JCTEI
JOURNAL OF CLINICAL TRIALS AND EXPERIMENTAL INVESTIGATIONS
Year: 2025 Volume: 4 Issue: 1

ORIGINAL ARTICLE

10.5281/zenodo.15069860

Imaging modalities in the diagnosis and monitoring of IgG4-Related disease: Utilization patterns and clinical implications

Rabia Deniz[1], Cemal Bes[1]

1. University of Health Sciences Başakşehir Çam and Sakura City Hospital, Department of Rheumatology, Istanbul, Turkey

Correspondence
Rabia Deniz, Başakşehir Çam and Sakura City Hospital, Department of Rheumatology, Başakşehir Olimpiyat Bulvarı Yolu, 34480, Istanbul, Turkey,

e-mail
dr.rabiadeniz@gmail.com

Received: 9 February 2025
Revised: 1 March 2025
Accepted: 9 March 2025
Published: 19 March 2025

Keywords
- Immunoglobulin G4-related disease
- imaging
- computed tomography
- magnetic resonance imaging
- positron emission tomography

ORCID ID of the author(s):
RD: 0000-0003-4537-894X
CB: 0000-0002-1730-2991

Abstract

Objective: Immunoglobulin G4-related disease (IgG4-RD) is a chronic fibroinflammatory disorder affecting multiple organ systems, often requiring imaging for diagnosis and monitoring. Despite its critical role, an optimal imaging strategy, including modality preference and follow-up intervals, remains undefined. This study evaluates the utilization patterns of different imaging modalities in IgG4-RD.

Materials and methods: This retrospective, single-center study included 18 patients diagnosed with IgG4-RD according to ACR/EULAR criteria between May 2020 and December 2024. Clinical, laboratory, histopathological, and imaging data were collected. Computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET-CT) were analyzed for diagnostic and follow-up trends. Patients were stratified based on the presence of acute kidney injury (AKI) at diagnosis.

Results: At diagnosis, CT (83.3%) was the most frequently used modality, followed by PET-CT (61.1%) and MRI (27.8%). Combined imaging was performed in 66.6% of cases initially but declined during follow-up. The choice of the first follow-up imaging differed between patients with and without AKI (p=0.072). Notably, follow-up imaging intervals were significantly shorter in AKI patients (30.5 vs. 49 months, p=0.049). Over time, PET-CT use decreased, while MRI became the preferred modality. Despite these variations, no standardized follow-up approach was observed.

Conclusions: Our findings indicate a shift from multimodal to single-modality imaging during follow-up, with variations based on AKI status. The lack of a standardized imaging protocol indicates the need for consensus guidelines to enhance disease monitoring and optimize patient outcomes.

Cite as: Deniz R, Bes C. Imaging modalities in the diagnosis and monitoring of IgG4-Related disease: Utilization patterns and clinical implications. J Clin Trials Exp Investig. 2025;4(1):1-6.

Introduction

Immunoglobulin G4-related disease (IgG4-RD) is a chronic, immune-mediated fibroinflammatory condition characterized by tumefactive lesions, dense lymphoplasmacytic infiltration with IgG4-positive plasma cells, and storiform fibrosis (1,2). It can affect multiple organ systems, including the pancreas, bile ducts, salivary glands, kidneys, and retroperitoneum, often mimicking malignancies or other inflammatory disorders. The diagnosis of IgG4-RD relies on a combination of clinical, serological, histopathological, and imaging findings. Among these, imaging plays a crucial role in detecting organ involvement, guiding biopsies, and assessing treatment response. Various imaging modalities, such as CT, magnetic resonance

In certain clinical scenarios, such as periaortitis or retroperitoneal fibrosis, obtaining a histopathological confirmation through biopsy may be high-risk or technically unfeasible. In such cases, imaging plays a crucial diagnostic role, offering non-invasive means to support clinical suspicion and guide management decisions. Additionally, considering that IgG4-RD patients may present with acute kidney injury, the choice of imaging modality must take into account contrast-induced nephropathy risks, necessitating the careful selection of appropriate imaging techniques.

CT, MRI, and FDG-PET/CT are among the leading modalities employed in the diagnosis and follow-up of IgG4-RD. However, there is no established consensus regarding the optimal imaging strategy, including whether a single modality or a combination should be preferred in specific scenarios, or the ideal interval for follow-up imaging. Despite the increasing recognition of imaging's role in IgG4-RD, a standardized algorithm for its diagnostic and monitoring use remains undefined.

