What Do Cars, TVs, and Lung Cancer Have in Common?

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Q: What is there in common among cars, televisions, and lung cancer?
A: In each instance, Japan outperforms the United States.

Most Americans are aware that technical experts from Consumer Reports magazine consistently rank televisions and automobiles manufactured by Japanese companies higher than their US counterparts, but I believe that neither Consumer Reports nor US physicians—including so-called lung cancer “thought leaders”—understand how much better lung cancer treatment results are in Japan.

A 2009 study reports 65.7% 5-year survival following pulmonary resection of lung cancer at the National Cancer Center Hospital (NCCH) in Tokyo. Such excellent survival is not unique. A 2011 Japanese Joint Committee for Lung Cancer Registry report on more than 11,000 resected cases reports a 5-year survival of 69.6%, improved over results from a decade earlier. A PubMed search retrieved no comparable postsurgical survival results in any national registry or cancer center in Europe or the United States. Superior results in Japan might be partly attributed to a more fastidious application of en bloc resection combined with systematic nodal dissection, but evidence suggests that the primary reason for strikingly improved survival lies in widespread application of lung cancer screening in Japan. This phenomenon is reflected in the NCCH-Tokyo patients. More than half had lung cancers detected by population screening and another fourth were incidental findings on radiographic studies.

In the United States, outside of a small number of research trials in Philadelphia in the 1950s; at the Mayo Clinic, Johns Hopkins, and Memorial Hospital in the 1970s; and in the recent I-ELCAP, PLCO, and NLST trials, little screening for lung cancer has been performed. In total, these studies screened only about 300,000 individuals. The first US population lung cancer screening, based upon guideline recommendations, began in 2012.

In contradistinction, enormous numbers of individuals have been screened in large research studies, pilots, and population screenings in Japan. Chest roentgenographic (CXR) screening in Japan extends as far back to the 1940s, with annual CXR mandated by the Tuberculosis Control Laws. The Tokyo Metropolitan Government Study of 1953 screened more than 1.8 million individuals using CXR. Lung cancer screening for individuals above age 40 was added in 1987 under the Health and Medical Services Law for the Elderly.

In 2005, Professor Tomotaka Sobue reported on the history of lung cancer screening in Japan at the 12th International Conference on Screening for Lung Cancer in Nara, Japan, and estimated that more than 7.8 million Japanese over the age of 40 had annual CXR screening. This number is almost certainly much higher now. Between 1987 and 1998, 2,323,455 people in Okayama Prefecture alone were screened. Although public health policy was implemented initially in the absence of data showing reduction in national population mortality, a series of case-control studies with matching controls, taken from more than 1 million Japanese screened annually with CXR in five large studies between 1982 and 2001, showed evidence of substantial reduction in lung cancer population mortality. Estimates of lung cancer percent mortality reduction from these studies ranged between a low of 28% ($P = .07$) from the Japanese Lung Cancer Screening Research Group to statistically significant 20% to 30% (Gunma Prefecture), 41% (Okayama Prefecture), 46% (Miyagi Prefecture), and 60% (Niigata Prefecture).

In the late 1980s, Japanese researchers began to study progressively lower-dose CT scans as a more sensitive screening modality. Ohmatsu of the National Cancer Hospital East reported results of the Anti-Lung Cancer Association (ALCA) study, comparing two methods of screening in 45,000 individuals. The percentage of patients detected by CXR vs CT in stage IA was 42% vs 74%, mean
tumor size was 30 vs 17 mm, and 5-year survival was 49% vs 80% in the two groups.

In 2007, Sone reported 84% 10-year survival in CT-detected lung cancers in Nagano, Japan. Nakayama reported interim results of the Japanese Lung Cancer Screening Research Group, a multi-institutional, non-concurrent cohort study of 137,000 that screened individuals by CXR vs CT with a case-control arm. Eighty-four percent of CT cases were detected in stage I with a 5-year survival of 92%. Sub-centimeter cancers had 100% 5-year survival, better than that of cancers larger than 30 mm ($P = .05$). Lung cancer mortality rates appeared to decrease with increasing duration of annual CT follow-up.

In a series of 210 lung cancers detected by CT screening in Hitachi, Japan, published in 2012 by Nawa et al, 5-year survival was 90% (97% in stage IA patients).

The benefits of population screening are not limited to public health, but also extend to research science. Access to large numbers of small, early-stage cancers have allowed Japanese investigators to study and report on a large and rapidly growing body of data on the pathology and natural history of lung cancers, which informs clinical diagnosis, staging, and treatment. Results suggest that many adenocarcinomas arise in areas of atypical hyperplasia and progress to lepidic, in situ carcinomas that cannot be seen on CXR, but appear as nonsolid nodules or “ground glass opacities” (GGOs) on CT scans. On serial examinations, these lesions typically grow slowly, with long volume-doubling times, but in many cases “collapse” into GGOs with solid components, ie, part-solid nodules. Noguchi has described progression from noninvasive, in situ, class-A adenocarcinomas into class C–F invasive neoplasms. Radiologic-pathologic correlative series have shown that GGOs typically represent noninvasive Noguchi A adenocarcinomas with rare nodal or systemic metastasis. Development of a solid component on serial CT scans corresponds with invasion across the alveolar basement membrane (Noguchi class C), increasing risk of metastasis and reduced survival. Early results of published surgical series suggest that patients with screen-detected cancers might benefit not only from markedly improved survival, but also from less invasive, limited surgical resections that spare lung tissue and require no adjuvant chemotherapy or radiation therapy. Growing evidence from Japanese investigators also suggests that modern radiation therapy methods may replace surgical resection, at least in elderly patients or those with comorbid illnesses.

Because CT screening in Japan has not been restricted to older patients with current or prior heavy smoking histories, Japanese investigators have also observed the incidence and characteristics of lung cancer in nonsmokers. Based upon a higher than expected incidence of lung cancer, some US epidemiologists have hypothesized that lung cancer biology is different in Asian female nonsmokers. But since very few American female nonsmokers have been CT-screened, there is no real basis for such a comparison. The utility of screening in nonsmokers and younger adults is a critically important research question since more than 25,000 American nonsmokers die of lung cancer each year. These individuals are currently excluded from consideration of screening in screening guidelines.

To sum up, while US medicine insisted upon delay to obtain randomized controlled trial evidence of mortality reduction from lung cancer screening, Japan moved forward to population screening decades earlier, based on results of what is considered lower-level evidence by methodologists. Who was right? That is a question best answered by Japanese and American lung cancer patients and their families.

A caution: there are substantial gaps in this narrative, based on a literature search of English-language articles. The author's understanding of the complexities of the healthcare system in Japan is limited and insufficient to provide a comprehensive explanation of why the Japanese national policy for lung cancer screening differs so much from ours. It would be helpful if experts on Japanese national cancer screening policy would comment on this important question for Cancer Network readers.