Utility of plasma tumor marker levels in management of patients with appendiceal adenocarcinoma

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Background

- Due to the rarity of appendiceal adenocarcinomas (AA), systematic study of these tumors has been limited. Thus, guidelines for the diagnosis and treatment of AA are often based on other related tumor types such as colorectal cancer
- However, given that AA has been shown to be molecularly and functionally distinct, there is a need for focused clinical data to guide disease management
- In AA, tumor marker levels are used by some practitioners to monitor response to treatment and aid in diagnosis. This study evaluates the association of elevated tumor marker levels with survival outcomes

Patients and Methods

- The MDACC database was queried to identify patients with AA between 1997 to 2022
- Patients with reported values for the tumor markers CEA (n=1228), CA 19-9 (n=1042), and CA-125 (n=1067) were then selected for analysis
- Elevation of tumor markers was defined as above the laboratory upper limit of normal (CA-125 > 37 U/mL, CA 19-9 > 37 U/mL, and CEA > 3 ng/mL and survival outcomes were compared with a log-rank (Mantel-Cox) test
- This analysis was repeated while controlling for tumor grade, which was defined by low-grade: well, well to moderately differentiated and high-grade: moderate, moderate to poor, and poorly differentiated
- Mutational profile was available for 334 patients, and was analyzed to check for association with tumor marker levels

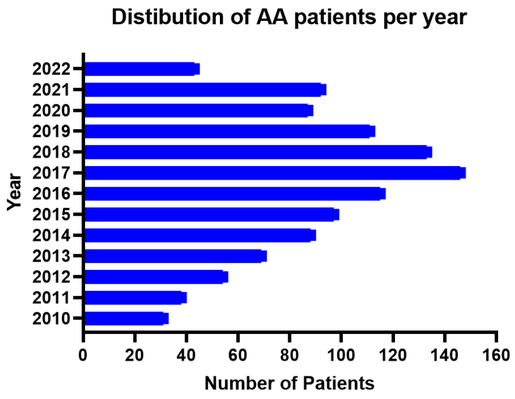


Fig 1. MDACC Appendiceal Adenocarcinoma patients distribution by year

Results

- Elevated CEA was predictive of overall survival in all patients with median survival not-yet-reached for those with normal CEA, not-yet-reached for those with elevated CEA (HR: 3.7, p < 0.0001) and 99.8 months for those with highly elevated CEA (101 ng/ml; more than 90th percentile of CEA level) (HR: 9.0, p < 0.0001)
- Given that tumor grade is the primary driver of prognosis in AA, This analysis was repeated while controlling for tumor grade
- Elevated levels of CEA was strongly predictive of overall survival for patients with low-grade tumors (HR: 19.3, 59, respectively, p < 0.0001 for each) & high grade (HR: 2.9, 6.6, respectively, p < 0.0001 for each)

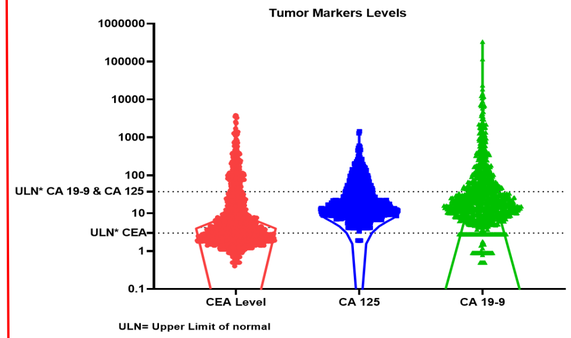


Fig 2. Tumor marker levels distribution

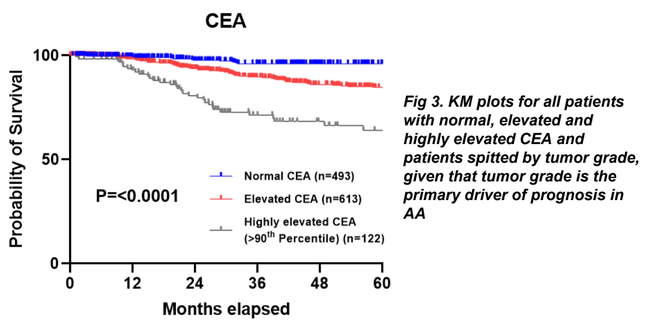
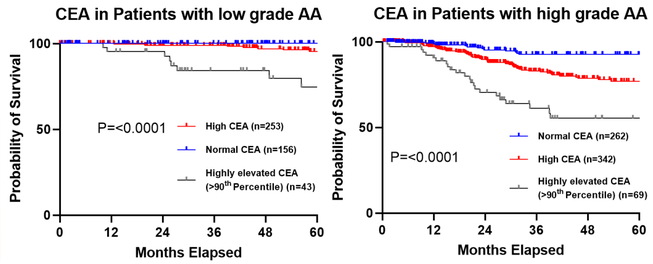