This study aims to retrospectively analyze the imaging modalities utilized for the diagnosis and follow-up of IgG4-RD patients monitored in our center. By evaluating the imaging approaches used in real-world clinical practice, we seek to provide insights into the role of different modalities in the diagnostic process and long-term management of IgG4-RD. The findings may contribute to optimizing imaging-based strategies for disease assessment and monitoring.

Materials and methods

Study design and participants

This study was designed as a retrospective, single-center, descriptive, observational conducted using records of all consecutive diagnosed with IgG4-RD accoridng to ACR/EULAR criteria (3) and followed between May 2020 and December 2024. Information related to demographics, clinical and laboratory findings, results of histopathologic evaluation and imaging methods used at diagnosis and durin follow-up were collected from patient charts and electronic records. Patients were divided into two groups based on the presence of acute kidney injury (serum creatinine level higher than 1.2 mg/dL for female and 1.3 mg/dL for male patients) at the diagnosis. Patients whose clinical, laboratory, or imaging data were inaccessible or incomplete were excluded from the study.

Assessment of imaging studies

All imaging modalities, including CT, MRI, and FDG-PET/CT, were assessed for their use in diagnosis and follow-up. Their combined usage, preference order, and frequency of repetition were recorded. Additionally, the time interval between imaging studies and the chosen modality were documented for each patient.

Ethical approval

The study protocol was approved by the Institutional Research Ethics Committee (Project number 12.01.2024/145), and written informed consent was not required due to the retrospective design of the study.

Statistical analysis

Data were evaluated for homogenicity of distrubitoun with Kolmogorov Smirnov test and presented as median values with ranges for continuous variables and as percentages for categorical variables. Differences in continuous variables between groups were analyzed using Mann Whitney U test, while differences in categorical data frequencies were analyzed using the χ^2 test. A p-value of <0.05 was considered statistically significant. Statistical analyses were performed using SPSS Statistics for Windows, version 28.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 18 patients diagnosed with IgG4-RD were included in the study, of whom 17 (94.4%) were male and 1 (5.6%) was female (**Table-1**). The median age at diagnosis was 48.5 years (range: 39–77), and the median disease duration was 37 months (range: 3–61). AKI at the time of diagnosis was observed in 10 patients (55.6%). The use of imaging modalities were given in Table 1 at diagnosis, T**able 2** according to presence of AKI at admission, and **Table 3** according to follow-up visits. Regarding imaging modalities, CT was the most frequently used technique at diagnosis (83.3%), followed by PET-CT (61.1%) and MRI (27.8%).

Table 1: Patient characteristics and laboratory parameters

Parameters	Patients (n=18)
Female/Male (n,%)	1/17 (5.6/94.4)
Age, year (median, range)	52 (43-77)
Age at diagnosis, year (median, range)	48.5 (39-77)
Disease duration, months (median, range)	37 (3-61)
Acute kidney injury at diagnosis (n, %)	10 (55.6)
Remmision at last visit (n, %)	16 (88.9)
Diagnostic evaluation at diagnosis	
Biopsy (n, %)	8 (44.4)
C-reactive protein mg/L (median, range)	65.7 (0.9-450.7)
Erythrocyte sedimentation rate mm/h (median, range)	49.5 (7-192)
Rheumatoid factor positivity (n, %)	0/11
Serum IgG4 positivity. (n, %)	1/12 (8.3)
PET-CT (n, %)	11 (61.1)
CT (n, %)	15 (83.3)
MRI (n, %)	5 (27.8)

* PET-CT: positron emission tomography-computed tomography, CT: computed tomography, MRI: magnetic resonance imaging

Combined imaging modalities were utilized in 12 patients (66.6%) at diagnosis, but their use decreased during follow-up, with a shift towards single-modality imaging, particularly CT or MRI.

When comparing follow-up imaging between patients with and without AKI at diagnosis, the first follow-up imaging modality demonstrated a trend toward statistical significance (p=0.072) and given in Table 2). In the AKI group, PET-CT was used in 4 patients (44.4%), CT in 3 patients (33.3%), PET-CT combined with MRI in 1 patient (11.1%), and CT combined with MRI in 1 patient (11.1%). In contrast, among patients without AKI, CT and MRI were each used in 3 cases (42.9%), while PET-CT was used in 1 case (14.3%). No significant differences were detected in subsequent follow-up imaging between the two groups.

