Verona, 23 of March, 2026

IgG4-Related Disease

Department of Medicine
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IgG4-Related Disease

1. Severe fibro-inflammatory condition
2. Involving possibly every human organ system
3. Tendency to form tumefactive lesions *("mass-forming")*
4. Histopathological features bear striking similarities across the involved organs *(similarly to sarcoidosis)*
5. Elevated serum IgG4
6. Response to steroids
7. Frequent relapses
8. Loss of function, if not treated

IgG4-Related Disease

Histopathologic Hallmarks of IgG4-RD

Pathology

Major

- Dense lympho-plasmacytic infiltrate
- Fibrosis, arranged at least focally in a storiform pattern
- Obliterative phlebitis

Minor

- Phlebitis without obliteration of the lumen
- Increased numbers of eosinophils

Immunochemistry

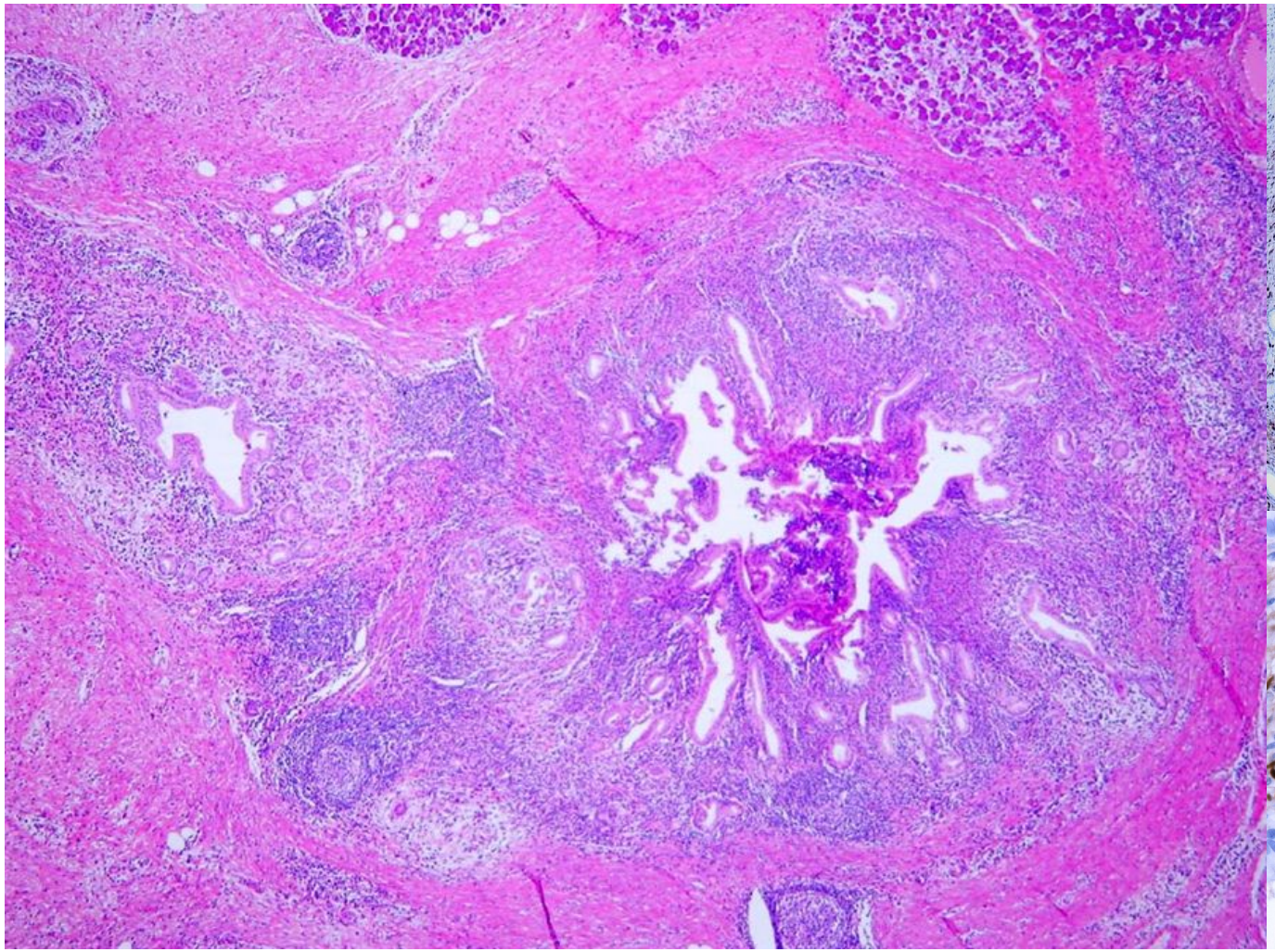
↑ numbers of IgG4+ plasma cells

and/or

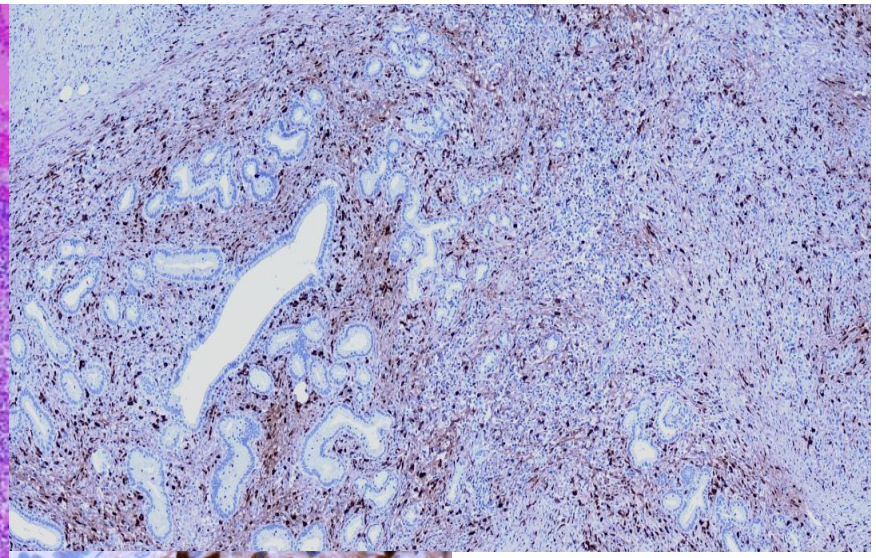
elevated IgG4:IgG ratio

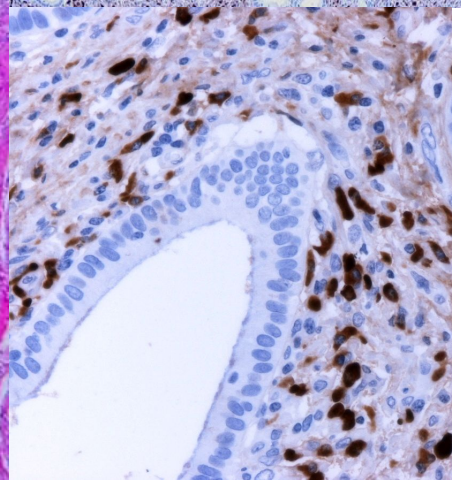
IgG4-Related Disease

Pancreatic Involvement – Autoimmune Pancreatitis type 1



histology of surgical specimens





Immunochemistry for IgG4 plasmacells

Zamboni G, Capelli P, *Pathology,* Verona

IgG4-Related Disease

Nomenclature (=organs involved)

