Western Surgical Association
2020 Annual Meeting
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4:00pm – 6:15pm Pacific Time
– Virtual Meeting –
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12. MOLECULAR PERITONEAL STAGING (MUTANT KRAS DNA) IN PANCREATIC ADENOCARCINOMA: RESULTS FROM A PROSPECTIVE TRIAL

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Background: Pancreatic ductal adenocarcinoma (PDAC) is an aggressive malignancy requiring accurate staging for appropriate treatment recommendations. Standard imaging (CT/MRI) fails to detect synchronous peritoneal dissemination (PD) in 1/3 of patients. Addition of laparoscopic exploration and peritoneal lavage (PL) with cytology may increase PD detection, but is limited by cellular yield and low sensitivity. Since 1/2018, we have used a ddPCR cell-free DNA assay to detect mutant KRAS (mKRAS) in peripheral blood, as >90% of PDAC tumors harbor mKRAS. This assay has successfully identified patients at high risk of occult hematogenous metastases. Given the yield of our clinically available blood assay, we aimed to determine the ability and utility of mKRAS detection in PL fluid via a prospective peritoneal staging trial.

Methods: Patients with non-metastatic PDAC after initial imaging undergoing staging laparoscopy with PL by a single-surgeon under an IRB-approved prospective trial were included. Gross metastases identified on laparoscopy were biopsied for pathologic review. PL was performed with instillation of 1000ml saline which was agitated, aspirated, and sent for cytologic examination, CA19-9/CEA levels, and mKRAS DNA assay. PL fluid was spun, pelleted, and DNA was extracted. ddPCR was used to detect mKRAS copies. Results were considered positive if mKRAS copies were present. Clinically positive laparoscopy was defined as gross metastases or positive cytology. PL fluid mKRAS status was compared to gross findings, CA19-9/CEA levels, and cytology.

Results: Sixty-five patients were prospectively studied with median follow-up of 6.5 months. In total 18/65 (28%) patients had clinically positive laparoscopy. This did not correlate with elevated serum CA19-9, present in 43 (66%) patients. Cytology was positive in 10 (15%) patients and 11 (17%) patients had gross metastatic disease at laparoscopy. Of patients with gross disease only 3/11 (27%) had correlative positive cytology. PL fluid CA19-9 or CEA levels were elevated in 24/65 (37%) patients and this associated with clinically positive laparoscopy findings (p=0.021). 29 (45%) patients had mKRAS detected in PL fluid with a mean of 56 mutant copies/20uL. Positive mKRAS was associated with clinically positive laparoscopy (67% vs 33%, p=0.034), with higher copy numbers in clinically positive patients (295 vs 6, p=0.030). Peritoneal mKRAS was positive in an additional 17 clinically negative patients (36%) with only 3/17 (18%) demonstrating elevated PL fluid CA19-9/CEA levels.

Conclusion: This is the only study assessing mKRAS DNA in peritoneal fluid of patients undergoing staging laparoscopy for PDAC and shows that a high proportion of patients have detectable mKRAS. In our study, standard clinical peritoneal staging identified 1/3 of patients with synchronous PD however cytologic examination had poor sensitivity. There was high correlation with PL fluid CA19-9/CEA elevation and mKRAS with clinically positive findings. However, a significant proportion of clinically negative laparoscopy patients have detectable mKRAS suggesting that current standard peritoneal staging is likely too insensitive and the addition of mKRAS PL fluid staging may improve detection rates of occult PD. Longer follow up for correlation with peritoneal recurrence and disease progression is necessary to fully elucidate the power of this assay, however the current findings are provocative and deserve additional study.