto the other side, unlike those with other brain tumors or acoustic neurinomas. It seems to be also because with neurologically good condition, they remembered things well and were cooperative with the survey questions.

Overall, epidemiologic studies conducted so far on the relationship between mobile phone use and diseases have not found relationship between the use and cancer genesis [6,8,9]. Moreover, studies on Denmark [10] and Sweden [11] reported that there was no significant relationship between brain tumors and electromagnetic waves emitted by a mobile phone. Also, a case-control study (Interphone study) initiated as an international set of case-control studies in 13 countries around the world [26] focusing on mobile phone use and the risk of brain tumors, showed no risk of gliomas and meningiomas associated with mobile phone use [10,11], which agrees with the findings of this study.

On the other hand, a study reported borderline levels of effects on the risk of gliomas and the use of analog cellular phones, with 432 cases of brain tumor and salivary gland cancer diagnosed in Finland in 1996, with five controls per case [17]. In addition, a case-control study published in 2003 (1617 cases) reported the association of analog mobile phone use with brain tumors [14]. Health hazards, such as an increase in standardized mortality ratio [33] pursuant to the increase of the time of usage [29]and an increase of ocular melanoma occurrence [30] were reported additionally [34].

Overall, findings of studies conducted so far show inconsistent results on the link between electromagnetic waves emitted by mobile phones and brain tumors. Such conflicting results can be attributed to ecological error, inaccuracy of exposure evaluation, and failure to control the information on confounding variables.

In the case where the body side of usual mobile phone use agreed with the location of a glioma (ipsilateral use) for all the respondents, the aOR (95% CI) for the lifetime years of use, the cumulative hours of use, the average daily frequency of receiving a call, and the average daily frequency of sending a call were 1.25 (0.55 to 2.88), 1.77 (0.32 to 1.84), 1.52 (0.56 to 4.10), and 3.13 (0.83 to 11.31), respectively. On the contrary, in the case of disagreement, they showed aOR (95% CI) that was slightly lower. The results correspond to findings of other research on acoustic neurinomas [35] and gliomas [14]. However, some studies on gliomas and meningiomas did not show the increase in risk [11]. In addition, a study involving 678 cases and 3553 controls selected from Sweden, Denmark, Norway, Finland, and two regions in the UK found no relationship of risk with duration of mobile phone use, lifetime years of use or number of calls. Nevertheless, it reported that the risk of brain tumor on the same side of the head as mobile phone use was raised for use for 10 years or longer [36].

In the present study, the analysis result showed an RR of 1.43 (p=0.01). The study conducted by Inskip et al. [9] showed an RR of 0.9 (p=0.77) in gliomas, a Japanese study an RR of 0.72 (p=0.001) in acoustic neurinomas [23] and an Israeli study an RR of 1.32 (p=0.001) in parotid gland tumors [16], respectively. This showed a consistency among different studies to suggest a stronger association in the same laterality.

The limitations of this study were as follows: First, it is not

possible to exclude the possibility of recall bias that might be caused by the patients' untruthful response, avoidance, memory loss, or exaggeration as to some exposure factors of the questionnaire that included the situation in which the patients knew already they belonged to the patent group. Thus, this study excluded subjects aged 70 or older for the seeming difficulty of deriving accurate responses due to their advanced age. Second, it is probable that selection bias worked because persons relatively more interested in mobile phone radiation participated, and responses could differ between the self-respondents and the proxy respondents. Therefore, this study carried out analysis according to the types of respondents. Third, old subjects of this study aged 60 or older rarely use mobile phones, compared with the young. Therefore, the possibility should be considered that a proper number of samples failed to be obtained. Fourth, during the selection of the patient group, given the dead who died of serious conditions, selection bias may have resulted from including in this study only patients who survived the research period. Thus, it is possible that findings of the current study, which included only mild cases, but excluded the lost, have been underestimated.

Despite the many limitations mentioned above, this case-control study, could secure comparability between the two groups as much as possible. The patient group and the control group were selected by the same standard from the same source population, and the same method was applied to the process of obtaining necessary information from the questionnaire survey. That is, variability could be reduced in collecting information on risk factors since the institutions of the nine hospitals that participated in the research used the standardized common protocol. Furthermore, it was possible to explore the dose-response relationship by grasping the frequency and duration of use, using the personal exposure to the mobile phone found from an additional questionnaire survey on. Such were educational achievement, the type of respondent, the use of dye, alcohol drinking, the use of computer, and the use of electric blanket as well as sex, age, and residential region. This study has the advantage of being the first large-scale research ever performed in Korea on the relationship between gliomas and mobile phone radiation.

Future studies with longer time users and to elucidate the biological mechanism are needed.

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Conflict of Interest

The authors have no conflicts of interest associated with material presented in this paper.