Table 2: Patient characteristics and laboratory parameters according to presence of acute kidney injury at diagnosis

	AKI at diagnosis (n=10)	No AKI at diagnosis (n=8)	p- value
Female/Male (n,%)	1/9 (10/90)	0/8 (0/100)	0.556
Age, year (median, range)	56 (46-77)	48 (43-66)	0.138
Age at diagnosis, year (median, range)	55 (44-77)	43 (39-66)	0.058
Disease duration, months (median, range)	30.5 (3-61)	49 (4-60)	0.004
Remmision at last visit (n, %)	7 (87.5)	9 (90.0)	0.706
Diagnostic evaluation at diagnosis			
Biopsy (n, %)	5 (50.0)	3 (37.5)	0.480
C-reactive protein mg/L (median, range)	75.1 (49.2-450.7)	39.8 (0.9-140.0)	0.317
Erythrocyte sedimentation rate mm/h (median, range)	65.5 (32-192)	35.5 (7-86)	0.280
PET-CT (n, %)	6 (60.0)	5 (62.5)	0.648
CT (n, %)	8 (80.0)	7 (87.5)	0.568
MRI (n, %)	3 (30.0)	2 (25.0)	0.618

* PET-CT: positron emission tomography-computed tomography, CT: computed tomography, MRI: magnetic resonance imaging

Table 3: Use of imaging modalities and combinations at diagnosis and follow-up

Imaging modality	At diagnosis (n=18)	1st follow-up imaging (n=16)	2nd follow-up imaging (n=12)	3rd follow-up imaging (n=10)	4th follow-up imaging (n=3)	5th follow-up imaging (n=2)
PET-CT	1 (5.6)	5 (31.3)	3 (25.0)	2 (20.0)	1 (33.3)	0
CT	3 (16.6)	6 (37.5)	3 (25.0)	2 (20.0)	2 (66.7)	1 (50.0)
MR	2 (11.2)	3 (18.8)	5 (41.7)	6 (60.0)	0	1 (50.0)
PET-CT+CT	9 (50.0)	0	0	0	0	0
PET-CT+MRI	0	1 (6.3)	0	0	0	0
PET-CT+CT+MRI	1 (5.6)	0	0	0	0	0
CT+MRI	2 (11.2)	1 (6.3)	1 (8.3)	0	0	0
Time after last imaging, month (median, range)	N/A	3 (1-19)	6.5 (2-13)	7.5 (3-16)	3 (1-12)	7.5 (4-11)

* PET-CT: positron emission tomography-computed tomography, CT: computed tomography, MRI: magnetic resonance imaging

However, the interval between follow-up imaging was significantly shorter in patients with AKI (30.5 vs. 49 months, p=0.049).

At the last follow-up visit, remission was achieved in 16 patients (88.9%). The median interval between imaging studies progressively increased with each subsequent follow-up, with a median duration of 3 months (range: 1–19) for the first follow-up, 6.5 months (range: 2–13) for the second, and 7.5 months (range: 3–16) for the third. Notably, the use of PET-CT decreased over time, whereas MRI became the preferred modality in later follow-ups.

Discussion

The IgG4-RD is a complex, multisystem fibroinflammatory condition characterized by tumefactive lesions, storiform fibrosis, and infiltration of IgG4-positive plasma cells (4). Despite its growing recognition, the role of imaging modalities in both diagnosis and monitoring remains a subject of ongoing debate (5-9). Our study highlights the utilization trends of CT, MRI, and PET-CT in real-world clinical practice, revealing significant variations in follow-up strategies.

Our study demonstrated that CT was the most frequently employed imaging modality at diagnosis (83.3%), while PET-CT (61.1%) and MRI (27.8%) were also used, albeit with declining follow-up rates. These findings are consistent with previous studies that have underscored the diagnostic value of PET-CT in detecting multi-organ involvement in IgG4-RD (10-15). Zhang et al. demonstrated that PET-CT could identify additional organ involvement not detected by conventional imaging, thus improving diagnostic accuracy (16). Similarly, Zhao et al. confirmed that PET-CT effectively delineates disease extent and guides biopsy selection (17).