Organ system/tissue	Preferred name
Pancreas	Type 1 autoimmune pancreatitis (IgG4-related pancreatitis)
Eye	IgG4-related ophthalmic disease is the general term for the periocular manifestations of this disease. There are several subsets, outlined below.
Lacrimal glands	IgG4-related dacryoadenitis
Orbital soft tissue (orbital inflammatory pseudotumor)	IgG4-related orbital inflammation (or IgG4-related orbital inflammatory pseudotumor)
Extraocular muscle disease	IgG4-related orbital myositis
Orbit with involvement of multiple anatomic structures	IgG4-related pan-orbital inflammation (includes lacrimal gland disease, extraocular muscle involvement, and other potential intraorbital complications)
Salivary glands (parotid and submandibular glands)	IgG4-related sialadenitis or, more specifically, IgG4-related parotitis or IgG4-related submandibular gland disease
Pachymeninges	IgG4-related pachymeningitis
Hypophysis	IgG4-related hypophysitis
Thyroid (Riedel thyroiditis)	IgG4-related thyroid disease
Aorta	IgG4-related aortitis/periaortitis
Arteries	IgG4-related periarteritis
Mediastinum	IgG4-related mediastinitis
Retroperitoneum	IgG4-related retroperitoneal fibrosis
Mesentery	IgG4-related mesenteritis
Skin	IgG4-related skin disease
Lymph node	IgG4-related lymphadenopathy
Bile ducts	IgG4-related sclerosing cholangitis
Gallbladder	IgG4-related cholecystitis
Liver	IgG4-related hepatopathy (refers to liver involvement that is distinct from biliary tract involvement)
Lung	IgG4-related lung disease
Pleura	IgG4-related pleuritis
Pericardium	IgG4-related pericarditis
Kidney	IgG4-related kidney disease. The specific renal complications should be termed tubulointerstitial nephritis secondary to IgG4-related disease and membranous glomerulonephritis secondary to IgG4-related disease. Involvement of the renal pelvis should be termed IgG4-related renal pyelitis.
Breast	IgG4-related mastitis
Prostate	IgG4-related prostatitis

Stone J et al, *Arthritis Rheum*, 2012; **64(10)**:

HIGH SERUM IgG4 CONCENTRATIONS IN PATIENTS WITH SCLEROSING PANCREATITIS

HIDEAKI HAMANO, M.D., SHIGEYUKI KAWA, M.D., AKIRA HORIUCHI, M.D., HIROSHI UNNO, M.D., NAOYUKI FURUYA, M.D., TAIJI AKAMATSU, M.D., MANA FUKUSHIMA, M.D., TOSHIO NIKAIDO, PH.D., KOHZO NAKAYAMA, PH.D., NOBUTERU USUDA, M.D., AND KENDO KIYOSAWA, M.D.

Why

...

We previously found that the serum of some patients with sclerosing pancreatitis had a polyclonal band in the rapidly migrating fraction of gamma globulins.

Hypothesis

...

Because high serum IgG4 concentrations are found in only a limited number of conditions, such as atopic dermatitis,[17] some parasitic diseases,[18] and pemphigus vulgaris and pemphigus foliaceus,[19] we sought to determine whether serum IgG4 concentrations are high in patients with sclerosing pancreatitis but not in patients with other diseases of the pancreas or biliary tract.

2001;344:732-8.

The New England Journal of Medicine

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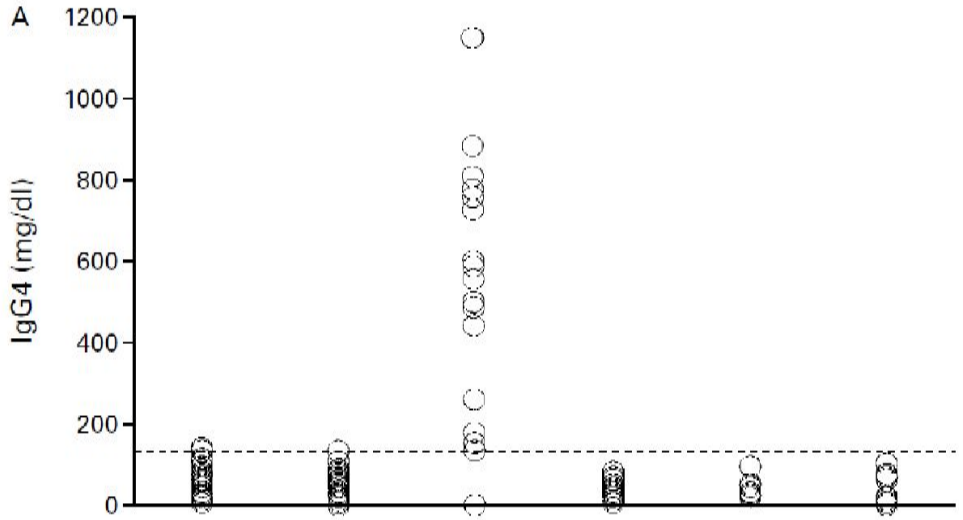


IgG4 cut-off 135 mg/dl Vs. pancreatic cancer

Sensitivity	95%
Specificity	97%
Accuracy	95%

2001;344:732-8.

