

Another interesting subject is the one related to the impact of the number of harvested lymph nodes on the overall survival in patients with central cholangiocarcinoma. According to Gugliemi's study, the median overall survival seems to be significantly influenced by this parameter (14). Therefore, in the study conducted by this author on a group of 62 patients submitted to surgery with curative intent for hilar cholangiocarcinomas, cases in which more than three lymph nodes were harvested reported a significantly improved overall survival when compared to those in which 1 to 3 nodes had been harvested or to those in which lymph node dissection was not performed ($p < 0.01$). Moreover, the authors demonstrated that the overall survival was not influenced by the station in which metastatic disease had been found (N1 versus N2 versus N3, $p = 0.66$). In multivariate analysis the authors demonstrated that the radicality of resection as well as the lymph node ratio were the only significant prognostic factors for the long term outcomes (14).

In order to offer a better chance to receive a tailored treatment after resection and to improve the long term outcomes of these patients, the Chinese authors created a formula in which they introduced the number of lymph node metastases, the serum levels of CEA and the surgical margins, these three parameters being the most significant ones in multivariate analysis for survival (15). These parameters were quoted with 1 point if the resection margin was positive, if the lymph nodes presented metastases and if the serum level of CEA was higher than 15 ng/ml, and 2 points if the resection margin was negative, if the lymph nodes did not present metastatic disease and if the serum levels were lower than 15 ng/ml. According to the value of this score, the 169 cases introduced in this study were classified in three categories – high risk, middle risk and low risk, the three categories reporting a significant difference in terms of survival (15).

Another aspect which was intensively studied in patients with hilar cholangiocarcinomas is related to the influence of lymph node micrometastases on the overall survival. In the study conducted by Taniguchi *et al.* and published in 2006 (16) the authors included 28 patients submitted to surgery for hilar cholangiocarcinomas in whom the histopathological studies demonstrated the absence of lymph node metastases; totally, the authors harvested 423 regional lymph nodes which were immunostained with antibodies against cytokeratins 8 and 18. After performing this method the authors reported the presence of micrometastatic deposits in 11 of the 28 patients (corresponding to 14 of the 423 harvested lymph nodes). In univariate analysis the presence of micrometastatic disease was significantly correlated to the tumoral stage at diagnostic, with the histopathological degree of differentiation, as well as with the presence of venous invasion; moreover, micrometastatic disease significantly affected the overall survival rate; therefore the five year overall survival rate was 21.8% in cases with micrometastatic disease and 66.5% in cases with no micrometastatic deposits ($p = 0.02$). Therefore, the authors concluded that immunohistochemical studies should be routinely performed among patients with negative nodes in order to identify the subset of cases presenting micrometastatic lesions (16).

CONCLUSIONS

Hilar cholangiocarcinomas remain an aggressive subtype of digestive malignancies associated with poor rates of survival in the absence of radical surgical treatment. In order to improve the outcomes of these patients and to provide an adequate staging of the tumoral process, regional lymph node dissection is mandatory. Moreover, certain authors proposed stratifying the cases after calculating a risk score which might further assure a tailored treatment.

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