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Cigarette smoking increases risk of early morbidity after hepatic resection in patients with hepatocellular carcinoma

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Abstract

Aims: Cigarette smoking is an important risk factor for the development of postoperative pulmonary complications after major surgical procedures. The objective of this study was to investigate whether preoperative smoking has any impact on early morbidity after liver resection for hepatocellular carcinoma (HCC).

Methods: Data of 425 consecutive patients undergoing partial hepatectomy for HCC was retrospectively reviewed. Smoking and drinking habits, biochemical tests, tumor status, operation data, and any postoperative complications occurring before discharge from the hospital were documented. The risk factors promoting postoperative complications were analyzed by univariate and multivariate methods.

Results: The overall morbidity rate was 40% (170 of 425). 166 patients were current smokers (39%). By multivariate analysis, liver cirrhosis (Risk Ratio (RR) 4.0, 95% confidence interval (CI) 2.0–8.0), smoking status (RR 3.0, 95% CI 1.7–5.1), PY of smoking (RR 1.3, 95% CI 1.1–1.9), preoperative platelet count (RR 1.6, 95% CI 1.4–2.0) and major hepatectomy (RR 1.4, 95% CI 1.1–1.8) were independent risk factors of postoperative morbidity (all $p < 0.05$). Liver failure, bile leakage, intractable ascites, chest and wound infection were more frequently occurred in smokers than non-smokers. Current smokers had higher postoperative morbidity than non- & former smokers in patients with normal liver and those with liver cirrhosis ($p = 0.047$ and $p < 0.001$, respectively).

Conclusions: Cigarette smoking is an independent risk factor for the development of liver-related and infectious complications in patients undergoing partial hepatectomy for HCC, especially in those with liver cirrhosis.

Keywords: Morbidity; Complication; Hepatectomy; Smoking; Hepatocellular carcinoma

Introduction

With advancement of surgical techniques and perioperative intensive care, in-hospital mortality after partial hepatectomy for hepatocellular carcinoma (HCC) has decreased greatly.[1–3] However, the relative high morbidity after surgery remains problematic. In HCC resection, most of the patients have chronic liver disease with liver fibrosis, cirrhosis and thus impaired liver function.[4] Few serious complications might occur after partial hepatectomy, such as liver failure, massive bleeding and biliary injury, etc., and once occurred, they might be catastrophic and expensive.

Smoking is a major health risk, and accounts for at least 20% of all deaths in developed countries.[5] Cigarette carries more than 4000 toxic substances which causes hazardous adverse effects on almost every organ in the body.[6] Its effects on cardiac, circulatory and pulmonary functions were mostly investigated perioperatively. Nicotine and carbon monoxide in common tend to create imbalance between oxygen consumption and availability, potentially resulting in hypoxemia in vital organs.[7–9] Smoking also

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impairs pulmonary function and wound healing after surgery,[5,10–12] and has been shown to increase the risk of anastomotic leakage after colorectal surgery.[13] Although hepatologists have traditionally paid scant attentions to the deleterious effects of smoking, there is increasing evidence that cigarette smoking may promote liver fibrosis, cirrhosis and favors hepatocarcinogenesis by excreting a variety of pro-inflammatory substances.[6,14–18] Our aim was to investigate whether preoperative smoking habits has any effects on postoperative complications, especially liver-related complications, in liver cancer surgeries.

Patients and methods

Patients

The pre-, intra- and postoperative data of 443 patients undergoing curative resection for HCC in our hospital was collected in a computerized database between January 2008 and May 2011. The data which were collected for each patient included age, gender, pre-existing cardiac, pulmonary or diabetic disease, smoking and alcohol habits. 12 patients with diagnosed coronary atherosclerotic heart disease and 6 with severe pulmonary dysfunction were excluded from the study, since preoperative comorbidities might retard the recovery of these patients. Finally, 425 patients were enrolled into the study. Patients were asked if they smoke regularly and, if so, at what age they started, numbers of cigarettes smoked per day (average), and how many years of smoking. Biochemical testing data was recorded before the surgery. The study was approved by the Ethic Committee of the First Affiliated Hospital of Medical College, Xi'an Jiaotong University.

Diagnosis and treatments

The diagnosis of HCC was made by computed tomography (CT) scan, ultrasonography and/or a serum alpha-fetoprotein (AFP) level greater than 20 ng/ml preoperatively, and confirmed by pathological examination postoperatively. Resection criteria were constant over the study period. Hepatic resection was the treatment of patients with HCC when available based on the general condition, tumor status, preoperative liver function, as well as the future remnant liver parenchymal. Curative resection was defined as complete excision of the tumor with tumor-free surgical margins. All resected tumors were examined pathologically for the degree of differentiation of HCC, vascular invasion, surgical margin, tumor number and maximum size.

Measurement of exposure to tobacco and alcohol

Smoking data included pack-years smoked (PY) [[the average number of packages of cigarettes smoked per day multiplied by the number of years smoked]. Tobacco exposure was characterized as none (<100 cigarettes during their lifetime), <20 pack-years or ≧20 pack-years.[19,20] A regular smoker was defined as one who smokes at least 1 cigarette per day for over 1 year and a current smoker as one who smokes within 1 year of the date of surgery.[21] The patients were divided into current smokers and non-smokers who had either never smoke or had stopped for at least 1 year. Alcohol drinking/abuse was defined as alcohol consumption of at least 50 g (1 tael) per day for at least 1 year.[22]

Postoperative morbidity

Postoperative morbidity was defined as any complications occurred during the hospital stay after surgery. The complications included liver failure, bleeding, biliary complications, sepsis of any organ/space surgical-site, pulmonary, cardiac and wound complications, etc. Pleural effusion and ascites included as morbidity were defined as that requiring diuretics or paracentesis. Bile leakage was defined according to the International Study Group of Liver Surgery as bilirubin concentration in the drain fluid at least 3 times the serum bilirubin concentration or macroscopic bile from surgical drains on or after postoperative day 3 or as the need for radiologic or operative intervention resulting from biliary collections or bile peritonitis.[23,24] The definition of any organ/space surgical-site infection was based on postoperative findings of purulent drainage from a drain without macroscopic bile discharge or confirmed by reoperation or ultrasonography-guided drainage.[23] The severity of complications was classified according to Dindo-Clavien score.[25]

Statistical analysis

Data were expressed as mean ± standard error (S.D.) or median and ranges for numerical variables or percentages for nominal variables. Mann–Whitney U test or *t* tests were used to compare numerical variables, and the Chi–Square test or Fisher's exact test was carried out to compare nominal variables between the groups. Those variables with a *p* value less than 0.05 by univariate analysis were enrolled into further multivariate analysis. Multivariate analysis was performed with forward stepwise logistic regression. Statistical analysis was carried out using SPSS 17.0. $p < 0.05$ was considered statistically significant.

Results

Patient characteristics

Baseline characteristics of the study population were summarized in Table 1. Liver cirrhosis was present in 73% of the patients due to high HBV infection rate (78%). Smoking habits were present in 166 patients (39%) at surgery, with an average of 17 cigarettes smoked