Molecular Stability, Regression, and Progression in Pancreatic Cysts Over Time

Vinay Chandrasekhara[1], Sara A. Jackson[2], Nicole Toney[2], Christina Narick[2], Sydney Finkelstein[2]
1. Mayo Clinic, Rochester, MN, United States. 2. Interpace Diagnostics, Pittsburgh, PA, United States

BACKGROUND:

- Molecular testing of pancreatic cyst fluid has proven to be useful for differentiating high-risk from low-risk cystic lesions
- The stability of molecular markers in pancreatic cyst fluid over time is unknown
- We reviewed molecular results from patients who have underwent serial pancreatic cyst fluid analysis over time to better understand how DNA abnormalities (DNA Ab), or the lack thereof, may remain stable, regress, or progress to cumulative levels associated with high risk of malignancy

METHODS:

- A database of more than 38,000 patients who underwent molecular testing in pancreatic cyst fluid (Interpace Diagnostics) was searched to identify individuals who underwent ≥2 endoscopic ultrasound-guided fine needle aspirations
- Patients had DNA analysis as part of their standard of care between April 2012 and March 2019 and were categorized as having 0, 1, or multiple (2-3) DNA Ab, which included any one of three key DNA Ab categories:
    - Elevated DNA quantity
    - KRAS
    - Tumor suppressor gene loss of heterozygosity (TSG-LOH) at 10 genomic loci

DNA Ab detected on Initial EUS-FNA	DNA Ab detected on Final EUS-FNA	Patients (N)	% Subgroup Total	Median time between Initial and Final EUS-FNA (year)
Total 0 DNA Ab		**2315**		
	0	1879	81%	1.64
	1	406	18%	1.40
	≥2	30	1%	1.38
Total 1 DNA Ab		**923**		
	0	562	61%	1.51
	1	327	35%	1.19
	≥2	34	4%	1.15
Total ≥2 DNA Ab		**94**		
	0	36	38%	1.51
	1	39	41%	0.914
	≥2	19	20%	0.548
Grand Total		**3332**		

Table 1: Patients who underwent serial testing for three DNA Ab over time, grouped by the number DNA Ab detected on the initial EUS-FNA and the number of DNA Ab detected on the final follow-up EUS-FNA.

RESULTS:

3332 total patients underwent serial pancreatic cyst fluid analysis.

2315 patients (69.5%) initially had 0 DNA Ab.

- 99% of these patients had non-worrisome levels of DNA Ab at a median time of 1.5 years later, with 81% remaining at 0 DNA Ab and 18% developing only 1 DNA Ab
- Only 1% progressed to have cumulative (≥2) DNA Ab in this timeframe

923 patients (27.7%) initially had 1 DNA Ab.

- The majority (96%) of these had non-worrisome levels of DNA Ab at follow-up of 1.4 years, with 61% regressing to 0 DNA Ab and 35% retaining only 1 DNA Ab
- Only 4% progressed to have cumulative (≥2) DNA Ab in this timeframe

94 patients (2.8%) initially had multiple (≥2) DNA Ab.

- 20% of these patients retained multiple DNA Ab at a median follow-up of 0.5 years
- 41% of these patients regressed to 1 DNA Ab at a median of 1.5 years follow-up
- 38% regressed to 0 DNA Ab at a median of 0.9 years follow-up

CONCLUSIONS:

- Most patients who have non-worrisome levels of DNA Ab (0-1) will continue to have non-worrisome levels at 1.5 years follow-up
- Given the high negative predictive value for test results based on the lack of cumulative DNA damage, these data suggest that in patients with pancreatic cysts that contain no DNA abnormalities, surveillance intervals may be lengthened beyond 1 year
- Although molecular regression can occur in patients with multiple (≥2) DNA Ab, a significant fraction of these patients will retain their cumulative DNA damage over time, consistent with higher risk disease