J Gastroenterol 2003; 38:982–984
DOI 10.1007/s00535-003-1175-y

Journal of
Gastroenterology

Rapid communication

A new clinicopathological entity of IgG4-related autoimmune disease

Terumi Kamisawa[1], Nobuaki Funata[2], Yukiko Hayashi[2], Yoshinobu Eishi[3], Morio Koike[3], Kouji Tsuruta[4], Atsutake Okamoto[4], Naoto Egawa[1], and Hitoshi Nakajima[1]

Table 1. Distribution of IgG4-positive plasma cells in the organs and tissues of eight patients with IgG4-related autoimmune pancreatitis

IgG4-positive plasma cells	Pancreas	Peripancreatic tissues	Bile duct	Gallbladder	Liver	Stomach	Duodenum	Colon	Lung	Salivary gland	Lymph node	Bone marrow
>30/HPF	1, 2, 3, 4, 5, 6, 7, 8	1, 2, 3, 4, 5, 6	1, 3, 4, 5, 6, 7, 8	1, 4, 5, 7, 8	6, 7	1, 3, 6		8		1	1, 2, 3, 5, 6	
30–10/HPF			2	2, 3, 6	1	5, 8		7			4	1, 5
10–5/HPF						2, 4	1, 3, 6			2		
<5/HPF							2, 4, 5		3			

Numbers in the table denote patients 1 to 8 with autoimmune pancreatitis
HPF, high-power field

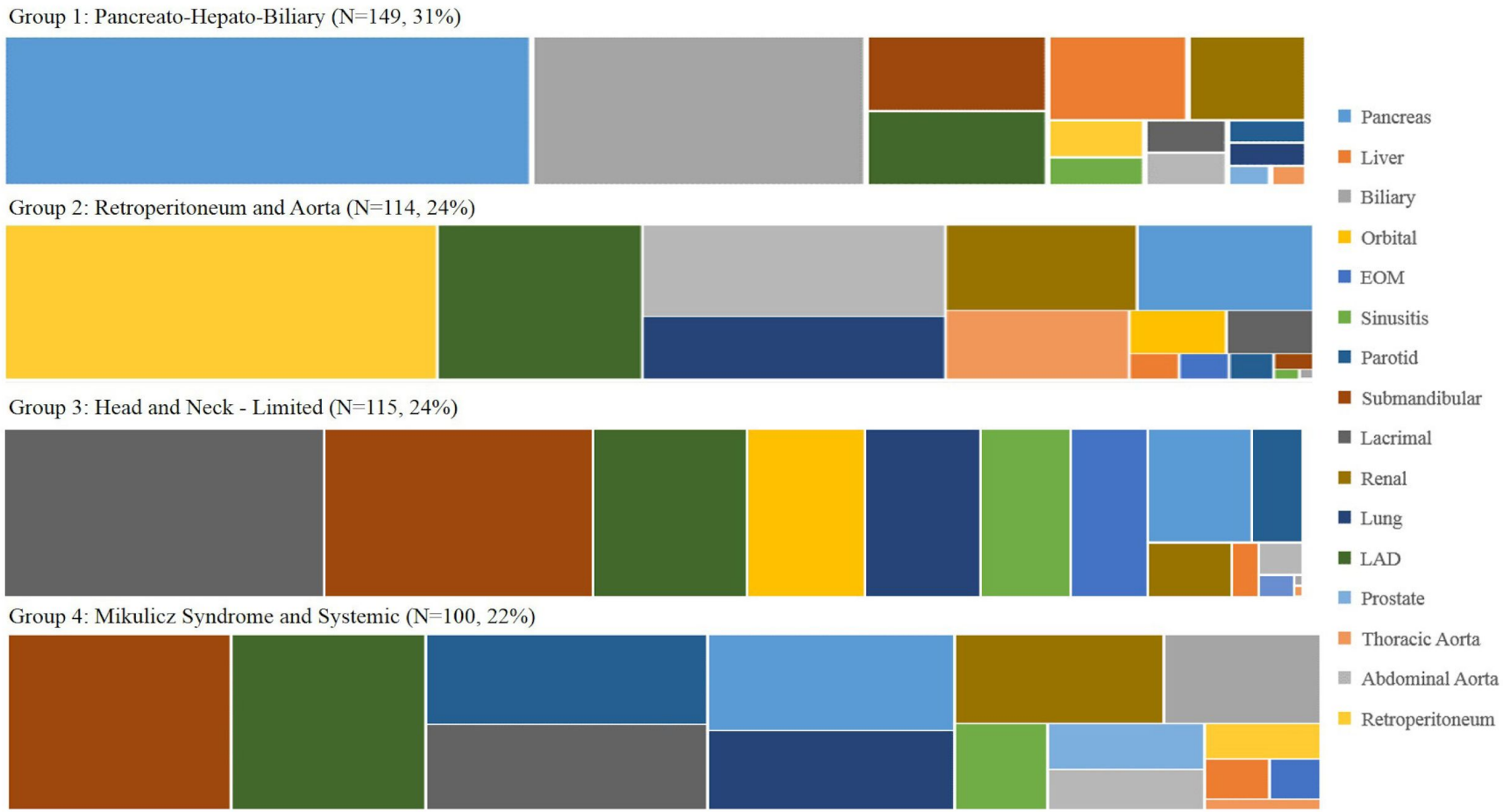
Conclusions.

