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A predictive model of metachronous colorectal cancer occurrence in Lynch syndrome

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Background

Lynch Syndrome (LS) correlated colorectal carcinoma (CRC) patients show a tendency towards the development of multiple and metachronous lesions and, for this reason, a surgical prophylactic treatment, as total colectomy, is warranted. Considering the quality of life of patients treated with total colectomy, it is essential to determine risk factors of metachronous CRC. Aim of the study was to evaluate through a predictive model the patients that could really benefit from a surgical prevention.

Methods

We considered LS or suspected LS CRC patients enrolled by our Institutional Register of Hereditary Colorectal Tumors and submitted to a surgical resection of CRC, excluding those who had a total colectomy. Patients were characterized according to their genotype (MLH I, MSH2 and MSH6), sex and clinical features (age at diagnosis, tumour site, stage, grading, presence of colorectal adenomas and of extracolonic cancers) and were stratified in 4 mutually exclusive groups according to family characteristics: A) MMR gene mutation positive; B) Amsterdam criteria (ACI-II) positive, but mutation negative; C) AC-like and D) high risk. In order to identify a model for predicting metachronous CRC occurrence, for each patients' group a stepwise unconditional logistic regression model was fitted. All the regression equation included terms for gender, age in continuous as blocked terms. The predictive accuracy was assessed using the area under the receiver operating characteristics curve (AUC).

Results

A total of 1,604 CRC patients (M/F=1.02, 16.5% <40 yrs old) were considered (600 in group A, 117 B, 530 C and 357 D). During the follow-up, 181 developed metachronous CRC (11 %) and 354 (22%) an extracolonic cancer. The risks of metachronous CRC at 10 years were 21%, 16%, 16%, and 14% for group A, B, C and D, respectively. The predictive variables in the final model comprised for each group were: A) MLHI mutation, the presence of colorectal adenomas and then occurrence of extracolonic cancers, B) occurrence of extracolonic cancers, C) high tumor grade and presence of colorectal adenomas. No significant predictors were identified for group D. AUC values, as a measure of discrimination of the various models, were 0.72, 0.78 and 0.76 for group A, B and C, respectively.

Conclusions

Metachronous CRC is a long-term moderate risk in LS patients. This suggests to recommend a prophylactic colectomy only to selected patients with well defined characteristics.

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