

Student: Tom Moore

Title: Prognostication in hepatic resection for colorectal metastases in Christchurch, New Zealand

Supervisor(s): Dr Dean Harris

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Introduction:

Colorectal cancer is the second highest cause of cancer related death in New Zealand, and along with Australia we have the highest rate of bowel cancer death in the developed world. Each year 43 in every 100,000 New Zealanders are diagnosed with colon cancer. The liver represents the most frequent site of metastatic spread with 25% of patients having evidence of spread to the liver at the time of presentation, with a further 40-50% of patients developing liver metastases after resection of the primary tumour.

The 5-year survival rate for all patients diagnosed with a colorectal cancer is estimated at 65%, dropping to 11% if distant metastases are present. Only about 10-20% of patients with metastatic spread to the liver have disease that is amenable to resection. For these patients surgical resection with curative intent is the treatment of choice and improves 5-year survival rates in the range of 38-58%.

There are many prognostic scores in use worldwide that look to predict survival after liver resection, and not only are they important from a patient point of view, but they also allow clinicians to stratify patients into risk categories, which aids in deciding the best management plan for each patient. This is particularly useful because they can help to predict which patients are most likely to benefit from liver resection of colorectal cancer metastases.

Aims:

The aims of this research were to:

1. Audit the outcomes of all patients with colorectal cancer who had liver metastases resected at Christchurch Hospital from 2005-2014.
2. Evaluate the Fong, Nordlinger, Basingstoke, and Memorial Sloan-Kettering Cancer Center (MSKCC) Nomogram prognostic tools to stratify patient's outcomes after resection of liver metastases in our population.

By validating the scores in our population we hope that they can then be used to guide patient management and provide insight into which patients are most likely to benefit from resection of their liver metastases.

Methods:

Patients were identified from a prospectively collected database from the Department of Surgery, who underwent resection for radiological evidence of liver metastases from colorectal cancer at Christchurch Hospital from 2005-2014. Patient notes were reviewed for additional data including, age at operation, pre and post-operative blood results, blood tumour marker (CEA), stage and differentiation of the primary bowel tumour, size and number of liver metastases, time interval from primary resection to liver resection and use of chemotherapy within 8 weeks either side of hepatic resection as well as the chemotherapy used. The Fong, Nordlinger and Basingstoke prognostic scores were calculated and the MSKCC nomogram was used to calculate survival probabilities.

The date of death was identified from records and the time of last contact was identified from the date of last clinical letter to permit assessment of overall survival with a Kaplan-Meier survival analysis. The date of recurrence was taken as that of the radiological study first identifying new lesions. Cancer specific survival was not able to be assessed due to the time constraints of the project precluded analysis of death certificates for cause of death.

The data was analysed by a statistician for overall survival and disease free survival as well as outcomes for each stratification of the respective prognostic scores.

Results:

132 patients underwent liver resection for colorectal metastases between 2005 and 2014. The overall survival in our population was measured from the date of liver resection. The 2-year survival was 87.4% and the overall 5-year survival was 53.8%. These results place our patient population at the upper end of overall survival range compared to recent studies.

The Fong Score places patients into one of six categories based on prognosis. Our population compares favorably with the Fong Score original outcomes. For example, in risk category four, the second worst prognostic category and the poorest category any patient in our population made it into, predicts 3 and 5-year overall survival at 38% and 25 % respectively with our population showing survival rates at 63% and 24% respectively. The trend in the Fong Score is consistent with our population, however the statistical assessment suggested no clear difference between the scores.

The Nordlinger Score provided similar results to that of the Fong Score, with each patient placed into a low, intermediate or high-risk category. The Nordlinger score predicts overall 2-year survival for low, intermediate and high risk groups at 79, 60 and 43% respectively. For each of those categories the overall 2-year survival in our population was, 91, 91 and 72% respectively.

The Basingstoke score does however separate our population into 3 statistically significant groups with the intermediate and high risk groups having median survivals of 6 and 3.5 years respectively with the median survival not yet reached at 6 years follow up for the low risk group.

Conclusion:

Several prognostic models have been developed to predict survival or recurrence in after liver resection in the setting of colorectal cancer metastases. We successfully applied 4 approaches and validated them in our patient population. The outcomes from the population exceeded our expectations and place our unit's outcomes at the upper end of the published literature with regard to colon cancer free survival and the chances of being alive 5 years on from a diagnosis of advanced liver metastatic colorectal cancer.

We identified that the Fong score was able to separate our population but the differences did not reach significance, though this may relate to the small numbers of patients included in the study and the very small numbers in some of the categories. The Nordlinger score however was able to separate with statistical significance those with low and intermediate score and those with a high risk of recurrence. Those in the high-risk group had a median survival of 2.5 years as opposed to 6 years in the intermediate group. The Basingstoke prognostic index did separate 3 clear groups with widely disparate survival. This has successfully validated and identified the score most clinically useful for our population for preoperative assessment of prognosis. This will enable us to identify a number of patients who may not have minimal benefit from liver resection, avoiding them having unnecessary surgery, those likely to have a very good outcome and a group who may benefit from additional treatment such as chemotherapy or more advanced staging.

In the future we hope to assess our data for additional simpler prognostic scores such as the neutrophil/lymphocyte ratio to see if this will add further insight to outcome. The data will also allow clinical outcomes in detail to be linked with a current translational project assessing the use of cell free tumour DNA in the blood stream (liquid biopsy). We hope this will further enhance the very high outcomes from liver resection that Christchurch has.