Preliminary Short Communication

Prognostic Nomogram for Colorectal Cancer after Radical Resection in Japanese population

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INTRODUCTION

Nomogram is a clinically useful tool to predict prognosis of the patients or other clinical event for individuals, and has been widely applied in the field of medical oncology¹⁾. In previous reports, some nomograms that predict survival or recurrence rate of colorectal cancer have been established²⁻⁷⁾. However, to date, most nomograms of colorectal cancers have been developed by using clinical data from the western patients and only from small sample size study from East Asia. In addition, the external validations of the results have not been satisfactory implemented in these studies⁸⁾.

In this regard, we conducted a study to establish a more precise nomogram that would be able to predict long term outcomes in patients who have undergone curative resection with lymph node dissection for colorectal cancer. We obtained the development data from prospective randomized clinical trials, and validation of the obtained results was performed by using data from the Cancer Institute Hospital in Japan. The nomogram developed in this study would be the first in East-Asian population with the largest sample size in all other previous tools. It would also provide surgeons with a lot of benefit in their practice. In this preliminary report, we show the study design and the method to establish statistical pre-

dictive model to prevent publication bias.

PROTOCOL DIGEST OF THE STUDY

Purpose

Our goal was to develop the prognostic nomograms for predicting long-term survival in Japanese patients who underwent curative resection for colorectal cancer.

Patients

We prepared two independent datasets in this study; one is the development data and the other is validation data. A total of 5530 individual patients' data were pooled as the development data from three phase 3 trials of Japanese Foundation for Multidisciplinary Treatment of Cancer (JFMC) studies (JFMC 7, JFMC 15, and JFMC 33) and a total of 2346 individual patients' data were obtained for external validation of established nomogram from Cancer Institute Hospital of Japanese Foundation Cancer Research. The results of each clinical trial had already been reported in peer review journals⁹⁻¹¹⁾. Briefly, JFMC 7 and JFMC 15 trials were performed to evaluate the long-term utilization of oral fluorinated pyrimidines as adjuvant chemotherapy for patients with colorectal cancer, comparing the overall survival with the surgery alone arm. JFMC 33 evaluated survival benefit of receiving tegafur (UFT, 300 mg/m²/day as tegafur)/leucovorin (LV, 75 mg/day) for 5 consecutive days per week for 18 months compared with the standard tegafur regimen.

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Data Collection and Variables

In order to develop prediction model, all clinically important information was extracted from case-report forms of the targeted clinical trial or from the hospital medical records. Specifically, patients' age, gender, primary site, tumor size, TNM stage and distance of margin on resected specimen, surgical procedure, degree of lymph node dissection, residual tumor, histological findings, postoperative complication and adjuvant chemotherapy. Furthermore, survival time, timing of recurrence and site were investigated as outcomes.

This study was approved by the Institutional Review Board of the Cancer Institute Hospital and the Japanese Foundation for Multidisciplinary Treatment of Cancer.

Statistical analyses and the model development

All datasets have been already finalized and analyses have been completed. Detailed results of overview of this integrated data will be published elsewhere after scrutinized examination and model based analysis of all the retrieved results.

The prediction models for OS and DFS were developed using Cox regression model. When the type of relapse was analyzed as an outcome, we used the logistic regression model. Backward selection approach with Akaike's Information Criterion was adopted for the variable selection of each prediction model. Main effects and interaction terms for each possible variable were considered as a candidate for the selection. Candidate variables were ranked according to their frequency of selection in the bootstrap samples. If variables were selected in >60% of bootstrap sample, we included them as a final set of predictors in the model.

Internal and External Validation

Performance of each prediction model was evaluated based on the discrimination and calibration measure. For the discrimination, we used Chambless and Diao's c-statistic¹²⁾ for the survival model and c-statistic for the logistic model. Calibration plot and its slope were also studied. Internal validation was conducted using bootstrap and we calculated optimism-corrected performance for each performance measure. As an external validation, the constructed prediction model was applied to the clinical data of the Cancer Institute Hospital and the Japanese Foundation for Multidisciplinary Treatment of Cancer. After the validation, the model updating may be considered.

We followed TRIPOD guideline¹³⁾ for developing and reporting the prediction model.

Completion of nomogram based on pooled data, and progress of the study

Data collection, integration of data from the three clinical trials (JFMC 7, 15 and 33), development of no-

mogram, and internal validation of the nomogram have already been completed. Currently, clinical data from the Cancer Institute Hospital have been collected and fixed. Thereafter, external validation of the nomogram will be conducted. All final results will be published elsewhere through an intense discussion with all the contributors.

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Conflict of interest statement

None declared.

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