The Use of Immunohistochemistry for IgG4 in the Diagnosis of Autoimmune Pancreatitis: A Systematic Review and Meta-analysis

Seung Bae Yoon,¹ Sung-Hoon Moon,² Jong Hyeok Kim,² Tae Jun Song,³ and Myung-Hwan Kim³

¹Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, South Korea ²Department of Internal Medicine, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, South Korea

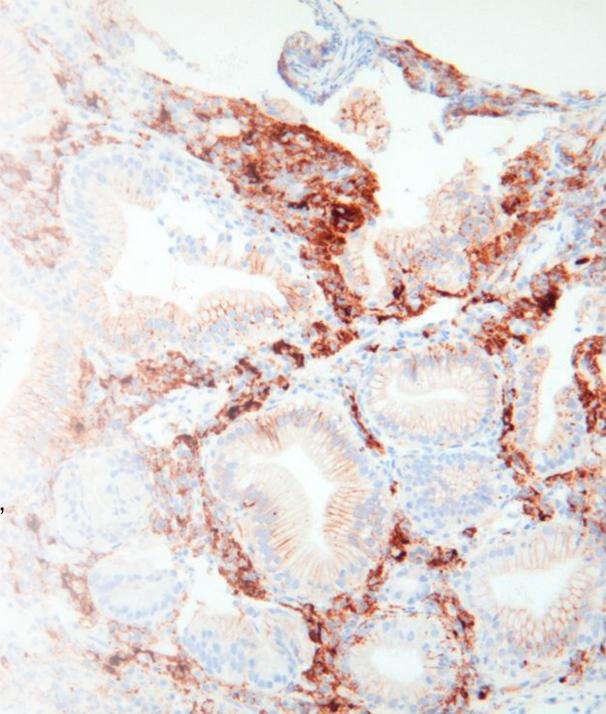
³Department of Internal Medicine, University of Ulsan, College of Medicine, Asan Medical Center, Seoul, South Korea

Declaration of Interest

The authors have no conflicts of interest.

