Assessment of Universal Mismatch repair (MMR) or Microsatellite Instability (MSI) testing in colorectal cancers.

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MMR deficient colorectal tumors can be present both as sporadic and as part of inherited cancer syndrome- the Lynch Syndrome. Approximately 15% of sporadic Colorectal cancers carry impaired mismatch repair mechanism. Germ line mutation in this repair mechanism is the basis for Lynch syndrome- the hereditary colon/ uterine cancer syndrome. Lynch syndrome is present in 5-6% of Colorectal cancer patients.

MMR deficient tumors exhibit different biology and response to treatment in addition to predisposing patients to multiple tumors in their lifetime if this is inherited genetically. MMR deficiency in tumor is also predictive of response to Immunotherapy in Stage IV setting. Most of the MMR deficient tumors are sporadic in nature and are not heritable.

MMR deficiency is assessed by Immunohistochemistry (IHC) or DNA analysis for MSI.

Recently the recommendation has been for universal testing for MMR in all colorectal cancer patients versus testing only those who are at risk for Lynch Syndrome (younger age, strong family history, personal history of uterine cancer)

ASCO guidelines published in 2014 endorses universal screening for Lynch syndrome in all patients with Colorectal cancer- “Tumor testing for DNA mismatch repair (MMR) deficiency with immunohistochemistry for MMR proteins and /or MSI should be assessed in all the CRC patients. As an alternate strategy, tumor testing should be carried out in individuals with CRC younger than 70 years, or those older than 70 years who fulfill any of the revised Bethesda guidelines”

Although the recommendation has been endorsed by organizations like National Comprehensive Cancer Network (NCCN), the universal acceptance, even in academic institutions have been woefully low. A recent study done on 152993 patients with CRC showed that the MMR testing in CRC cancer patients have been done in just 28% of the patients. This large study was funded by the grant from National Institutes of Health and National Cancer Institute

Methodology-

All the patients diagnosed at Truman Medical Center with colorectal adenocarcinoma, stages 0 to IV in the years 2015-2017 were identified from tumor registry for analysis.

A total of 102 patients were identified for the study. 20 were excluded based on other histology like carcinoid.

Total number of patients analyzed in this study: 82

Breakdown by stage-

Stage 0: 8 (9.5%)
Stage 1: 10 (12%)
Stage II: 12 (15%)
Stage III: 23 (28%)
Stage IV: 27 (33%)

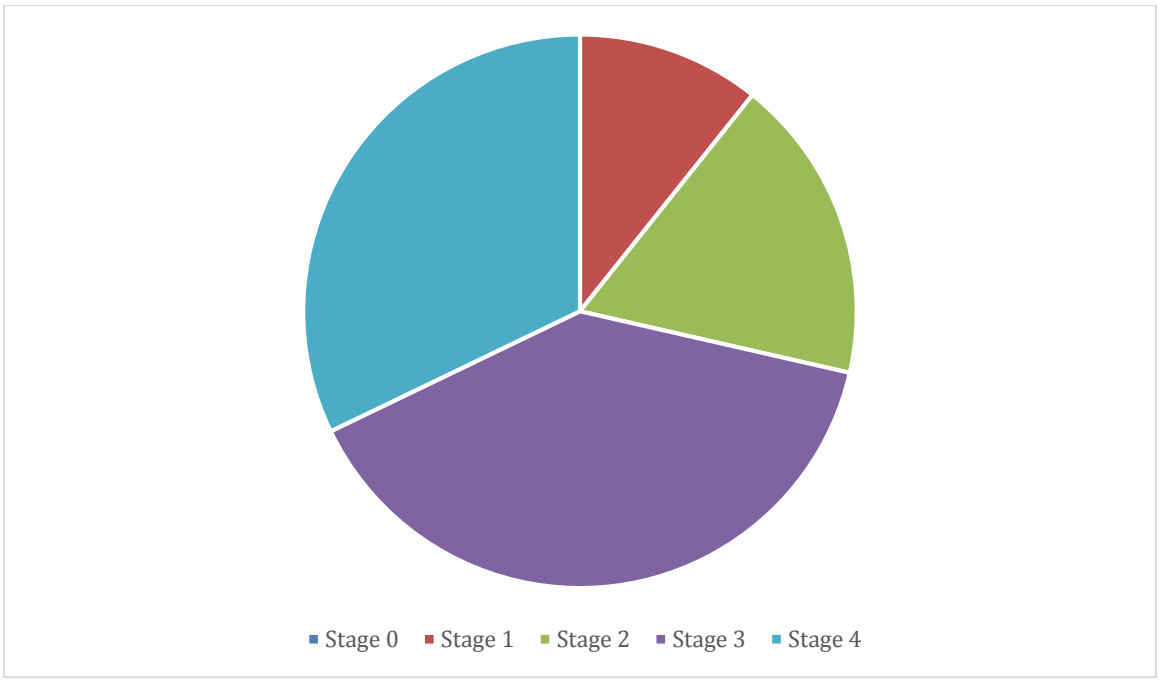
Stage unknown: 2 (2.5%)

MMR deficiency was testing by both IHC and DNA analysis for MSI.

