

Validation of onco-assist survival prediction tool in stage I, II and III colon cancer among Asian patients

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ABSTRACT

Clinical calculators and predictors are now commonly used in clinical practice to predict most accurate clinical outcome and provide guidance for appropriate therapy. One of the most commonly used calculator is onco-assist. This study was conducted to compare onco-assist prediction of the patients diagnosed with colon cancer Stage I, II and III. Data was retrospectively collected from 88 patients of colon cancer diagnosed over the period of 11 years (2008 to 2018) and registered at Nuclear Institute of medicine and radiotherapy (NIMRA), Hospital, Jamshoro Sindh. These patients received primary surgical therapy without any neo-adjuvant systemic chemotherapy. Survival assessed on onco-assist prediction algorithm using the defined parameters and compared with the actual survival according to the grade of the tumour. The clinical calculator onco-assist incorporated seven variables: gender, age number of lymph nodes examined, number of tumor-involved lymph nodes, T = (1-4), grade (low / high), adjuvant chemo received (yes / no) if yes then only 5FU or 5FU plus Oxaliplatin based. Onco-assist predicted five-year survival rate in well differentiated tumours with and without chemotherapy as 84% and 80% respectively, in moderately differentiated tumour with and without chemotherapy as 78% and 76% respectively. For poorly differentiated tumours the predicted survival rate with and without chemotherapy was 73%. While actual achieved survival was 35%, 52% and 17% for well, moderately and poorly differentiated cancers. This clinical calculator onco-assist includes limited parameters and limited adjuvant therapy options thus the prediction of cancer survival following surgery in stage I –III colon cancer does not appear to accurately predict outcome in Asian population.

Key Words: colon cancer; Onco-assist, survival calculator, adjuvant chemotherapy.

INTRODUCTION

Colorectal cancer (CRC) is one of the leading cancer throughout the world both in developed and developing countries. The primary curative treatment is surgical resection of the tumor followed by adjuvant therapy. The American Joint Committee on Cancer (AJCC), has endorsed clinical calculators and nomograms for providing the most tailored treatment plan along with precise estimate of clinical outcome of cancer patients. Using the clinico-pathological parameters, these nomograms predict chance of recurrence after surgery for operable colon cancer (ie Stage I, II and III).(1) Commonly used tools for survival prediction usually predict outcome of patients for five years relatively more accurately in patients of colon cancer after diagnosis and primary treatment.(2) The exact prediction of

survival is a difficult undertaking for oncology team and also a prime concern of the patient and the family.(2-3). Onco-assist is one of the prediction tools which provide survival rates for colon cancer, based upon biological markers and adjuvant treatment.

The prediction of the risk recurrence in colon cancer is generally based upon the observations made according to the clinic-pathological factors and patients factors including performance status, weight loss and tumor grade while in recurrent and metastatic cases the anatomic sites of metastases and overall health status of the patient provide useful information which can help in prediction of clinical outcome including disease specific and overall survival(4).

Early operable cases undergoing complete resection of stage I or II disease, the characteristics of a primary colon cancer, such as initial stage of tumor, and histological grade can provide valuable information regarding the clinical behavior of malignant tumor (5). Not only tumour biological markers and patient characteristics but also genetic signature of the cancers can help in prediction of the recurrence and general clinical outcome. These prognostic factors provide precise guide for management and therapy(6). However, in any case a single factor cannot predict clinical outcome neither guide treatment.

The prediction after primary surgery is a difficult task. Combination of tumour and treatment factors can potentially predict it. There is data available suggesting usefulness of onco-assist in colorectal cancer. However, there is limited literature available on validating its usefulness in Pakistani population. Thus this study was conducted based on a retrospective review of the clinical data.

METHODOLOGY

This was a retrospective observational study conducted at Nuclear Institute of medicine and radiotherapy (NIMRA), Jamshoro, Pakistan. Data was retrospectively collected from case files. Complete information of the variables for Onco-assist including age, gender, grade, T (ie tumor size), N (ie number lymph nodes examined and number of lymph nodes positive) and adjuvant chemotherapy (only 5FU/ 5FU plus Oxaliplatin) was available for 88 patients of colon cancer stage 1, II and III. These patients were registered and underwent treatment from 2008 till 2018. These patients received primary surgical therapy without any neo-adjuvant systemic chemotherapy. After their diagnosis, they received treatment as per hospital policy. Then the survival assessed on onco-assist prediction algorithm for colon cancer on the defined parameters and the actual survival compared to onco-assist predicted survival, according to the histological grade of the tumour. Patients of stage IV colon and recto-sigmoid tumors were excluded.

Data was collected and analyzed by using SPSS version 19.0. 5-year Median survival was calculated by using Kaplan Meier Method and compared with the median predicted survival.

RESULTS

The clinical calculator onco-assist incorporated seven variables including gender, age number of lymph nodes examined, number of tumor-involved lymph nodes, T = (1-4), grade (low / high), adjuvant chemo received (yes / no) if yes then only 5FU or 5FU plus Oxaliplatin based. Onco-assist predicted five-year survival rate according to grades, where well differentiated without having adjuvant chemotherapy was 80% and with chemotherapy was 84%, while moderately differentiated tumours

if without receiving chemotherapy predicted to have 76% 5-year survival and if receiving chemotherapy, it was 78%. Poorly differentiated tumours on the other hand predicted to have 73% 5-year survival regardless of adjuvant chemotherapy.

However actual 5- year survival rate in well-differentiated (n = 27) tumours was 30.7%, moderately differentiated (n =46) was 52.3% and for poorly differentiated (n =15) was 17%. A summary of the comparison is given in Figure 1.

