Bibliographic reference	**The American journal of gastroenterology** **2000 95 (3) PAGES 712-714** **Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery** **Dickey, W., Hughes, D. F.et al.**
Study type	Cohort
Study quality	Could the selection of patients have introduced bias? UNCLEAR – not reported if a consecutive sample used Is there concern that the included patients do not match the review question? NO Could the conduct or interpretation of the index test have introduced bias?. NO Is there concern that the index test, its conduct, or interpretation differ from the review question? NO Could the reference standard, its conduct, or its interpretation have introduced bias? NO Is there concern that the target condition as defined by the reference standard does not match the review question? NO Could the patient flow have introduced bias? YES – 24 were excluded but explanation not given
Number of patients	53
Patient characteristics	Inclusion criteria: Presence of villous atrophy and positive IgA EMA Exclusion criteria: IgA deficiency, Non-compliance with diet or biopsy Age at diagnosis – mean (range): 51 years (16 – 81 years) Gender (M/F): 14/39 Immunoglobulin A (IgA) deficiency: None Time on gluten-free diet – mean (range) : 12 months Assessed by: Dietitian for adherence
Intervention	IgA EMA by indirect immunofluorescence using primate oesophagus (Biodiagnostics, Upto-upon-Severn, England) with a titer of ≥ 1.5 as cut-off Duodenal biopsy Dietitian assessment
Comparison	NA

Bibliographic reference	**The American journal of gastroenterology** **2000 95 (3) PAGES 712-714** **Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery** **Dickey, W., Hughes, D. F.et al.**
Length of follow up	12 months
Location	Northern Ireland
Outcomes measures and effect size	Resolution of gastrointestinal and non-gastrointestinal symptoms 48/53 (90.6%) IgA EMA – number testing negative At 3 months = 13/53 (58% At 6 months = 50/53 (75%) At 9 months = not reported At 12 months = 46/53 (87%) Duodenal biopsy TVA/STVA at baseline (n = 41) At 12 months = 13 were normal, 18 had PVA and 10 were non-responders (persistent TVA/STVA) PVA at baseline (n = 12): At 12 months = 7 were normal, 1 was Marsh grade 1 and 4 were non-responders (persistent PVA) Growth in children and young people Not reported Complications of coeliac disease Not reported Dietary adherence 5/53 (9.4%) reported as non-adherent

Bibliographic reference	**The American journal of gastroenterology** **2000 95 (3) PAGES 712-714** **Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery** **Dickey, W., Hughes, D. F.et al.**
	Impact on carers Not reported Health-related quality of life Not reported
Source of funding	None reported
Comments	All responders were adherent to GFD, non-responders were non-adherent Of 79 candidates for inclusion, 2 were EMA negative at baseline due to IgA deficiency, and 62 test EMA positive at baseline, 9 did not have a full 12 months of GFD, only 53 EMA + at baseline were followed up Study did not report on agreement or correlation between serology and biopsy
Bibliographic reference	**Autoimmunity** **2007 40 (2) PAGES 117-121** **Two-year follow-up of anti-transglutaminase autoantibodies among celiac children on gluten-free diet: comparison of IgG and IgA** **Martin-Pagola, Ainhoa, Ortiz-Paranza, Lourdeset al.**
Study type	Cohort
Study quality	Could the selection of patients have introduced bias? YES – unclear if a consecutive sample was used Is there concern that the included patients do not match the review question? NO Could the conduct or interpretation of the index test have introduced bias?. NO Is there concern that the index test, its conduct, or interpretation differ from the review question? NO

Bibliographic reference	**The American journal of gastroenterology** **2000 95 (3) PAGES 712-714** **Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery** **Dickey, W., Hughes, D. F.et al.**
	Could the reference standard, its conduct, or its interpretation have introduced bias? NO Is there concern that the target condition as defined by the reference standard does not match the review question? NO Could the patient flow have introduced bias? NO
Number of patients	93
Patient characteristics	Inclusion criteria: ESPGHAM diagnosis of CD with HLA-DRB! Typing and GFD adherent Exclusion criteria: Non-adherence to GFD Age at diagnosis – mean (range): 3.56 years (0.94 – 17.5) Gender (M/F): 35/58 (62.4% female) Immunoglobulin A (IgA) deficiency: Not reported Time on gluten-free diet – mean (range): 2 years Assessed by: Not reported
Intervention	IgA anti-tTG IgG anti-tTG Both determined by immunoprecipitation radioassays. S25 labeled human recombinant tTGase was incubated with 3µl of serum at 4oC overnight and immune complexes were precipitated with a 25% (v/V) suspension of protein-A agarose (Amersham Biosciences, Barcelona, Spain) for IgG or a 20% (v/v) suspension of agarose-conjugated IgA specific antibodies (Sigma cat. No. A2691) St Louis, MO) for IgA. Cut-off values were set as the sum of the mean and 3/SD of the index values of 50 serum samples from the general population.
Comparison	NA
Length of follow up	24 months
Location	Spain
Outcomes measures and effect size	Resolution of gastrointestinal and non-gastrointestinal symptoms (reported as remission)