Fig 3. KM plots for all patients with normal, elevated and highly elevated CEA and patients spitted by tumor grade, given that tumor grade is the primary driver of prognosis in AA



- Elevated CA 125 was predictive of overall survival in all patients with median survival not-yet-reached for those with normal CA 125, 99.8 months for those with elevated CA 125 (HR: 4.7, p < 0.0001) and 69.8 months for those with highly elevated CA 125 (98 U/mL; more than 90th percentile of CA 125 level) (HR: 8.3, p < 0.0001)
- Elevated levels of CA 125 was strongly predictive of overall survival for patients with low-grade tumors (HR: 5.2, 8.7, respectively, p < 0.0001 for each) & high grade (HR: 4.9, 8, respectively, p < 0.0001 for each)

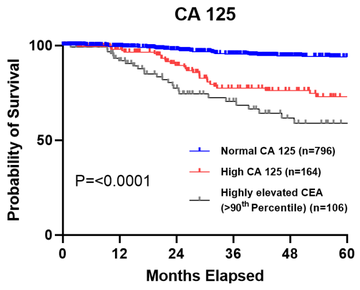
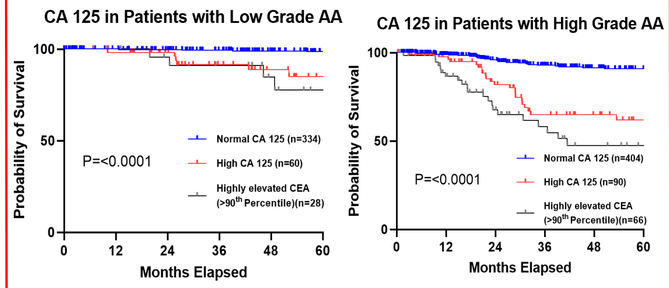


Fig 4. KM plots for all patients with normal, elevated and highly elevated CA125 and patients spitted by tumor grade, given that tumor grade is the primary driver of prognosis in AA



- Elevated CA19-9 was predictive of overall survival in all patients with median survival not-yet-reached for those with normal CA19-9, not-yet-reached for those with elevated CA19-9 (HR: 2, p = 0.0008) and 105 months for those with highly elevated CA19-9 (338 U/mL; more than 90th percentile of CA19-9 level) (HR: 4.7, p < 0.0001)
- Elevated levels of CA19-9 was strongly predictive of overall survival for patients with low-grade tumors (HR: 7, 22, respectively, p < 0.0001 for each) & high grade (HR: 1.6, 2.7, respectively, p =0.09, p=0.0003 respectively)
- A Logistic regression analysis model was built for the mutational profiles using 334 patients' mutational analysis data, However, no statistical significance were found for both univariate and multivariate analysis between normal and elevated levels of tumor marker levels

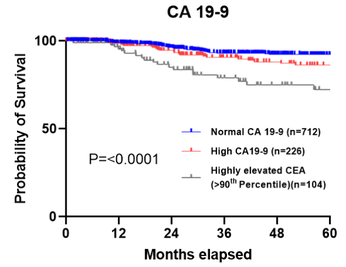
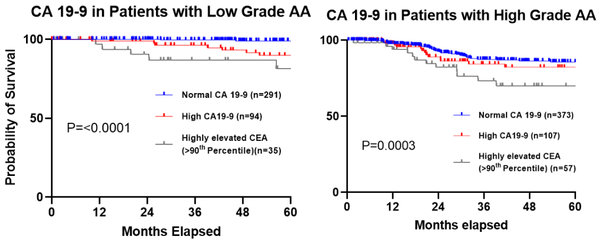


Fig 5. KM plots for all patients with normal, elevated and highly elevated CA19-9 and patients spitted by tumor grade, given that tumor grade is the primary driver of prognosis in AA



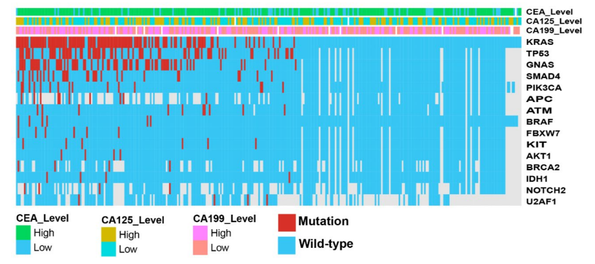


Fig 6. Heatmap plot considering gene mutations of all patients and how they align with CEA, CA125, CA199 levels (n=334)

Conclusions

- In summary, these data from a retrospective analysis highlight the utility of using tumor marker levels in conjunction with tumor grade to more accurately predict prognosis in appendiceal adenocarcinoma patients

Acknowledgement

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