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Risk for Glioma Triples With Long-Term Cell Phone Use CME/CE

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Clinical Context

During the last decade, there has been a dramatic global increase in wireless communication use, resulting in greater exposure to radiofrequency electromagnetic fields (RF-EMF). Health risk concerns center on the brain, which is the main target of RF-EMF during use of mobile or cordless phones.

Some evidence suggests the possibility of increased brain tumor risk associated with use of wireless phones, but findings to date have been mixed and inconclusive. The International Agency on Research on Cancer (IARC) at the World Health Organization concluded that RF-EMF exposure is "possibly" a human carcinogen.

Study Synopsis and Perspective

Long-term use of both mobile and cordless phones is associated with an increased risk for glioma, the most common type of brain tumor, the latest research on the topic concludes.

The new study shows that the risk for glioma was tripled among those using a wireless phone for more than 25 years and that the risk was also greater for those who had started using mobile or cordless phones before age 20 years.

"Doctors should be very concerned by this and discuss precautions with their patients," study author Lennart Hardell, MD, PhD, professor, Department of Oncology, University Hospital, Örebro, Sweden, told *Medscape Medical News*.

Such precautions, he said, include using hands-free phones with the "loud speaker" feature and text messaging instead of phoning.

The study was published online October 28 in *Pathophysiology*.

Pooled Data

The recent worldwide increase in use of wireless communications has resulted in greater exposure to RF-EMF. The brain is the main target of RF-EMF when these phones are used, with the highest exposure being on the same side of the brain where the phone is placed.

The new study pooled data from 2 case-control studies on histopathologically confirmed malignant brain tumors. The first included patients 20 to 80 years old diagnosed from 1997 to 2003, and the second included those 18 to 75 years old diagnosed between 2007 and 2009. Patients came from 6 oncology centers in Sweden.

Patients were matched with control participants of the same gender and approximate age who were randomly drawn from the Swedish Population Registry.

All participants filled out a questionnaire detailing exposure to mobile phones and cordless desktop phones.

The analysis included 1498 cases of patients with malignant brain tumors; the mean age was 52 years. Most patients (92%) had a diagnosis of glioma, and just more than half of the gliomas (50.3%) were the most malignant variety --- astrocytoma grade 4 (glioblastoma multiforme). Also included were 3530 control participants, with a mean age of 54 years.

The analysis showed an increased risk for glioma associated with use for more than 1 year of both mobile and cordless phones after adjustment for age at diagnosis, gender, socioeconomic index, and year of diagnosis. The highest risk was for those with the longest latency for mobile phone use at 25 years.

Table. Glioma Risk With Mobile and Cordless Phone Use

Phone Use	**Odds Ratio (95% Confidence Interval)**
Mobile phone use > 1 year	1.3 (1.1 - 1.6)
Cordless phone use > 1 year	1.4 (1.1 - 1.7)
Mobile phone use > 25 years	3.0 (1.7 - 5.2)

The risk was increased the more that wireless phones were used. The odds ratios (ORs) steadily increased with increasing hours of use.

The risk for glioma was greatest in the most exposed part of the brain. The ORs were higher for ipsilateral exposure and for glioma in the temporal and overlapping lobes.

Furthermore, the risk was highest among participants who first used a mobile phone (OR, 1.8) or cordless phone (OR, 2.3) before age 20 years, although the number of patients and control participants was relatively small.

Developing Brain

As Dr Hardell explained, children and adolescents are more exposed to RF-EMF than adults because of their thinner skull bone and smaller head and the higher conductivity in their brain tissue. The brain is still developing up to approximately age 20 years, and until that time, it is relatively vulnerable, he said.

There was a higher risk for third-generation (3G) mobile phone use compared with other types, but this was based on short latency and rather low numbers of exposed participants, said the authors. 3G universal global telecommunications system mobile phones emit wide-band microwave signals, which "hypothetically" may result in higher biological effects compared with other signals, they write.

Such biological effects, said Dr Hardell, could include an increase in reactive oxygen species, which several articles have linked to cancer. The *p53* gene has also been implicated, he said.

The study's very high participation rate (86% for patients and 87% for control participants) makes it unlikely that selection bias influenced the results, said the authors.

Dr Hardell believes the new findings reinforce the message that EF-EMF emissions from wireless phones should be regarded as carcinogenic under IARC classifications and that current guidelines for exposure "should be urgently revised" to reflect that.

According to the IARC's 2013 report, there is a "causal" relationship between use of both mobile and cordless phones and that the risk for glioma is "possible."

Numerous studies have looked at the link between use of wireless phones and brain tumors. Studies by Dr Hardell and his colleagues dating back to the late 1990s have found a connection with mobile and cordless phones.

However, the INTERPHONE study (*Int J Epidemiol* 2011;39:675-694; *Cancer Epidemiol* 2011;32:453-464) failed to find strong evidence that mobile phones increase the risk for brain tumors.

In addition, a large prospective study (*Int J Epidemiol* 2013;42:792-802) found that mobile phone use was not associated with increased incidences of glioma, meningioma, or noncentral nervous system cancers in middle-aged British women.

According to Dr Hardell, this last study was limited because it used information at one point in time. "It is not a case-control study and has serious problems with the methods used," he told *Medscape Medical News*.

Evidence "Unconvincing"

Reached for a comment, L. Dade Lunsford, MD, Lars Leksell Professor of Neurosurgery, and director, Center for Image Guided Neurosurgery, University of Pittsburgh, Pennsylvania, said that the new study provides additional "but as yet unconvincing" evidence of a potential role of cell or cordless phone technologies in the pathogenesis of gliomas.