Bibliographic reference	**The American journal of gastroenterology** **2000 95 (3) PAGES 712-714** **Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery** **Dickey, W., Hughes, D. F.et al.**
	Not reported Response – defined as number of people testing negative on serology At 6 months IgA: 46/93 (49%) IgG: 59/93 (63%) At 24 months IgA: 82/93 (88%) IgG: 90/93 (96%) Biopsy – response = normal biopsy N = 41* Of those with Marsh 3a or 3b at diagnosis 4 (9%) were Marsh 2 12 (30%) were Marsh 1 25 (61%) were Marsh 0 Growth in children and young people Not reported Complications of coeliac disease Not reported Dietary adherence Not reported

Bibliographic reference	**The American journal of gastroenterology** **2000 95 (3) PAGES 712-714** **Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery** **Dickey, W., Hughes, D. F.et al.**
	Impact on carers Not reported Health-related quality of life Not reported
Source of funding	Funded by the Spanish Ministry of Health
Comments	Only 41 consented to a second biopsy after 2 year GFD Only those with elevated serology titers at baseline followed up Study did not report on agreement or correlation between serology and biopsy
Bibliographic reference	**Journal of internal medicine** **2004 256 (6) PAGES 519-524** **Antibody levels in adult patients with coeliac disease during gluten-free diet: a rapid initial decrease of clinical importance** **Midhagen, G., Aberg, A. K.et al.**
Study type	Cohort
Study quality	Could the selection of patients have introduced bias? NO Is there concern that the included patients do not match the review question? NO Could the conduct or interpretation of the index test have introduced bias?. Yes – unclear of exact timing of tests Is there concern that the index test, its conduct, or interpretation differ from the review question? NO Could the reference standard, its conduct, or its interpretation have introduced bias? NO Is there concern that the target condition as defined by the reference standard does not match the review question? NO

Bibliographic reference	**The American journal of gastroenterology** **2000 95 (3) PAGES 712-714** **Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery** **Dickey, W., Hughes, D. F.et al.**
	Could the patient flow have introduced bias? NO
Number of patients	20
Patient characteristics	Inclusion criteria: Diagnosed with CD with March 3 criteria Exclusion criteria: IgA deficiency Age at diagnosis – median (range): 62 years (29 – 86 years) Gender (M/F): 10/12 (54.5% female) Immunoglobulin A (IgA) deficiency: NA Time on gluten-free diet – mean (range) : 12 months Assessed by: Dietitian for adherence
Intervention	AGA (AGA was tested using UniCAP Gliadin IgA (Pharmacia Diagnostics, Uppsala, Sweden) and was defined as positive with a result >3 $mg_A\ L^{-1}$.) tTGgrh (Celikey®, tTGrh, IgA antibody assay (Pharmacia Diagnostics, Freiburg, Germany). It was defined by the producer as positive when >8 U mL^{-1}, negative when <5 U mL^{-1}, borderline between 5 and 8 U mL^{-1}) tTGgp (ImmuLisa®, tTGgp with guinea-pig-derived tTG (IMMCO, Buffalo, NY, USA). The result was defined by the producer as positive when >25 U, negative when <20 U, borderline when 20–25 U) IgA EMA (indirect immunofluoflourescence using monkey oesophageal tissue. Tissue sections from marmoset monkey oesophagus were mounted on microscopic slides. Undiluted sera and sera diluted 1 : 25 with phosphate-buffered saline (PBS) was applied to slides, which were incubated for 30 min at room temperature. After washing with PBS the sections were covered with fluorescein conjugated rabbit-antihuman IgA (Dako, Copenhagen, Denmark) for 30 min, washed with PBS and examined by fluorescence microscopy. Positive sera were further diluted (1 : 5, 1 : 10, 1 : 25, 1 : 100, 1 : 400 and 1 : 1600). Sera positive in dilution 1 : 10 or more were defined as positive

Bibliographic reference	**The American journal of gastroenterology** **2000 95 (3) PAGES 712-714** **Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery** **Dickey, W., Hughes, D. F.et al.**
	Biopsy (Three to four biopsy specimens were obtained during upper endoscopic examination of each patient from the lower part of the duodenum descendens with standard forceps. All biopsies were fixed in a 4% buffered formaldehyde solution. Fixation, embedding and cutting were carried out according to routine methods)
Comparison	NA
Length of follow up	12 months
Location	Sweden
Outcomes measures and effect size	Resolution of gastrointestinal and non-gastrointestinal symptoms (reported as remission) 16/18 (88.9%) Response – defined as number of people testing negative on serology <u>AGA IgA</u> at 3 months =9/114 (74%) at 6 months = 14/15 (93%) at 9 months = not reported at 12 months = 15/15 (100%) <u>IgA EMA</u> at 3 months =7/17 (41%) at 6 months = 13/17 (65%) at 9 months = not reported at 12 months = 14/16 (87%) <u>IgA tTGrh</u> at 3 months = 8/14 (57%)

