



COVID-19 and excess mortality of patients with liver cancer in France, January 2020–September 2022

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Dear Editor

Systematic reviews and meta-analyses reported a sharp reduction in cancer screening¹ and treatments^{2,3} during the 2020–2021 COVID-19 pandemic waves, but remained inconclusive for primary liver cancer (PLC). The authors hypothesized that the COVID-19 pandemic could have worsened PLC outcomes during the first three pandemic waves in France, and that PLC prognosis would have returned to previous levels with high COVID-19 vaccination uptake rates recorded after June 2021 (over 75 per cent)⁴. This study analysed the nationwide cohort of all newly recorded adult inpatients with PLC in France, between 1 January 2018 and 30 September 2022.

Patients discharged with PLC were separated into three groups according to the COVID-19 pandemic timeline and vaccination uptake in France: prepandemic phase, from 1 January 2018 to 31 December 2019; pandemic phase, from 1 January 2020 to 30 June 2021; and postpandemic phase, from 1 July 2021 to 30 September 2022. The main outcome measures were access to curative treatment (defined as liver resection, liver transplantation, and/or percutaneous ablation) and mortality. To address confounding by period and other sources of bias arising from the use of observational data, a propensity score matching analysis was also undertaken on the likelihood of being in the postpandemic phase, with use of a logistic regression model based on age, sex, PLC histology, late-stage cancer, malnutrition, decompensated cirrhosis, alcoholic liver disease, Charlson Co-morbidity Index score, and deprivation⁵.

Of 51 572 patients (median age 71 (i.q.r. 63–78) years; 74 per cent men), 37 685 (73.0 per cent) had hepatocellular carcinoma and 13 887 (27.0 per cent) intrahepatic cholangiocarcinoma. The incidence of PLC (median 907 (i.q.r. 857–946) new cases per trimester) remained stable during the pandemic waves ($P = 0.080$).

A total of 13 873 patients (27.0 per cent) had curative treatment for PLC, including surgery or liver transplantation (16.0 per cent) and/or percutaneous ablation (11.0 per cent). Otherwise, locoregional intra-arterial treatments, radiotherapy or systemic chemotherapies were given, without any curative treatment, to 25.0 per cent of patients. Finally, 15 029 patients (29.1 per cent) received palliative care without any cancer treatment and 9994 (19.0 per cent) had no specific treatment. The proportion of patients having curative treatment dropped in the pandemic and postpandemic phases ($P < 0.001$) (Fig. S1). Surgery and liver transplantation had the sharpest reduction in the postpandemic compared with the prepandemic phase (–5.0 per cent; $P < 0.001$). The proportion of patients who had locoregional intra-arterial treatments, radiotherapy or systemic chemotherapy, without any curative treatment, progressed during pandemic phase, and reached almost one-third of patients (31.0 per cent) in the postpandemic phase (+10.0 per cent). Patient and treatment characteristics are detailed in Table S1. Compared with patients treated in the prepandemic phase, and adjusted for age, sex, malnutrition, cancer stage, decompensated cirrhosis, severe co-morbidities, and deprivation index, the ORs for access to curative treatment were 0.90 (95 per cent c.i. 0.86 to 0.95; $P < 0.001$) and 0.69 (0.66 to 0.73; $P < 0.001$) for those treated in the pandemic and postpandemic phases respectively (Table S2).

Compared with the prepandemic phase, probabilities of 6-month survival were similar in the pandemic phase (60.3 (95.0 per cent c.i. 59.5 to 61.1) per cent; $P = 0.910$, log rank test) and decreased in the postpandemic phase (55.5 (54.5 to 56.5) per cent; $P < 0.001$) (Fig. 1). The corresponding adjusted HRs for death were 1.02 (95 per cent c.i. 0.99 to 1.05; $P = 0.200$) and 1.22 (1.18 to 1.26; $P < 0.001$) respectively (Table S3). The results remained stable in a 1 : 1 propensity-matched sample of 28 232

