



## Treatment of Hepatocellular Carcinoma in the Elderly: Slash or Burn?

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Hepatocellular carcinoma (HCC) is the sixth-most prevalent cancer in the world, rising to third when cancer-related mortality is factored in [1]. Currently, the median age of patients with HCC is 63 years; its incidence rates increase by 8% in persons with over 65 years, perhaps since aging itself is an accepted risk factor for the development of HCC [2]. Though the definition of ‘elderly’ is defined as 65 years according to the United Nations, some developed countries that have a population mean age over 70 have considered 75 as the threshold age for ‘elderly’ [3]. No matter the cut-off, patients over 65 years of age in general have poorer outcomes after open surgery and aggressive chemotherapy. Therefore, it is important to tailor treatment options for HCC in elderly patients.

According to most guidelines, first-line treatment options for HCC are surgical resection (SR), radiofrequency ablation (RFA), percutaneous ethanol injection therapy, liver transplantation, transarterial chemoembolization, transarterial radioembolization, targeted therapy, and radiotherapy [4]. SR and RFA are the most common choices for treating HCC in elderly patients according to diagnostic criteria such as Barcelona Clinic Liver Cancer (BCLC) stage, tumor size, nodules, location, and the degree of liver fibrosis [5].

RFA considered a minimally invasive technique that effectively eradicates cancer cells by high temperature, whereas SR is the conventional approach aimed at complete or partial resection of HCC-involved tissues [6]. RFA is considered to be safe and effective for tumors < 3 cm, whereas SR, which carries the usual risks of surgical procedures, is generally used for larger tumors.

The relative benefits of SR and RFA in elderly populations are not well understood. SR may have an improved survival rate in elderly patients (> 65 years) with tumors < 5 cm [7]. Another study reported that SR is effective, although RFA had good benefits in patients > 75 years [8]. Furthermore, RFA was reported to be effective elderly patients with early-stage HCC, with less major complications than SR [9].

In this issue of *Digestive Diseases and Sciences* [10], Kim et al. conducted a retrospective data review using the Korean Central Cancer Registry of the National Cancer Center, as well as death data from the National Statistical Office, identifying 9213 subjects who had registered between 2011 and 2016. Through excluding records with insufficient or conflicting data and choosing subjects  $\geq 65$  years old who had a tumor size < 3 cm, BCLC stage A, and who had undergone RFA or SR, the authors identified 366 subjects for analysis, 4% of the initial sample. The authors compared the relative efficacies of SR and RFA in HCC using the primary endpoints of overall mortality, liver-related mortality, and recurrence-free survival. By using propensity score, matching, and multivariable analysis, the study reported that the SR group had lower performance status but superior liver function. The RFA group had a higher average age (70 vs. 68 years) compared with the SR group; age > 70 years was significantly associated with increased overall mortality. Between the groups, overall mortality rates were similar (HR 1.397, 95% CI 0.940–2.076,  $P=0.097$ ) and liver-related mortality was also the same (log rank  $P=0.130$ ), although recurrence-free survival was longer in the SR group (log rank  $P=0.038$ ). In patients > 75 years old, using subgroup analysis for which matching was not possible due to the small number in the SR group, overall and liver-related mortality, and recurrence-free survival were all similar.

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Even though the patient number was relatively small, the results provided valuable insights into the relative merits of RFA and surgery in elderly patients with relatively small and early-stage HCC in a real-world East Asian setting, suggesting that in the elderly population, RFA is similar to SR in terms of overall and liver-related mortality, in particular in patients > 75 years old. Last but not least, the choice of HCC treatment options depends on the stage at diagnosis, tumor size, and liver function. Since the BCLC stage remains most useful factor used to choose treatment option in elderly patients with tumors > 3 cm and BCLC stage > A, further study will be needed to determine the optimum treatment modalities in these patients.

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