MRI usage in our cohort increased during follow-up, suggesting a preference for its non-ionizing nature and superior soft-tissue contrast. This aligns with Zheng et al., who emphasized MRI's role in distinguishing IgG4-related abdominal and pelvic involvement from malignancies (18). However, the lack of a standardized follow-up strategy remains a significant gap, necessitating consensus guidelines to optimize imaging protocols.

A unique aspect of IgG4-RD is its potential to affect the vasculature, particularly the aorta, leading to IgG4-aortitis and periaortitis. Our study identified variations in imaging modality selection between patients with and without acute kidney injury (AKI), a finding supported by Nikiphorou et al. and Jayachamarajapura et al. who detailed the challenges in diagnosing IgG4-related aortic involvemen (2,19). PET-CT has been reported to have superior sensitivity in detecting vascular inflammation, while MRI is advantageous for assessing wall thickening and fibrosis (20,21). The increased use of MRI in later follow-ups in our study suggests

a growing preference for non-invasive methods to evaluate chronic vascular involvement and status of mass lesion.

The classification criteria established by the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) provide a structured approach to diagnosing IgG4-RD (3). These criteria emphasize a combination of clinical, serological, histopathological, and radiological findings, underscoring the indispensable role of imaging. The criteria highlighted that proper integration of imaging findings significantly enhances diagnostic specificity. In our study, stratification based on AKI status revealed distinct imaging preferences, reinforcing the importance of personalized diagnostic strategies.

The lack of a uniform imaging follow-up strategy in IgG4-RD is a crucial issue, as evidenced by the variable imaging intervals observed in our study. The progressively increasing time intervals between follow-up imaging suggest that clinicians rely on clinical remission rather than predefined imaging protocols. This supports the necessity of standardized guidelines, particularly for high-risk patients, such as those with vascular involvement or renal impairment. Studies emphasized the role of multimodality imaging in monitoring inflammatory aortic aneurysms, a principle that could be extended to IgG4-RD (22-24).

Additionally, the role of imaging in treatment response evaluation remains underexplored. Our findings align with Zhang et al., who reported that PET-CT could effectively monitor steroid-induced metabolic changes in IgG4-RD (16). Future research should focus on defining optimal imaging intervals and modality selection based on disease phenotype and risk stratification.

Conclusions

In conclusion, our study highlights the evolving landscape of imaging in IgG4-RD, with a notable shift from multimodal imaging at diagnosis to single-modality approaches during follow-up. The findings underscore the need for standardized imaging protocols that consider disease phenotype, organ involvement, and treatment response. Given the increasing role of PET-CT in initial diagnosis and MRI in follow-up, future guidelines should integrate these modalities to ensure optimal patient management. Further prospective studies are warranted to establish evidence-based imaging algorithms that enhance diagnostic accuracy and long-term disease monitoring.

Conflict of interest

The authors report no conflict of interest.

Funding source

No funding was required.

Ethical Approval

The study protocol was approved by the Institutional Research Ethics Committee (Project number 12.01.2024/145).

Informed consent

No written informed consent was needed due to retrospective design of this study..

Acknowledgment:

None

Peer-review

Externally. Evaluated by independent reviewers working in at least two different institutions appointed by the field editor.

Data availability

The authors confirm that the data supporting the findings of this study are available within the article.

Contributions

Research concept and design: **RD, CB**

Data analysis and interpretation: **RD**

Collection and/or assembly of data: **RD**

Writing the article: **RD**

Critical revision of the article: **RD, CB**

Final approval of the article: **RD, CB**

All authors read and approved the final version of the manuscript.

All authors read and approved the final version of the manuscript.

