

# Upfront Surgery Or Neoadjuvant Chemotherapy For Colorectal Liver Metastases? A Machine-learning Decision-tree To Identify The Best Potential Policy

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**Background :** How to select patients for neoadjuvant chemotherapy rather than upfront surgery is still controversial in case of colorectal-liver-metastases(CLM). A model to assess the best potential candidates to upfront or neoadjuvant strategies was developed by machine-learning.

**Methods :** Consecutive CLM patients at first hepatectomy were enrolled and grouped whether they had upfront surgery (UFS) or neoadjuvant therapy then surgery (NEOS). Baseline differences were weighted by Inverse-Probability-Weighting(IPW); survival analyses and risk predictions were estimated. A mortality risk model was built by Random-Forest(RF) to assess the best-potential-treatment(BPT) for each patient. A classification-and-regression-tree(CART) was developed to automatically identify the characteristics of BPT-upfront and BPT-neoadjuvant candidates.

**Results :** Between 2005 and 2019, 448 patients were enrolled: 95 UFS and 353 NEOS. Baseline differences were weighted by IPW, obtaining two balanced pseudopopulation: UFS=432 and NEOS=440. Mortality risk was not impacted by neoadjuvant therapy (HR 1.44, 95%CI: 0.95-2.17, p=0.07). A mortality prediction model was fit by RF, showing an AUROC of 75.2%. NEOS was the BPT for 245 patients, while UFS for 203. At CART, planning a R1vasc surgery was the main factor determining who were best candidates for NEOS and UFS, followed by primitive tumor localization, number of metastases, age, sex, RAS status and pre-operative CEA. In case of R1vasc, patients with CEA=>10, or those with lower CEA but being female or being male with a tumor located in the right colon, were the best candidate to UFS.

**Conclusions :** Upfront resection should be carefully reconsidered resulting the BPT in several complex conditions compared to NEOS.

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