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Table S1. Numbers of subjects contacted, included and not included in the study

	Cases	Controls
AMC	166	188
HUSH	42	53
KCC	84	92
KUH (Anam)	153	181
KUH (Ansan)	132	154
KUH (Guro)	121	147
SMC	57	63
SNUH	104	132
SPH	38	41
Total	897	1051
Not included in the study	612	766
Refused	142	354
Excessive pain[a]	465	7
No match partner[b]	5	405
Included in the study	285	285

AMC, Asan Medical Center; HUSH, Hallym University Sacred Heart Hospital; KCC, Korea Cancer Center Hospital; SMC, Samsung Medical Center in Seoul; SNUH, Seoul National University Hospital; SPH, Sanggye Paik Hospital.
[a]Some patients were excluded from the study because they were so ill that they were not able to answer the questionnaire.
[b]Some people in the control group were excluded from the study because they didn't make proper answers for the questionnaire.

Table S2. Risk of glioma for different levels of mobile phone use by ipsilateral and contralateral among self-respondents[a]

Variable and level of exposure		Ipsilateral				Contralateral			
		Cases (n=104)	Controls (n=93)	aOR (95% CI)[b]	*p*-trend	Cases (n=83)	Controls (n=85)	aOR (95% CI)[b]	*p*-trend
Use of mobile phones	Non-user[a]	28	38	1.00 (reference)	0.27	28	38	1.00 (reference)	0.60
	User	52	48	1.48 (0.67, 3.26)		27	44	1.28 (0.51, 3.20)	
Type of mobile phone use	Non-usera	28	38	1.00 (reference)	0.35	28	38	1.00 (reference)	0.36
	Analogue	2	3	0.64 (0.74, 5.65)		3	2	3.44 (0.39, 30.0)	
	Analogue+digital	31	25	2.49 (0.92, 6.73)		15	22	1.43 (0.49, 4.17)	
	Digital	18	20	1.03 (0.41, 2.62)		9	20	0.94 (0.30, 2.98)	
Lifetime years of use (mo)	Non-user[a]	28	38	1.00 (reference)	0.17	28	38	1.00 (reference)	0.42
	<48	7	4	1.71 (0.35, 8.38)		5	7	1.36 (0.28, 6.57)	
	48-84	12	22	0.76 (0.27, 2.11)		10	12	1.60 (0.50, 5.07)	
	>84	32	22	2.61 (0.97, 7.01)		12	25	1.04 (0.34, 3.12)	
Cumulative hours of use (hr)[c]	Non-user[a]	28	38	1.00 (reference)	0.14	28	38	1.00 (reference)	0.49
	<300	12	14	1.10 (0.37, 3.24)		9	13	1.40 (0.41, 4.72)	
	300-900	18	19	1.50 (0.55, 4.06)		8	12	1.88 (0.53, 6.63)	
	>900	21	15	1.79 (0.65, 4.89)		10	19	0.89 (0.27, 2.92)	
Monthly service fee (10^3 Korean won)	Non-user[a]	28	38	1.00 (reference)	0.03	28	38	1.00 (reference)	0.78
	<30	12	16	1.07 (0.36, 3.14)		11	13	1.74 (0.52, 5.80)	
	30- 49	26	23	1.61 (0.65, 3.95)		6	16	0.88 (0.25, 3.05)	
	50-80	8	6	1.58 (0.39, 6.36)		6	12	0.97 (0.22, 4.18)	
	>80	6	1	7.42 (0.68, 80.4)		4	2	3.49 (0.47, 25.8)	
Average daily receiving call	Non-user[a]	28	38	1.00 (reference)	0.07	28	38	1.00 (reference)	0.44
	≤2	9	11	1.22 (0.39, 3.79)		8	8	1.82 (0.49, 6.75)	
	3-5	16	20	1.03 (0.30, 2.82)		8	17	1.19 (0.36, 3.89)	
	6-9	11	7	1.83 (0.53, 6.27)		4	6	1.46 (0.27, 7.96)	
	≥10	16	10	2.48 (0.79, 7.74)		7	13	0.85 (0.21, 3.32)	
Average daily sending call	Non-user[a]	28	38	1.00 (reference)	0.05	28	38	1.00 (reference)	0.63
	≤2	10	13	1.17 (0.40, 3.46)		11	11	1.82 (0.56, 5.84)	
	3-5	22	21	1.39 (0.51, 3.77)		5	19	0.57 (0.15, 2.14)	
	6-9	6	10	0.77 (0.19, 2.99)		5	6	2.38 (0.46, 12.2)	
	≥10	14	4	5.38 (1.31, 22.1)		6	8	1.32 (0.27, 6.42)	
Average duration time (min)	Non-user[a]	28	38	1.00 (reference)	0.19	28	38	1.00 (reference)	0.51
	≤2	22	24	1.08 (0.47, 2.49)		14	24	1.33 (0.52, 3.40)	
	3-4	19	17	1.28 (0.52, 3.17)		8	11	1.06 (0.33, 3.35)	
	≥5	11	7	0.98 (0.28, 3.40)		5	9	0.81 (0.22, 2.96)	

aOR, adjusted odds ratio CI, confidence interval.

[a]Reference category is never or non-regular use of any type of mobile phone.

[b]aORs (95% CIs) were derived from unconditional logistic regression for 1:1-matched pairs, with results adjusted for area, education, hair coloring, alcohol drinking, computer use and electro-blanket use.

[c]For cumulative number and duration of calls category cut-off points were median and 75th percentile.