These results suggest that AIP is not simply pancreatitis but that it is a pancreatic lesion involved in IgG4-related systemic disease with extensive organ involvement. We propose a new clinicopathological entity, of a systemic IgG4-related autoimmune disease in which AIP and its associated diseases might be involved.

CLINICAL SCIENCE

Clinical phenotypes of IgG4-related disease: an analysis of two international cross-sectional cohorts

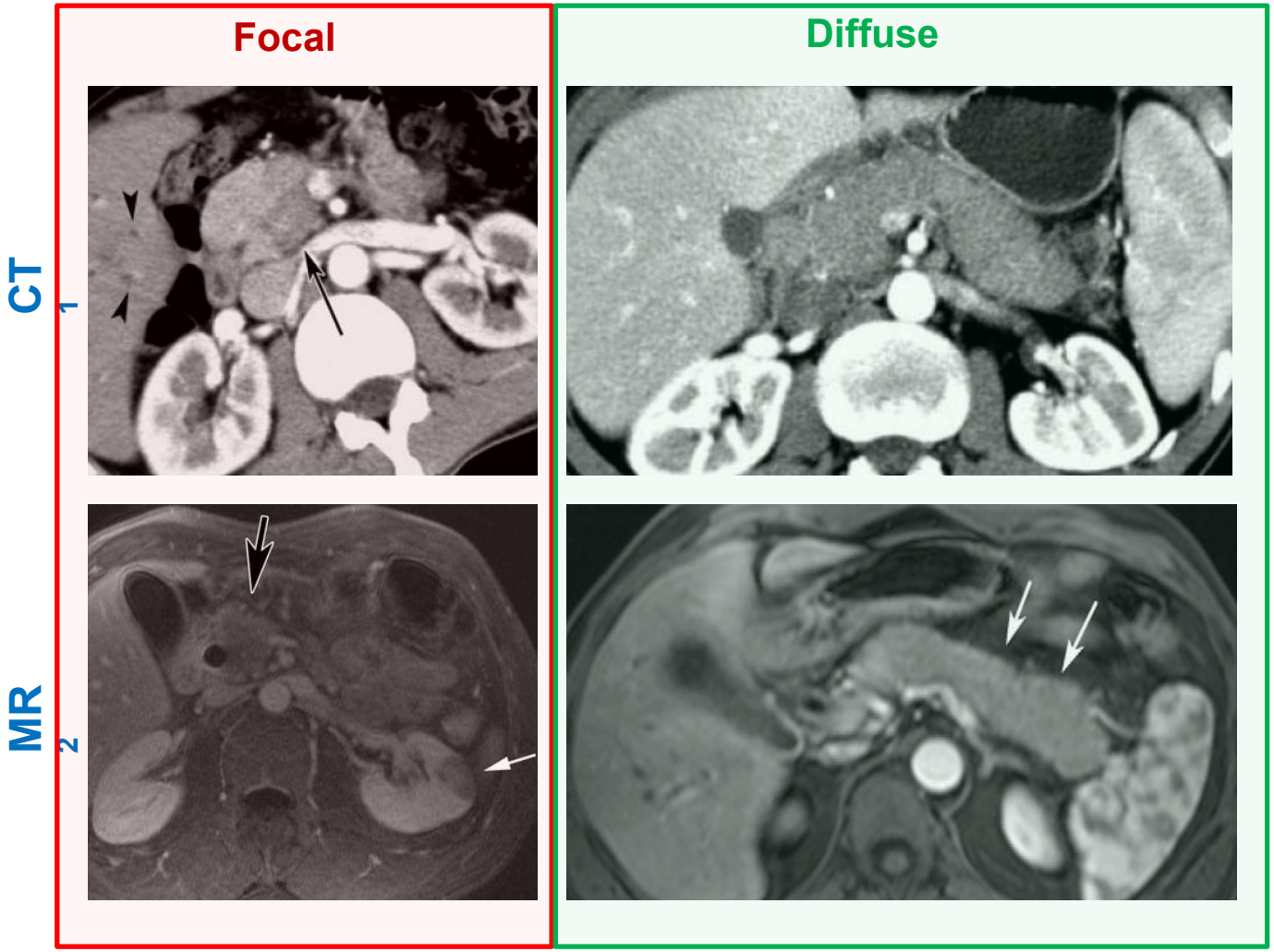
Zachary S Wallace,[1,2,3] Yuqing Zhang,[1,2,3] Cory A Perugino,[1,3] Ray Naden,[4] Hyon K Choi,[1,2,3] John H Stone,[1,3] for the ACR/EULAR IgG4-RD Classification Criteria Committee