A total of 29 patients out of 82 got MMR deficiency testing done. (35%)
Break down by the year 2015: 11 out of 28 patients (39%)
2016: 9 out of 30 patients (30%)
2017: 9 out of 24 patients (37%)

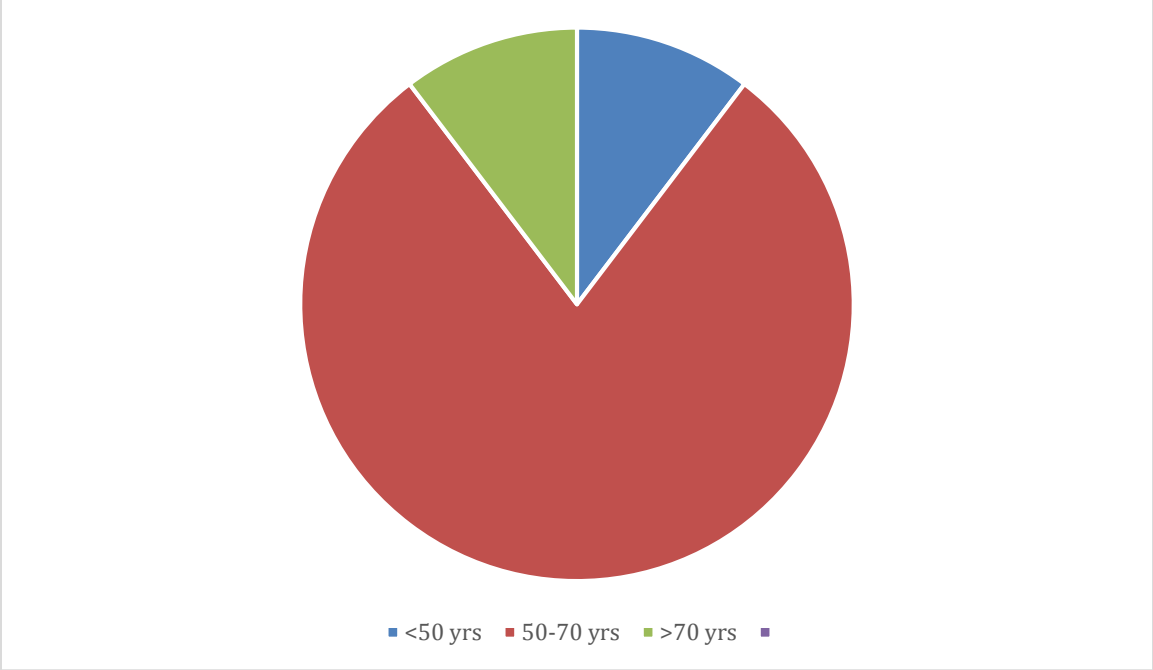
Number of MMR deficiency tests based on stage:

Stage 0: 0/8 (0%)
Stage 1: 3/9 (33%)
Stage 2: 5/12 (41%)
Stage 3: 11/23 (47%)
Stage 4: 9/27 (33%)



Number of MMR deficiency testing based on age:

< 50yrs: 3/7 (42%)
50-70 yrs.: 23/62 (37%)
> 70 yrs.: 3/13 (23%)



Conclusion:

Age group between 50-70yrs and Stage III patients accounted for most of the MMR deficiency testing. 42% of patients < 50 yrs. got their cancer specimen tested fro MMRI deficiency.

Testing for MMR deficiency, although, low at TMC is comparable to National Standards. As there has been increased awareness of this recommendation, testing for MMR deficiency has increase nationwide recently. The results shown above shows a steady plateau in testing at TMC over 3 years from 2015- 2017.

Recommendation-

1. Testing for all patients' colorectal cancer specimen, irrespective of stage, for MMR deficiency should be made a Reflex testing in all patients under the age of ≤ 70.
2. For patients >70 years treating clinician can advise for MMR testing based on the risk factor

References-

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