the placement of the needle, and the lack of electrostimulation. The design and use of sham acupuncture have been debated extensively in the acupuncture literature.[2] Our sham design sought to separate the nonspecific effects (ie, patient-provider contact, relaxation during resting, and patient expectations) from the specific effects of our electroacupuncture protocol (ie, de qi sensation, stimulation of specific painful areas, and use of electrostimulation). Hay suggested that our design could lead patients to perceive acupuncture differently. We argue that if the specific quality of the sensory stimulation in electroacupuncture affected patients' perceptions during the intervention and, as a result, modulated pain and other symptom distress (fatigue, anxiety, and depression), this was actually in the causal pathway of electroacupuncture's therapeutic effect and should not be controlled away. As we reported in our primary article[3] and in this specific article,[4] both electroacupuncture and sham acupuncture were perceived as credible (4.3 vs 4.0, $P = .54$), so we do not believe that electroacupuncture was perceived as more real than sham acupuncture by the participants.

FUNDING SUPPORT

No specific funding was disclosed.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

REFERENCES

1. Mao JJ, Farrar JT, Armstrong K, Donahue A, Ngo J, Bowman MA. De qi: Chinese acupuncture patients' experiences and beliefs regarding acupuncture needling sensation–an exploratory survey. *Acupunct Med*. 2007;25:158-165.
2. Langevin HM, Hammerschlag R, Lao L, Napadow V, Schnyer RN, Sherman KJ. Controversies in acupuncture research: selection of controls and outcome measures in acupuncture clinical trials. *J Altern Complement Med*. 2006;12:943-953.
3. Mao JJ, Xie SX, Farrar JT, et al. A randomised trial of electroacupuncture for arthralgia related to aromatase inhibitor use. *Eur J Cancer*. 2014;50:267-276.
4. Mao JJ, Farrar JT, Bruner D, et al. Electroacupuncture for fatigue, sleep, and psychological distress in breast cancer patients with aromatase inhibitor–related arthralgia: a randomized trial. *Cancer*. 2014;120:3744–3751.

Jun J. Mao, MD, MSCE
Department of Family Medicine and Community Health
Center for Clinical Epidemiology and Biostatistics
Perelman School of Medicine
University of Pennsylvania
Philadelphia, Pennsylvania

DOI: 10.1002/cncr.29115, Published online January 6, 2015 in Wiley Online Library (wileyonlinelibrary.com)

Prediction of Hepatocellular Carcinoma: Using a Complex Risk Model or Assisting for Smoking Cessation?

The conclusion reached by Flemming et al in their recent article that the ADRESS (age, diabetes, race, etiology of cirrhosis, sex, and severity)-hepatocellular carcinoma (HCC) risk model is useful in the prediction of the 1-year risk of HCC among patients with cirrhosis deserves comments.[1]

First, they failed to test a simple clinical variable, smoking, despite it being considered a dose-related contributing factor to the development of HCC.[2,3] In France, tobacco, hepatitis, and alcohol are the 3 main risk factors for HCC mortality, contributing mortality rates of 33%, 31%, and 26%, respectively, to HCC.[4] In a large European cohort, the population-attributable percentage for tobacco use among patients with HCC was found to be 47.6%, which is more than twice that of hepatitis C, which is considered to be the second most attributed risk factor (20.9%).[5]

Second, none of the 6 baseline clinical variables (age, diabetes, race, etiology of cirrhosis, sex, and severity of liver dysfunction) found to be independently associated with HCC in this model is amendable.[1] Moreover, to our knowledge there is no evidence to date that screening for HCC is beneficial.[6,7]

No one should ignore that the first priority, among 10, of the World Oncology Forum in the war against cancer is tobacco.[8]

FUNDING SUPPORT

No specific funding was disclosed.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

REFERENCES

1. Flemming JA, Yang JD, Vittinghoff E, Kim WR, Terrault NA. Risk prediction of hepatocellular carcinoma in patients with cirrhosis: the ADRESS-HCC risk model. *Cancer*. 2014;120:3485-3493.
2. Lee YC, Cohet C, Yang YC, Stayner L, Hashibe M, Straif K. Meta-analysis of epidemiologic studies on cigarette smoking and liver cancer. *Int J Epidemiol*. 2009;38:1497-1511.
3. Zhu K, Moriarty C, Caplan LS, Levine RS. Cigarette smoking and primary liver cancer: a population-based case-control study in US men. *Cancer Causes Control*. 2007;18:315-321.
4. Hill C, Doyon F, Mousannif A. Evolution of Breast Cancer Mortality in France From 1950 to 2006 [in French]. invs.sante.fr/display/

?doc=publications/2009/evolution_mortalite_cancer_france_1950_2006/index.html. Accessed September 17, 2014.
5. Trichopoulos D, Bamia C, Lagiou P, et al. Hepatocellular carcinoma risk factors and disease burden in a European cohort: a nested case-control study. *J Natl Cancer Inst*. 2011;103:1686-1695.
6. Braillon A. Hepatocellular carcinoma. *Lancet*. 2012;380:469; author reply 470-471.
7. Kansagara D, Papak J, Pasha AS, et al. Screening for hepatocellular carcinoma in chronic liver disease: a systematic review. *Ann Intern Med*. 2014;161:261-269.
8. Stop cancer now! *Lancet*. 2013;381:426-427.