Ann Rheum Dis 2019;**78**:406–412

Autoimmune Pancreatitis Type 1

CT and MR findings

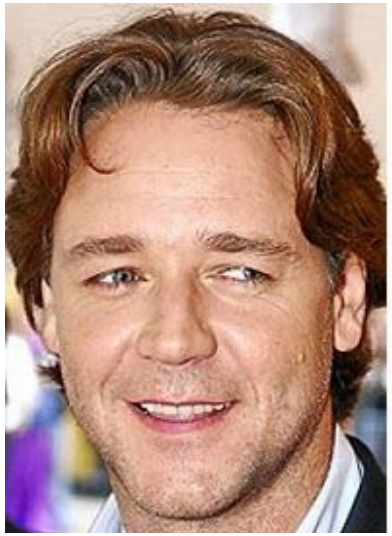


[1]Manfredi et al, *Radiology*, 2008; **247(2)**: 435-443

[2]Manfredi et al, *Radiology*, 2011; **260(2)**:

Autoimmune Pancreatitis Type 1

"The" Decisional Key



Russell Crowe

Ben Mckenzie

It seems a neoplasia at imaging

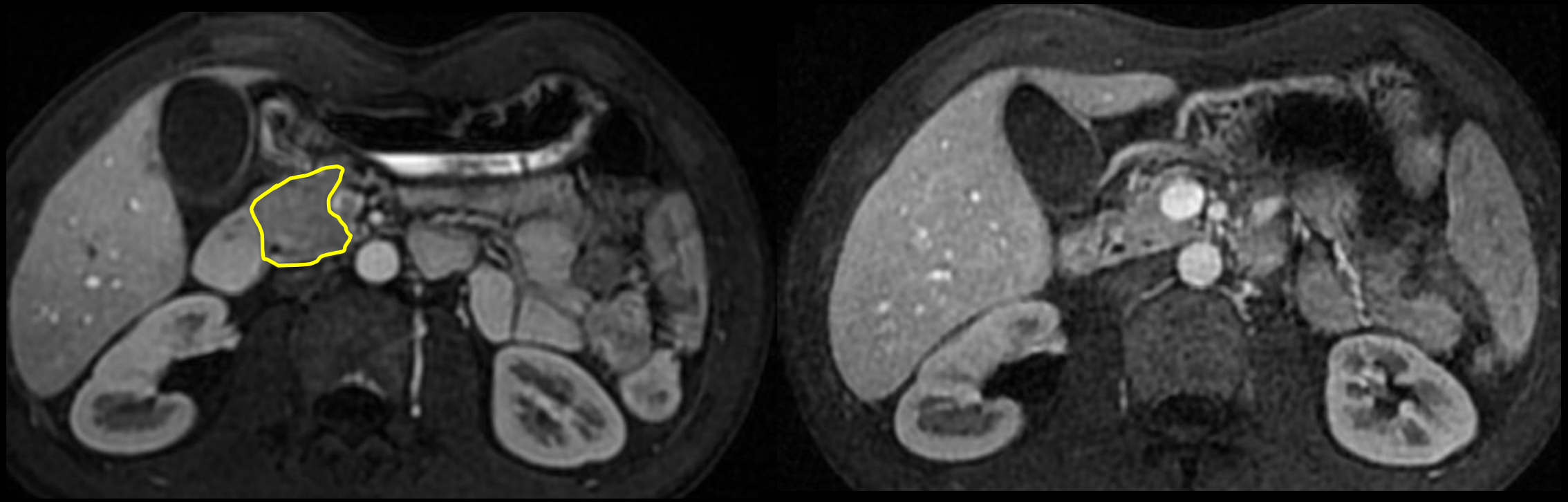
make the correct diagnosis

To avoid to treat "neoplasia" with steroids