Limitations of Onco-assist clinical calculator:

- The 5 year estimate of colon cancer specific survival without adjuvant chemotherapy calculated by using data derived from End Results (SEER) registry between 1988 and 1997 for Surveillance, Epidemiology(7). Thus for the patients from the 1990s causing a stage shift in the modern days due to newer imaging modalities.
- A number of factors considering the risks and benefits of adjuvant chemotherapy in colon cancer patients(8) according to ESMO and NCCN guidelines not considered i.e. lymph-vascular invasion, peri-neural invasion, perforation, obstruction, co-morbidities and surgical margin status all of which can influence the likelihood of recurrence were not included in the algorithm for prediction of survival outcome.
- The calculator only colon cancer not considering rectum, however majority of patients with sigmoid colon also involve rectum this sigmoid colon had to be excluded.

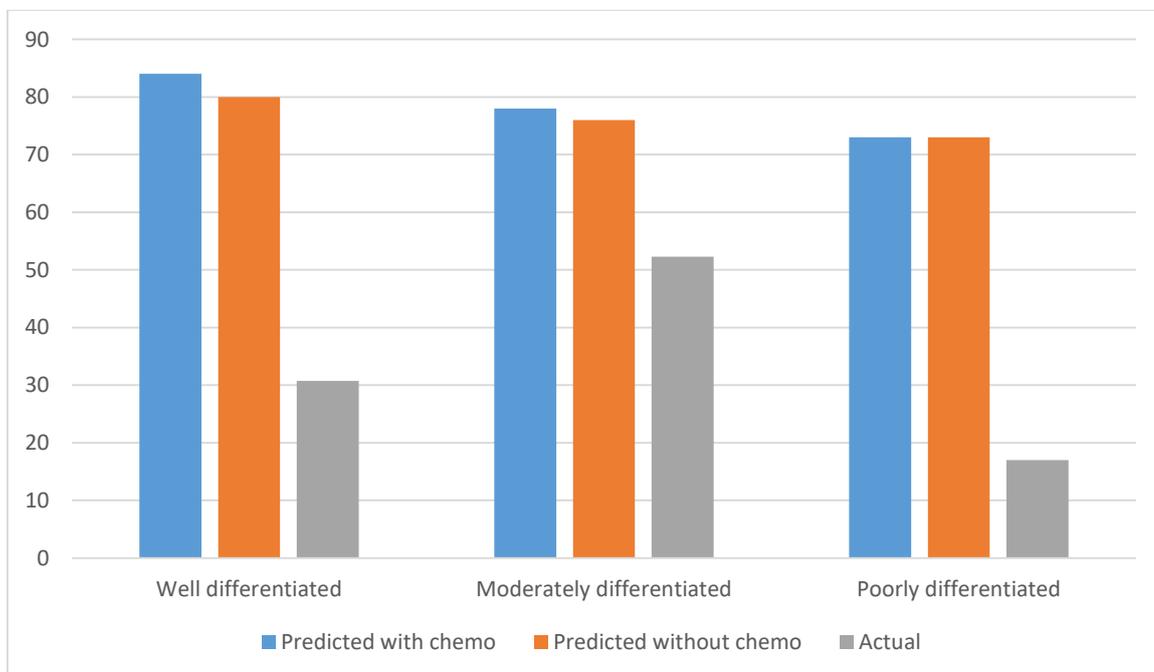


Figure 1. Onco-assist prediction of 5-year survival (%) in patients with colon cancer in Pakistani population versus actual observed 5-year survival rate (%).

DISCUSSION

Survival outcome of CRC has steadily improved from 1978 to 1999, this may be due to provision of modern surgical techniques and, the availability of modern chemotherapeutic drugs such as irinotecan and oxaliplatin for treatment of recurrent colon cancer in the most recent era.(4) The other factors such as improved screening facilities and diagnostic modalities including genomic testing has played important role.(9) In clinical practice role of adjuvant management is highly dependent on lymph node involvement age, gender, tumor size and grade of tumor. In addition, other high risk features including lymph vascular invasion, peri-neural invasion, perforation, obstruction, co-morbidities, tumor adherence and depth of invasion affect the decision of clinicians to treat patients with colon cancer and also remains a highly debated issue.(8)

Onco-assist is a well reputed and widely used online algorithm in breast cancer and validated by many studies(11). However, there is limited literature available validating it in colon cancer, which is a commonly found cancer globally. There is another tool with the title of Oncology Pro, which was derived from seven randomized controlled trials to predict survival outcome in patients receiving fluorouracil. The pooled analysis included 3302 patients. The review concluded that lymph node status, size of the tumour and the histological grades are the independent predictors of survival both disease specific and overall(5). However, there was no comparison was made with other tools. Colorectal cancer generally shows poor survival in developing countries due to late diagnosis and also possible aggressive tumour biology. Thus it is utmost important to develop such tools and validate them in populations independently so that the racial differences in clinical behavior of cancers can be addressed.

In our study onco-assist over-estimated survival while the actual achieved outcome was much less as compared to the predicted. This probably indicates that Asian population having aggressive tumor biology because in spite of getting standard treatment the overall survival is significantly different from onco-assist predicted. Secondly this calculator incorporates seven variables needs to be revised with inclusion of more sophisticated predictors and more specific variables in onco-assist in order to make it useful for Asian population. It is also recommended that emerging biomarkers need to be incorporated and validated for acceptance in the oncologic community.

CONCLUSION

This clinical calculator onco-assist for predicting cancer survival following surgery in stage I –III colon cancer is entirely different in case of Asian population. Larger studies with inclusion of more biomarkers are required to be conducted and also other algorithms need to be validated and compared in order to design a well fit model which can accurately predict clinical outcome in Asian population.

Ethical Consideration: The study was approved by the Local Research Ethical committee

Conflict of Interest: There is no conflict of interest.

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