Alain Braillon, MD, PhD
Hepatology and Public Health
University Hospital
Amiens, France

DOI: 10.1002/cncr.29182, Published online December 2, 2014 in Wiley Online Library (wileyonlinelibrary.com)

Reply to Prediction of Hepatocellular Carcinoma: Using a Complex Risk Model or Assisting for Smoking Cessation?

We appreciate Dr. Braillon's interest in our recent article.[1]

There is no argument that tobacco use is an important public health issue around the world. As we pointed out in our introduction, data exist that support an association between tobacco use and hepatocellular carcinoma (HCC).[2,3] However, the Scientific Registry of Transplant Recipients database does not contain information regarding smoking status. Given that the study participants are listed for liver transplantation and most transplantation programs have a policy prohibiting tobacco use, it is likely that the majority of patients in our study cohort were not active tobacco users. However, we do recognize that the lack of information regarding tobacco use in the Scientific Registry of Transplant Recipients limited our ability to explore this as a risk factor for HCC in this cohort of patients with cirrhosis.

We would argue that the risk of HCC in those using tobacco may not be as high as suggested. The case-control study quoted by Dr. Braillon[4] found a population-attributable fraction of tobacco use in HCC that was higher than that of hepatitis C and hepatitis B. However, several major limitations of that study, including the inability to identify the presence of cirrhosis (the undisputed highest risk factor for HCC) or the presence of diabetes,[5] make these results questionable. In addition, the interaction between tobacco use and viral hepatitis[3] was not explored. Furthermore, a meta-analysis of more than 100 studies[6] reported an odds ratio of developing HCC of only 1.51 (95% confidence interval, 1.37-1.67) in current smokers and a nonsignificant odds ratio of 1.12 (95% confidence interval, 0.78-1.60) in former smokers, which we believe would have been the majority of the patients in our cohort.

Finally, the goal of the ADRESS-HCC risk model is to provide an educational tool for HCC risk counseling in patients with cirrhosis of diverse etiologies regardless of whether the patient and their provider have elected to participate in an HCC surveillance program. Although high-quality evidence supporting a mortality reduction with HCC surveillance is minimal, surveillance is supported by all continental liver disease societies and therefore understanding the risk of HCC in an individual patient continues to be important in the management of patients with cirrhosis.

REFERENCES

1. Flemming JA, Yang JD, Vittinghoff E, Kim WR, Terrault NA. Risk prediction of hepatocellular carcinoma in patients with cirrhosis: the ADRESS-HCC risk model. *Cancer*. 2014;120:3485-3493.
2. Yu MC, Yuan JM. Environmental factors and risk for hepatocellular carcinoma. *Gastroenterology*. 2004;127(5 suppl 1):S72-S78.
3. Bosetti C, Turati F, La Vecchia C. Hepatocellular carcinoma epidemiology. *Best Prac Res Clin Gasteroenterol*. 2014;28:753-770.
4. Trichopoulos D, Bamia C, Lagiou P, et al. Hepatocellular carcinoma risk factors and disease burden in a European cohort: a nested case-control study. *J Natl Cancer Inst*. 2011;103:1686-1695.
5. Yang WS, Va P, Bray F, et al. The role of pre-existing diabetes mellitus on hepatocellular carcinoma occurrence and prognosis: a meta-analysis of prospective cohort studies. *PLoS One*. 2011;6:e27326.
6. Lee YC, Cohet C, Yang YC, Stayner L, Hashibe M, Straif K. Meta-analysis of epidemiologic studies on cigarette smoking and liver cancer. *Int J Epidemiol*. 2009;38:1497-1511.

Jennifer A. Flemming, MD, FRCP(C), MAS
Division of Cancer Care and Epidemiology
Department of Medicine
Queen's University
Kingston, Ontario, Canada
W. Ray Kim, MD
Division of Gastroenterology and Hepatology
Stanford University
Palo Alto, California
Norah A. Terrault, MD, MPH
Department of Medicine and the Liver Center
University of California at San Francisco
San Francisco, California

DOI: 10.1002/cncr.29183, Published online December 2, 2014 in Wiley Online Library (wileyonlinelibrary.com)

US Lung Cancer Trends by Histologic Type

Racial and ethnic disparities in lung cancer incidence remain a significant health concern.[1,2] In the United States, when compared with non-Hispanic white (NHW)