To avoid surgery for an "inflammatory" disease that fully responds to steroids

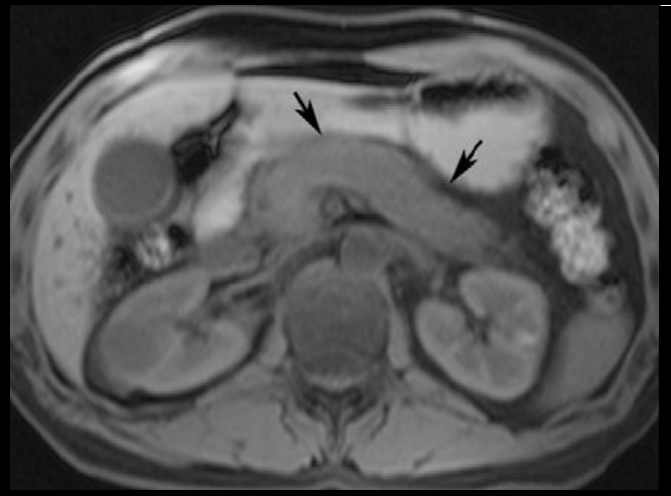
Autoimmune Pancreatitis Type 1

Response to Steroids

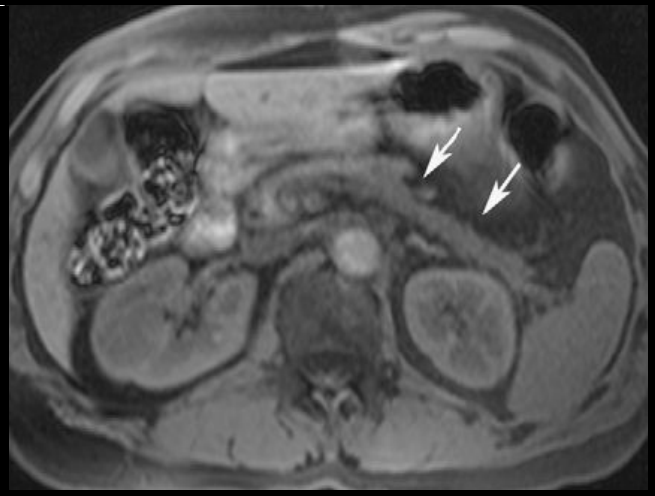


Autoimmune Pancreatitis Type 1

Response to Steroids and Relapse



August 2003

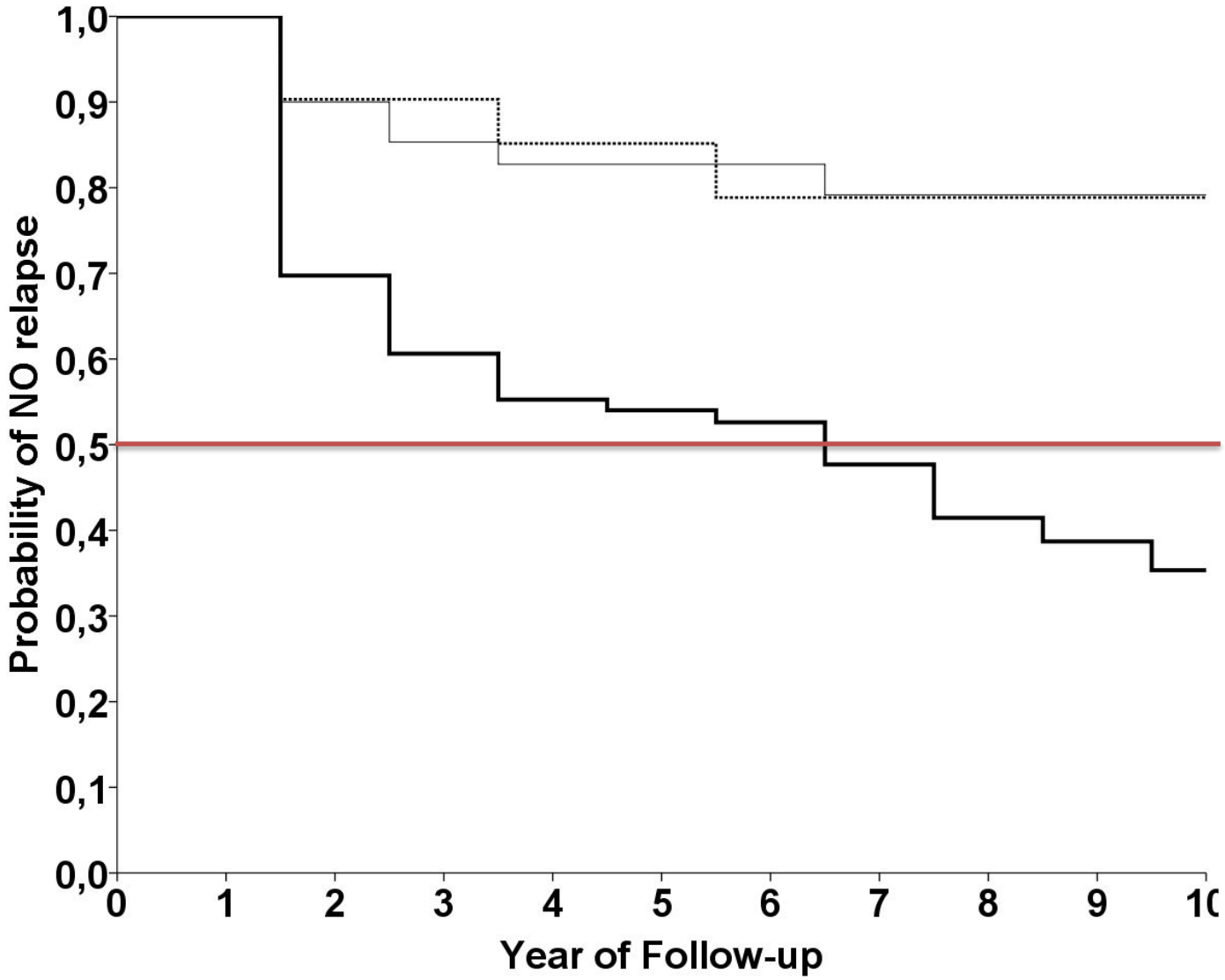


December 2003 *(after steroids)*

Manfredi et al, Radiology, 2011; 260(2): 428-436

Autoimmune Pancreatitis

Frequency of Disease Relapse Vs. Type



Type 2
117 pts (24%)

Type NOS
97 pts (20%)

Type 1 – IgG4 RD
269 pts (56%)

Verona AIP database, 496 patients, 22.7.2025

IgG4 Related Disease

The Clinical Needs

- To diagnose the disease – *probably largely underestimated*
- Differential diagnosis with cancer – *particularly in pancreatic-hepato-biliary phenotype*
- Early diagnosis – *“the earlier the disease is diagnosed, the better it can de treated”*
- Effective treatments – *maintenance therapy to avoid recurrences and disease progression*