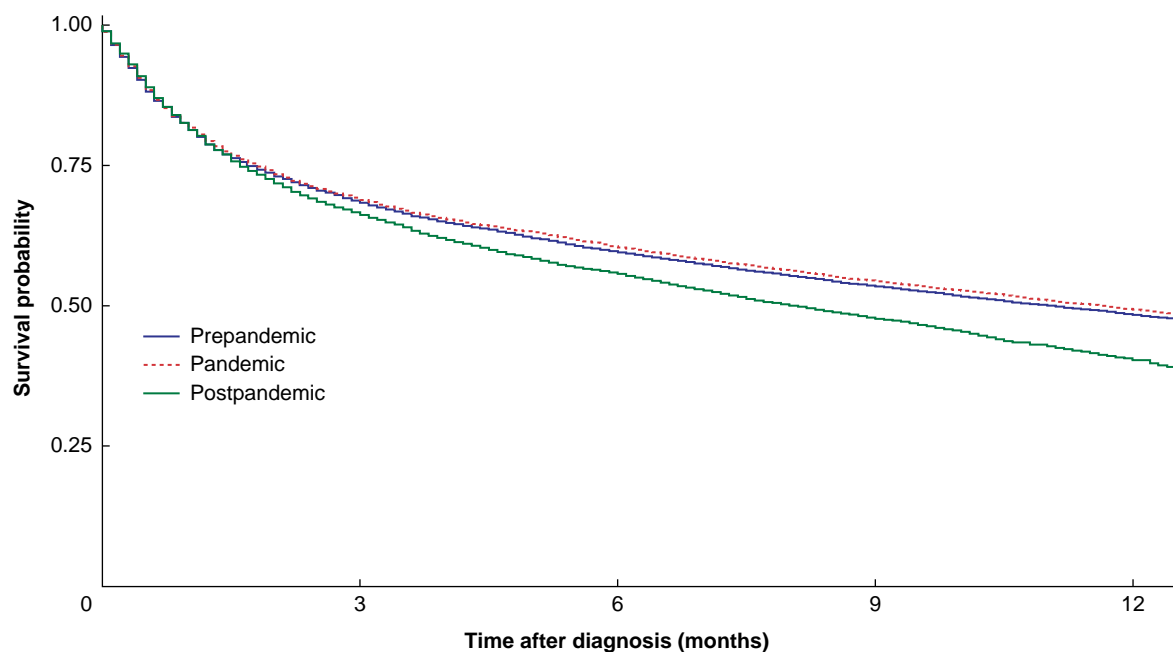


Fig. 1 Probability of 1-year survival of patients with primary liver cancer in France, 1 January 2018 to 30 September 2022

$P < 0.001$ (log rank test).

patients treated in the prepandemic and postpandemic phases (Fig. S2 and Table S4).

These results indicate that COVID-19 control measures had a detrimental impact on PLC mortality in France. The study also questions current adult PLC treatment in French hospitals. Future investigations should not only elucidate the reason for lower access to curative treatment, including liver surgery, transplantation, and percutaneous ablation in this patient group, but also how to rapidly set such access right in French hospitals.

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Author contributions

Stylianios Tzedakis (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Validation, Visualization, Writing—original draft, Writing—review & editing), Ortal Yzhaky Shapira (Conceptualization, Investigation, Visualization, Writing—original draft, Writing—review & editing), Michaël Schwarzingler (Conceptualization, Supervision, Validation, Visualization, Writing—review & editing), Sandrine Katsahian (Methodology, Resources, Supervision, Validation, Visualization, Writing—review & editing), Andrea Lazzati (Methodology, Supervision, Validation, Visualization, Writing—review & editing), Anthony Dohan (Methodology, Software, Supervision, Validation, Visualization, Writing—review & editing), Romain Coriat (CRediT contribution not specified), Philippe Sogni (Conceptualization, Formal analysis, Investigation, Methodology, Validation, Visualization,

Writing—review & editing), Stanislas Pol (Conceptualization, Methodology, Supervision, Validation, Visualization, Writing—review & editing), David Fuks (Conceptualization, Data curation, Investigation, Methodology, Resources, Supervision, Validation, Visualization, Writing—review & editing), and Vincent Mallet (Conceptualization, Formal analysis, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing—original draft, Writing—review & editing)

Supplementary material

Supplementary material is available at BJS online.

Disclosure

The authors declare no conflict of interest.

Data availability

The data that support the findings of this study are not publicly available owing to restrictions imposed by the National Commission for Computing and Liberties (Commission Nationale de l'Informatique et des Libertés).

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