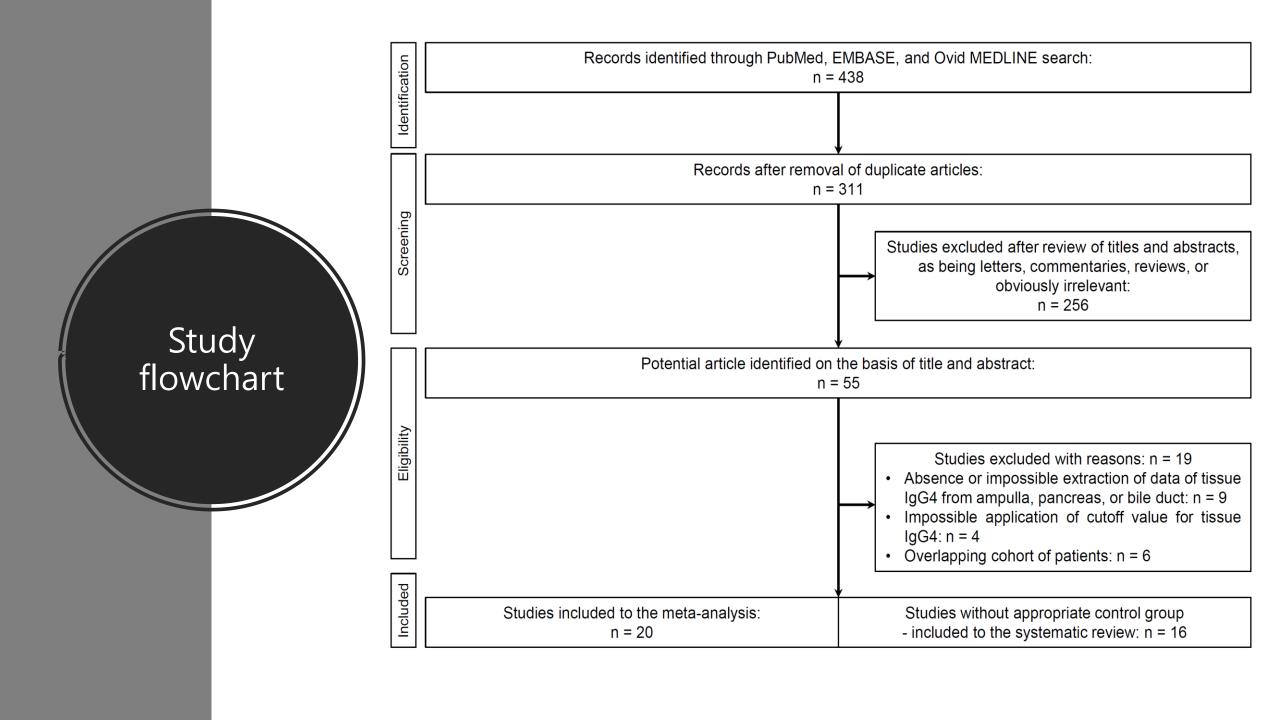
Background and Aim

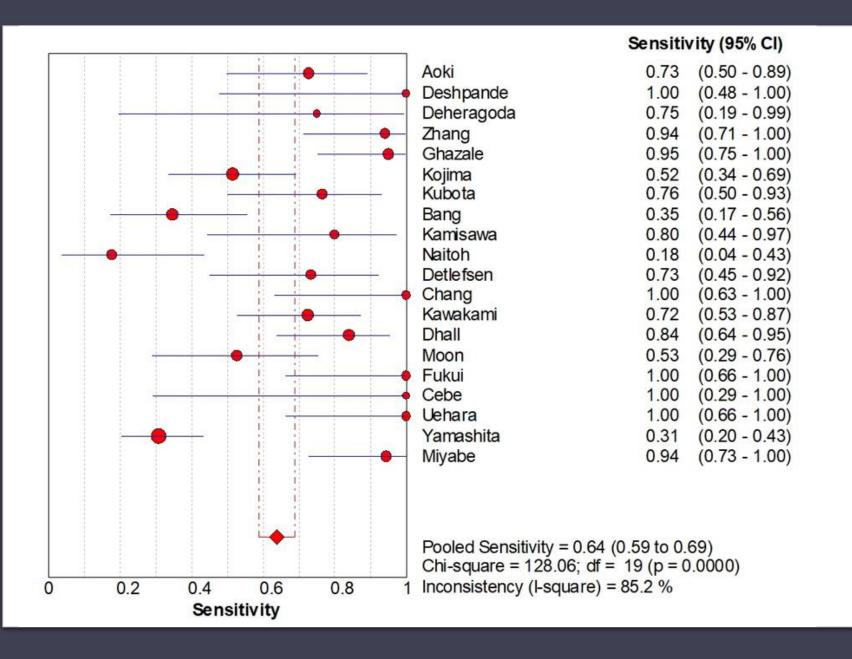
- 1. The diagnosis of autoimmune pancreatitis (AIP) remains challenging, especially when serum IgG4 is normal or imaging features are indeterminate.
- The aim of this study was to assess the diagnostic performance of IgG4 immunostaining of pancreatic, biliary, and ampullary tissues in the differential diagnosis of AIP.



Material and Methods

- A comprehensive literature search, using the PubMed, EMBASE, and Ovid MEDLINE databases
- Search terminology: ("autoimmune pancreatitis" or "lymphoplasmacytic sclerosing pancreatitis") and ("IgG4 immunostaining" or "tissue IgG4")
- Inclusion criteria: (1) studies providing detailed diagnostic criteria for AIP; (2) studies providing tissue IgG4 obtained from pancreas, bile duct, or ampulla; (3) studies providing the cut-off value for tissue IgG4; and (4) studies providing sufficient data to construct 2-by-2 tables





Pooled sensitivity

Specificity (95% CI) Aoki (0.83 - 1.00)Deshpande 0.88 (0.72 - 0.97)0.97 Deheragoda (0.83 - 1.00)0.88 (0.73 - 0.97)Zhang Ghazale 0.80 (0.28 - 0.99)1.00 (0.82 - 1.00)Kojima Kubota 1.00 (0.74 - 1.00)0.83 (0.59 - 0.96)Bang Kamisawa 1.00 (0.83 - 1.00)Naitoh 0.91 (0.59 - 1.00)Detlefsen 0.87 (0.60 - 0.98)(0.91 - 1.00)Chang 1.00 0.88 (0.72 - 0.97)Kawakami Dhall 1.00 (0.88 - 1.00)Moon 1.00 (0.96 - 1.00)Fukui 0.95 (0.76 - 1.00)Cebe 0.67 (0.22 - 0.96)**Uehara** 0.57 (0.34 - 0.78)Yamashita 0.96 (0.89 - 0.99)(0.82 - 0.97)Miyabe 0.91 Pooled Specificity = 0.93 (0.91 to 0.95) Chi-square = 66.46; df = 19 (p = 0.0000) Inconsistency (I-square) = 71.4 % 0 0.2 0.4 0.6 8.0 Specificity

Pooled specificity

Meta-regression for potential source of heterogeneity

Factors	RDOR	p value	95% CI
Subtype of AIP (type 1 AIP vs. AIP without subtyping)	2.69	0.218	0.54-12.37
Control group (pancreatobiliary cancer vs. oCP)	1.22	0.772	0.29-5.10
Sampling site (pancreas vs. bile duct/ampulla)	2.44	0.245	0.52-11.53
Sampling method (surgery vs. biopsy)	5.27	0.024	1.29-21.51
Counting method (1 HPF vs. ≥ 3 HPF)	0.73	0.777	0.07-8.02

RDOR, relative diagnostic odds ratio; CI, confidence interval; AIP, autoimmune pancreatitis; oCP, other chronic pancreatitis; HPF, high power field.

Conclusions

 IgG4 immunostaining of pancreatic, biliary, and ampullary tissue exhibited high specificity but moderate sensitivity for diagnosing AIP. Therefore, IgG4 immunostaining may be useful for supporting a diagnosis of AIP when AIP is clinically suspected, but the combination of imaging and serology does not confirm the diagnosis.

