A comparison of surgery alone versus surgery plus adjuvant chemotherapy in stage III colon cancer: Utilisation of tissue microarrays to elucidate BRAF and dMMR status in understanding real-world patient cohorts and outcomes

Shehara Mendis[1,2]*, **Christine Georges**[2,3]*, David Nickless[4], David Cheng[4], Javier Washington Queiros[4], Tanja Dimitrijevska[4], Mohammad Asghari-Jafarabadi[3,5], Raymond Yap[3], Paul McMurrick[3]

1. Oncology Research Department, Cabrini Health, Malvern 2. Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton 3. Cabrini Monash University Department of Surgery, Cabrini Health, Malvern 4. Cabrini Health, Malvern 5. School of Public Health and Preventive Medicine, Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton

*Joint first author

Background

Stage III colon cancer treated with oncologic resection alone has a cure rate of 50%.[1] The addition of adjuvant chemotherapy improves this cure rate to 70%. Despite the established role of adjuvant chemotherapy for stage III colon cancer, a significant proportion of patients do not receive adjuvant chemotherapy, as demonstrated in our preliminary study. For these patients, testing of mismatch repair (MMR) status was historically not standardised, and BRAF testing is still not currently standard of care.

Aim

This project aims to elucidate the significance of BRAF and dMMR status in stage III colon cancers patients that receive surgery alone (SA) versus surgery plus adjuvant chemotherapy (S+C).

Method

A retrospective analysis of prospectively collected data was carried out on patients undergoing surgery for Stage III colon cancer between 2010 and 2019 at Cabrini. Matched tissue microarrays (TMAs) were utilised to assess tumour MMR status and BRAF (V600E) mutation status via standard immunohistochemistry within SA and S+C groups.

Results

Only 53% and 16% of patients had MMR status or BRAF status, respectively, available on their original histopathology report. Combining histopathology reporting and TMA analyses increased this yield to 80% for MMR status and 91% for BRAF status.

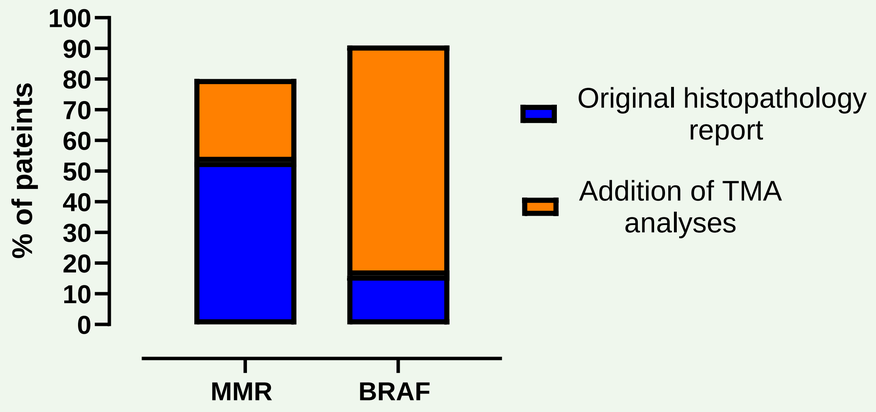

Figure 1. Percentage of patients with MMR and BRAF testing on original histopathology reports and with the addition of TMA analyses.

We found 33% SA patients and 12% S+C patients had dMMR (RR 2.78, 95% CI 1.79 to 4.30, p<0.001). In patients with proficient MMR (pMMR), SA patients had worse recurrence free survival (RFS) compared to S+C (HR 2.34, 95% CI 1.22-4.47, p=0.009), with no difference in RFS for dMMR patients between SA and S+C. When stratified by BRAF mutation status (BRAF mutant: 34% SA, 23% S+C), SA patients had inferior RFS compared to S+C patients regardless of BRAF status.