He noted that some features were not controlled for, including ionizing radiation exposure and family history.

As well, he said, the study has recall bias, with results possibly being affected by patients being anxious to solve the question of "why me?"

"It is of interest that the only study that used actual industry data of cell phone use (the Danish study [*Lancet Oncol* 2011;12:624-626; *Rev Environment Health* 2012;27:51-58]) was dismissed by the authors as 'uninformative'," he said. "Perhaps it was not supportive of the author's premise."

Although the study did not specify the side of the tumor, Dr Lunsford pointed out that roughly 90% of the world's population is right-handed and that most hold their mobile phone to their left ear in order to write with their dominant hand. "One could theorize then that left-sided tumors would predominate with the temporal lobe being most adjacent to the cell phone output."

Dr Lunsford also commented that both glial and Schwann cells are late-responding tissues and that the oncogenesis of such cells by mobile phone technologies remains unexplained. "If cell phones cause such tumors, why do patients not develop higher rates of ipsilateral basal or squamous cell cancers, or melanomas -- these are frequently dividing cell lines that theoretically ought to be even more susceptible."

Although the potential role of cell phones as an additional factor in oncogenesis "can't be dismissed out of hand," the use of this technology does save lives, stressed Dr Lunsford.

"Cell phone has provided an amazing safety net for citizens of almost all cultures across the world. The lives saved by the proliferation of cell phone communication [are] phenomenal -- emergency calls, quick first responders, warnings of severe weather are only a few examples."

Pathophysiology. Published online October 28, 2014. Abstract

Study Highlights

- The investigators pooled data from 2 case-control studies of malignant brain tumors from patients diagnosed in Sweden during 1997 to 2003 (diagnosis at ages 20 - 80 years) and 2007 to 2009 (ages 18 - 75 years).
- The investigators included only cases in which the tumor was confirmed by histopathologic examination.
- Population-based control participants were matched for age and gender.
- Questionnaires allowed determination of exposures to cell and cordless phone use.
- Unconditional regression analysis used the entire reference group, with adjustment for gender, age, year of diagnosis, and socioeconomic index.
- Response rates were 89% for patients (n = 1498) and 87% for control participants (n = 3530).

- Among the patients, 92% had glioma, of which 50.3% of these tumors were highly malignant glioblastoma multiforme (astrocytoma grade 4).
- Overall, mobile phone use was associated with a 30% increased risk for glioma (OR, 1.3; 95% CI, 1.1 - 1.6).
- For mobile phone use in the latency group of more than 25 years, the risk for glioma was tripled that in the control participants (OR, 3.0; 95% CI, 1.7 - 5.2).
- Use of cordless phones was associated with an overall 40% increased risk for glioma (OR, 1.4; 95% CI, 1.1 - 1.7), with risk increased further to 70% in the latency group of 15 to 20 years (OR, 1.7; 95% CI, 1.1 - 2.5).
- There were statistically significant increases in OR both per 100 hours of cumulative use, and per year of latency for mobile and cordless phone use.
- The risk was greatest for ipsilateral glioma (OR, 1.8 for mobile phone use; 95% CI, 1.4 - 2.2 and OR, 1.7 for cordless phone use; 95% CI, 1.3 - 2.1).
- In terms of location, the risk was greatest for glioma in the temporal and overlapping lobes, corresponding to the region of highest RF-EMF exposure.
- Beginning mobile or cordless phone use before age 20 years was associated with a higher risk for glioma compared with mobile or cordless phone use beginning at later ages.
- Although glioma risk was higher with use of 3G mobile phones, this was based on short latency and a small sample of exposed cases.
- Limitations of this study include possible recall bias or observational bias and relatively small numbers of patients and control participants in certain subgroups.
- Possible precautions to limit RF-EMF exposure during mobile or cordless phone use include using hands-free phones with a loud speaker and text messaging instead of telephoning.

Clinical Implications

- The risk for glioma is increased with cell and cordless phone use, based on an analysis of pooled case-control studies in Sweden.
- The risk associated with cell and cordless phone use is especially increased for ipsilateral glioma of the temporal and overlapping lobes, particularly for longer exposure starting at younger ages.

CME Test

To receive *AMA PRA Category 1 Credit™*, you must receive a minimum score of 75% on the post-test.

You are advising a mother regarding the safety of cell and cordless use in her teenaged children. According to the analysis of pooled case-control studies in Sweden by Hardell and Carlberg, which of the following statements about the overall risk for glioma associated with cell and cordless phone use is ***correct***?

- Overall, mobile phone use was associated with twice the risk for glioma
- Use of cordless phones was associated with an overall 20% increased risk for glioma

- Most of the patients in this study had low-grade gliomas
- RF-EMF exposure during mobile or cordless phone use could be limited by using hands-free phones with a loud speaker and text messaging instead of telephoning

According to the analysis of pooled case-control studies in Sweden by Hardell and Carlberg, which of the following statements about factors modifying the risk for glioma associated with cell and cordless phone use is ***correct***?

- Risk was greatest for glioma in the frontal lobe
- For mobile phone use in the latency group of more than 25 years, risk for glioma was triple that in the control participants
- Increases in risk per 100 hours of cumulative use were not statistically significant
- The study proved that glioma risk was statistically significantly higher with use of 3G mobile phones

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