Colorectal Cancer (CRC) in Patients from Rural Maine: Correlation of Molecular Profiles with Clinical Outcome.

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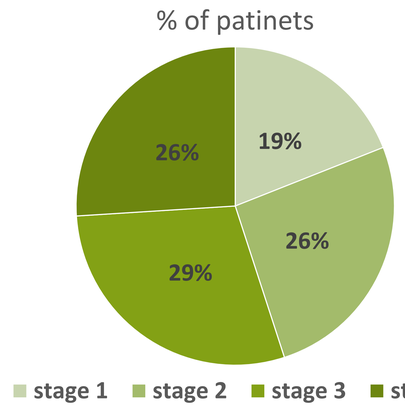
Abstract

The National Comprehensive Cancer Network (NCCN) recommends molecular testing for *BRAF*, *KRAS*, *NRAS* gene mutations and microsatellite instability (MSI) in CRC. In this study, mutational findings were correlated with clinical outcome in CRC patients from rural Maine. Mutational profiles of 192 CRC patients diagnosed in 2017 and 2018 were analyzed by next-generation sequencing (NGS). Mutational analysis included *BRAF* (exon 15) and RAS family biomarkers (*KRAS*/*NRAS* exons 2-4). MSI testing was performed using the MSI Analysis System. SPSS was used to perform Chi-square and Kaplan-Meier (log rank) survival analysis.

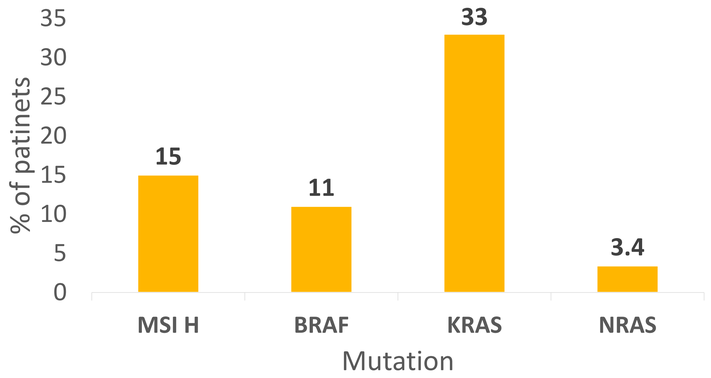
Median age at diagnosis was 66 years (range 28-100), with 57% men. Stage III disease was most frequently encountered (29%). MSI and *BRAF* mutation were seen in 15% and 11% of cases, respectively, with the majority being right sided. MSI-H tumors tended to be lower, stage I cancers. The majority (66%) of *BRAF* mutated tumors were also MSI-H. Approximately a third of tumors were *KRAS* mutated and less commonly associated with a poorly differentiated pathology. *NRAS* mutation was least common (3.4%) and associated with adverse outcome in stage 3 CRC patients. Median follow-up was 16 months, with 80% overall survival. Survival for low stages (1-2) was 100%, for stages 3 and 4 89% and 34%, respectively, with stage being a significant determinant of survival (p<0.001).

Introduction



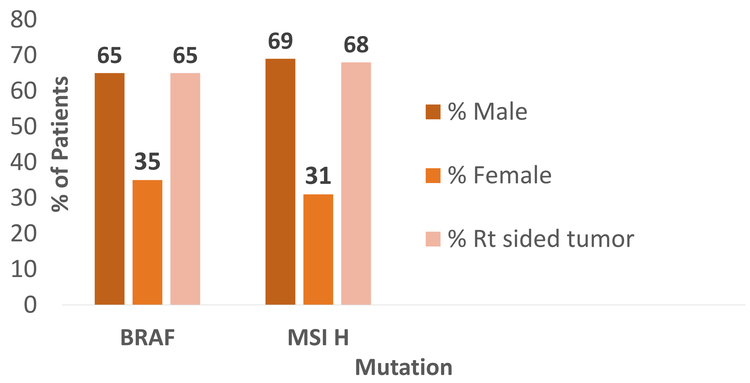
- **The pie chart above illustrates the stage wise distribution of the Colorectal cancer in our patient population**
- **We had 192 patients who were diagnosed with colorectal cancer between 207 and 2018 at our institution.**
- **57% were men and 43% were women**
- **Median age was 66 years**