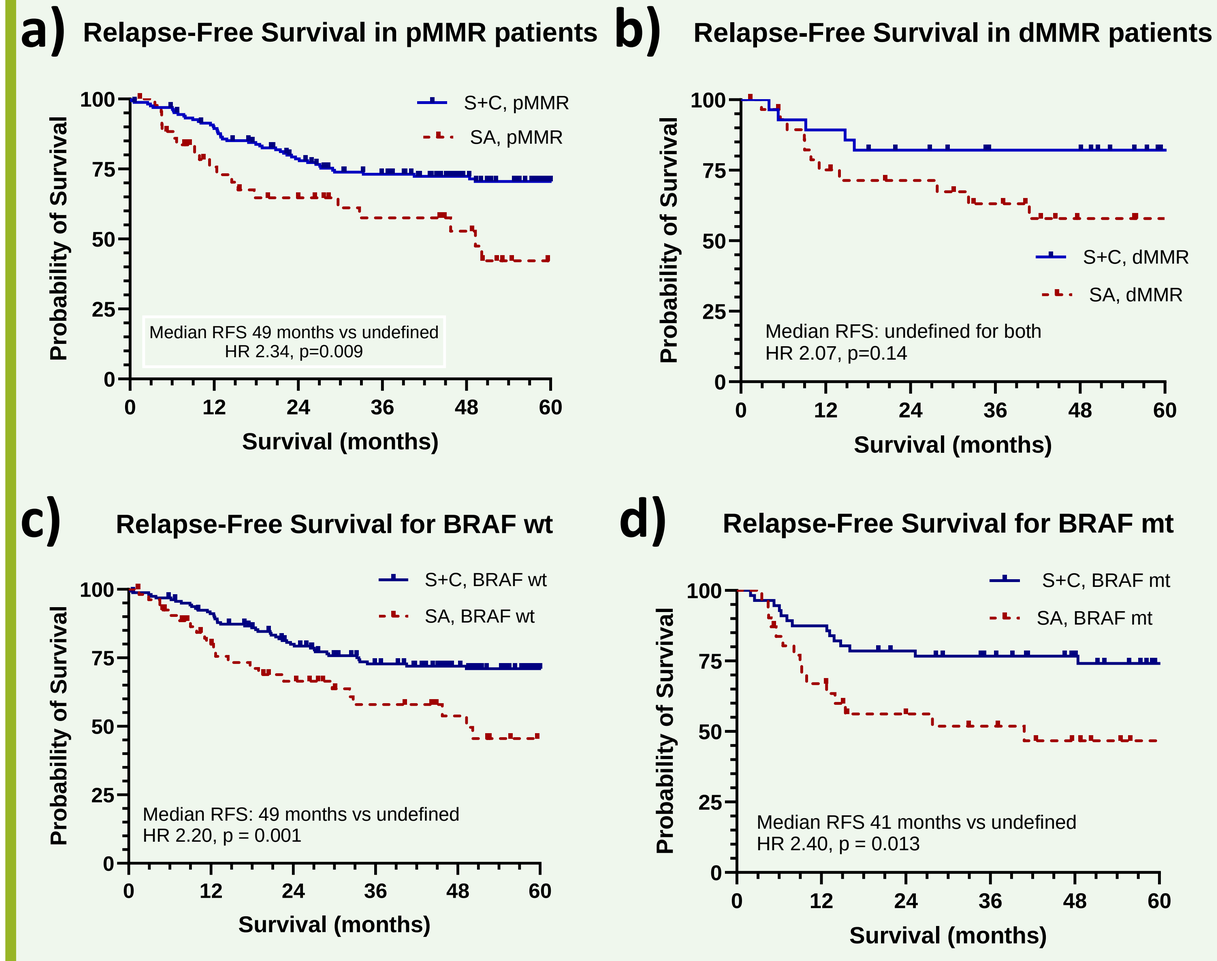

Figure 2. RFS in patients with pMMR a), dMMR b), BRAF wt c) and BRAF mt d), stratified into either S+C or SA.

Conclusion

Through utilisation of TMAs, we demonstrated clear detriment of lack of adjuvant chemotherapy in pMMR patients as compared to dMMR patients. TMAs are a useful tool for improving histopathologic characterisation of archival samples and demonstrating high frequency of BRAF mutations in a stage III colon cancer population.

References

Taieb J, *et al*. Refining adjuvant therapy for non-metastatic colon cancer, new standards and perspectives. Cancer treatment reviews. 2019;75:1-11.

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