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Expanded Mutation Profiling in Appendix Peritoneal Metastasis Has Prognostic and Therapeutic Utility When Managed with Cytoreductive Surgery/ Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC)

Authors

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caveat phrases in the original radiology interpretation. The studies were categorized into diagnostic, technically limited, or non-diagnostic studies.

Results: Studies performed using ASIR-V (375.6 mGy*cm [255.9, 501.4]) had a significantly lower DLP compared to those using FBP (695.3 mGy*cm [410.6, 1110.0]). The diagnostic quality was superior when performed using ASIR-V, with 90% (481/533) of studies being diagnostic, compared to 80% (452/562; P<.0001) in the FBP group.

Conclusions: CTPA performed using ASIR-V both reduced radiation dose as well as improved diagnostic confidence compared to CTPA performed using FBP. ■

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Expanded Mutation Profiling in Appendix Peritoneal Metastasis Has Prognostic and Therapeutic Utility When Managed with Cytoreductive Surgery/Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC)

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Type: Original Research

Background: The identification of relevant biological pathways and mutations is integral to improving outcomes in appendix peritoneal metastases (APM). Interrogation of cancers with Next Generation Sequencing (NGS) 50-gene mutation panels has become more widely utilized identifying prognostic and actionable mutations. This study is a dedicated analysis of the value of expanded mutation analysis in APM.

Methods: The IRB approved study included 51 APM patients where data was retrospectively collected from a CRS/HIPEC registry treated 2012-2018. Standard clinical 50-gene NGS analysis was performed in CLIA approved lab. All patients underwent CRS/HIPEC with mitomycin C delivered for 90 minutes at 41-42 C. Peritoneal Cancer Index (PCI), Completeness of Cytoreduction (CC) score, length of stay, progression free survival (PFS), overall survival (OS) were collected along with the rates and types of mutation in APM. OS and PFS analyses were performed on all, high grade (HG), and low grade (LG) APM, specifically evaluating the impact of smad4 and p53 mutations on survival.

Results: Eighty-four percent of APM had a mutation identified with 58% of cases harboring ≥2 mutations. Kras was most frequent, 66% of APM (88% LG 44% HG) and GNAS identified in 88% of LG APM. Smad4 or p53 mutation occurred in 25% of APM and a significant reduction in OS in all APM (22 vs 88 months p=0.0026) and HG APM (20 vs 47 months p=0.0502) was observed. Smad4 mutation was also associated with a significant reduction in PFS APM (p=0.0192). Actionable mutations were identified in 70% of APM.

Conclusion: Smad4 and p53 mutations were associated with more aggressive APM and maybe a useful tool in patient selection and outcome. Expanded mutation profiles is valuable in APM and further application is warranted. Research in Kras, p53 and smad4 pathways and drug development will benefit APM. ■

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Table 1.

p53 and/or SMAD4 mutations are associated with significantly reduced overall survival (OS) in all patients and high grade (HG) subgroup; SMAD4 mutations alone was associated with significantly shortened progression free survival (PFS) in all patients and high-grade subgroup. LG, low grade.

	WT P53 & SMAD4 (months)	+P53 OR +SMAD4 (months)	P VALUE
OS_{ALL}	88	22	<0.01
OS_{HG}	47	20	0.05
	WT SMAD4 (months)	+SMAD4 (months)	P VALUE
PFS_{ALL}	10	3.5	0.02
PFS_{HG}	6.5	1.5	0.01
PFS_{LG}	20	7.5	0.09