Mutational analysis



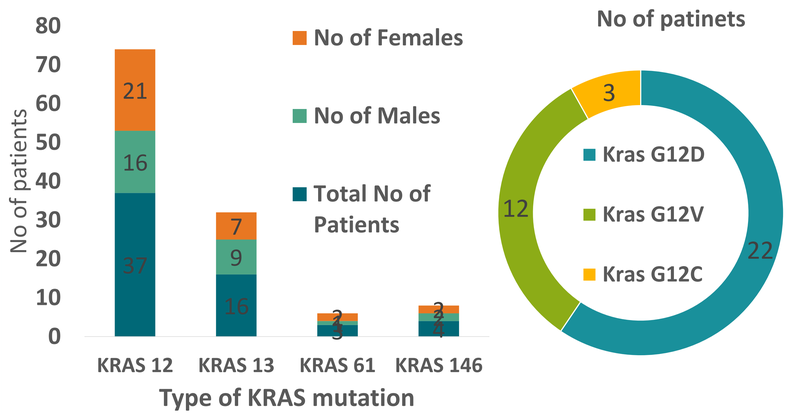
- The above graph illustrates the frequency of mutations in colorectal cancer in our population
- KRAS was the most common mutation present in 33% of patients
- NRAS was the least common mutation present in only 3.4% of patients
- Mutations were mutually exclusive

BRAF and MSI H



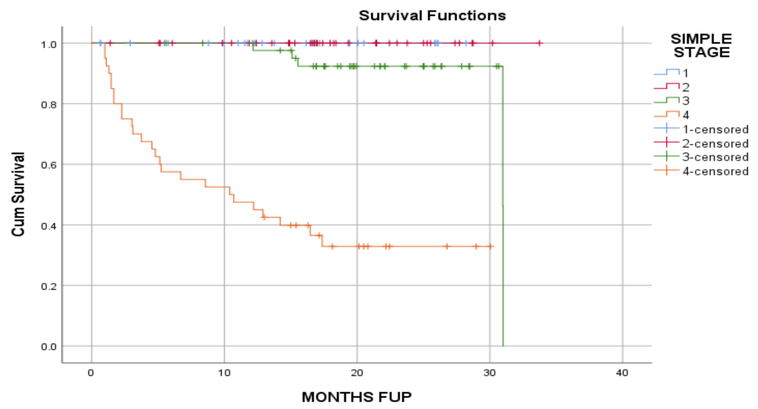
- **The above graph illustrates the frequency of distribution of MSI H and BRAF in our patient population**
- **MSI and *BRAF* mutation were seen predominantly in right sided tumors and more common in males than females**
- **MSI-H tumors tended to be lower, stage I cancers.**
- **The majority (66%) of *BRAF* mutated tumors were also MSI-H**
- **BARF mutation was more commonly seen in smokers**

KRAS Mutation



- The above columns illustrates the frequency of distribution of different types of KRAS mutations. The pie chart illustrates the distribution of variants of KRAS 12 mutations.
- KRAS Mutation was more common in females
- Was less commonly seen in poorly differentiated cancers
- KRAS 13 was more commonly seen in right sided tumors, never occurred in limited stage tumors

Survival



- **The above Kaplan Meyer curves illustrates the survival**
- **Survival was 100% in early stage cancers (stage 1&2)**
- **Survival for stage 3 and 4 - 89 % and 34 % respectively**
- **Stage of disease is a significant determinant for survival**

Conclusions

Results of clinical and overall molecular characteristics of patients from rural Maine were similar to those reported in the literature. Our future efforts will include analysis of the tumors from this dataset for additional mutations