References

1. Stone JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med. 2012;366(6):539-51.
2. Jayachamarajapura Onkaramurthy N, Suresh SC, Theetha Kariyanna P, Jayarangaiah A, Prakash G, Raju B. IgG4 related disease and aortitis: an up-to-date review. Scand J Rheumatol. 2023;52(3):306-16.
3. Wallace ZS, Naden RP, Chari S, Choi H, Della-Torre E, Dicaire JF, et al. The 2019 American College of Rheumatology/European League Against Rheumatism Classification Criteria for IgG4-Related Disease. Arthritis Rheumatol. 2020;72(1):7-19.
4. Zhang W, Stone JH. Management of IgG4-related disease. Lancet Rheumatol. 2019;1(1):e55-e65.
5. Sanchez-Oro R, Alonso-Munoz EM, Marti Romero L. Review of IgG4-related disease. Gastroenterol Hepatol. 2019;42(10):638-47.
6. Naik M, Hesni S, Tamimi A, Hameed M, Tomlinson J, Poo S, et al. Imaging manifestations of IgG4-related disease. Clin Radiol. 2023;78(8):555-64.
7. Kawano M, Saeki T. IgG4-related kidney disease--an update. Curr Opin Nephrol Hypertens. 2015;24(2):193-201.
8. Melenotte C, Seguier J, Ebbo M, Kaphan E, Bernit E, Saillier L, et al. Clinical presentation, treatment and outcome of IgG4-related pachymeningitis: From a national case registry and literature review. Semin Arthritis Rheum. 2019;49(3):430-7.
9. Ren H, Mori N, Sato S, Mugikura S, Masamune A, Takase K. American College of Rheumatology and the European League Against Rheumatism classification criteria for IgG4-related disease: an update for radiologists. Jpn J Radiol. 2022;40(9):876-93.
10. Negoto S, Tahara N, Nohara Y, Otsuka H, Tayama E. Utility of non-contrast MRI and FDG-PET/CT to assess inflammatory activity in IgG4-related abdominal aortic aneurysm. Eur Heart J Cardiovasc Imaging. 2024.
11. Takahashi H, Yamashita H, Morooka M, Kubota K, Takahashi Y, Kaneko H, et al. The utility of FDG-PET/CT and other imaging techniques in the evaluation of IgG4-related disease. Joint Bone Spine. 2014;81(4):331-6.
12. Nakatani K, Nakamoto Y, Togashi K. Utility of FDG PET/CT in IgG4-related systemic disease. Clin Radiol. 2012;67(4):297-305.
13. Cortes-Romera M, Sabate-Llobera A, Gamez-Cenzano C, Torras-Ambros J. [Usefulness of PET/CT in IgG4-related disease]. Med Clin (Barc). 2015;145(7):321-2.
14. Pucar D, Hinchcliff M. FDG PET vascular imaging in IgG4-RD: Potential and challenges. J Nucl Cardiol. 2022;29(6):2934-7.
15. Dai T, He YQ. CT and MRI features of multi-organ involvement in IgG4-related disease. Diagn Interv Imaging. 2023;104(5):261-2.
16. Zhang J, Chen H, Ma Y, Xiao Y, Niu N, Lin W, et al. Characterizing IgG4-related disease with (1)(8)F-FDG PET/CT: a prospective cohort study. Eur J Nucl Med Mol Imaging. 2014;41(8):1624-34.
17. Zhao Z, Wang Y, Guan Z, Jin J, Huang F, Zhu J. Utility of FDG-PET/CT in the diagnosis of IgG4-related diseases. Clin Exp Rheumatol. 2016;34(1):119-25.
18. Zheng Y, Elsayes KM, Waranch C, Abdelaziz A, Menias CO, Sandrasegaran K, et al. IgG4-related disease in the abdomen and pelvis: atypical findings, pitfalls, and mimics. Abdom Radiol (NY). 2020;45(8):2485-99.
19. Nikiphorou E, Galloway J, Fragoulis GE. Overview of IgG4-related aortitis and periaortitis. A decade since their first description. Autoimmun Rev. 2020;19(12):102694.
20. Fragoulis GE, Evangelatos G, Tektonidou MG. Vasculitis beyond aortitis in IgG4-related disease (IgG4-RD): case report and review of the literature. Clin Rheumatol. 2021;40(3):1167-73.
21. Lecler A, Sene T. MRI and ultrasonography are useful tools for a non-invasive diagnosis of IgG4-related disease. Ann Rheum Dis. 2022;81(3):e51.
22. Xu VYY, Bell M, Zahirieh A, Hsiao J, Higgins K, Ghorab Z, et al. A Challenging Diagnosis of IgG4-Related Disease When Understanding Limitations of Laboratory Testing Was Pivotal. Case Rep Med. 2017;2017:8748696.
23. Jolfayi AG, Salmanipour A, Heshmat-Ghahdarijani K, Meshgi S, Dastmardi M, Salehabadi G, et al. Imaging Findings in Cardiovascular Involvements of IgG4 Related Disease: A Systematic Review Study. Rheumatology (Oxford). 2025;64(3):943-51.
24. Czerniak S, Rao A, Mathur M. Multimodality pictorial review of IgG4-related disease in the abdomen and pelvis. Abdom Radiol (NY). 2023;48(10):3147-61.