Bibliographic reference	**The American journal of gastroenterology** **2000 95 (3) PAGES 712-714** **Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery** **Dickey, W., Hughes, D. F.et al.**
	at 6 months = 10/14 (71%) at 9 months = not reported at 12 months = 14/14 (100%) Biopsy – response = normal biopsy At 12 months = 16/18 (88.9%) Growth in children and young people Not reported Complications of coeliac disease Not reported Dietary adherence Not reported Impact on carers Not reported Health-related quality of life Not reported
Source of funding	Authors are research staff at Pharmacia Diagnostic manufacturers for some of the testing kits but they state no financial support was received.
Comments	1 person excluded for IgA deficiency and 1 not included in results as they stopped the GFD 2 participants did not have a repeat biopsy at 12 months,

Bibliographic reference	**The American journal of gastroenterology** **2000 95 (3) PAGES 712-714** **Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery** **Dickey, W., Hughes, D. F.et al.**
	Both non-responders at 12 months were in remission at follow-up biopsy but no timeframe reported Study did not report on agreement or correlation between serology and biopsy

Bibliographic reference	**Digestive diseases and sciences** **1999 44 (10) PAGES 2133-2138** **Clinical application of immunological markers as monitoring tests in celiac disease** **Fotoulaki, M., Nousia-Arvanitakis, S.et al**
Study type	Cohort (Prospective)
Study quality	Could the selection of patients have introduced bias? UNCLEAR – not reported if consecutive sample used Is there concern that the included patients do not match the review question? NO Could the conduct or interpretation of the index test have introduced bias?. NO Is there concern that the index test, its conduct, or interpretation differ from the review question? NO Could the reference standard, its conduct, or its interpretation have introduced bias? NO Is there concern that the target condition as defined by the reference standard does not match the review question? NO Could the patient flow have introduced bias? NO
Number of patients	30
Patient characteristics	Inclusion criteria: Diagnosis of CD according to EPSGHAN criteria

Bibliographic reference	**Digestive diseases and sciences** **1999 44 (10) PAGES 2133-2138** **Clinical application of immunological markers as monitoring tests in celiac disease** **Fotoulaki, M., Nousia-Arvanitakis, S.et al**
	Exclusion criteria: None reported Age at diagnosis – mean (range): 6 (1 – 24 years) Gender (M/F): 13/17 (56.7% female) Immunoglobulin A (IgA) deficiency: 3/30 (10%) Time on gluten-free diet – mean (range) : 12 months Assessed by: Not reported
Intervention	IgA EMA Ig ARA
Comparison	NA
Length of follow up	12 months
Location	Greece
Outcomes measures and effect size	Resolution of gastrointestinal and non-gastrointestinal symptoms Not reported Response – defined as the number of people testing negative on serology <u>IgA EMA</u> At 3 months = 17/30 (57%) At 6 months = 25/30 (83%) At 9 months = 17/30 (90%) At 12 months = 30/30 (100%) <u>Ig ARA</u> At 3 months = 23/30 (77%) At 6 months = 26/30 (87%)

Bibliographic reference	**Digestive diseases and sciences** **1999 44 (10) PAGES 2133-2138** **Clinical application of immunological markers as monitoring tests in celiac disease** **Fotoulaki, M., Nousia-Arvanitakis, S.et al**
	At 9 months = 30/30 (100%) At 12 months = 30/30 (100%) Growth in children and young people Not reported Complications of coeliac disease Not reported Dietary adherence Not reported Impact on carers Health-related quality of life Not reported
Source of funding	None reported
Comments	This study reports that ‘as the half-life of IgA is shorter than that of IgG, the IgA antibodies respond more rapidly to gluten changes in the diet and, therefore, are more appropriate for the follow-up of CD patients” IgA AGA and IgG AGA examined with home-made kits also studied so data were not used in this review Study did not report on agreement or correlation between serology and biopsy

Bibliographic reference	**Laboratory Medicine** **2011 42 (8) PAGES 497-501** **Importance of the educational environment in the evolution of celiac disease** **Samasca, G., Iancu, M.et al.**
Study type	Cohort (prospective)
Study quality	Could the selection of patients have introduced bias? UNCLEAR – not reported if a consecutive ample used Is there concern that the included patients do not match the review question? UNCEAR – age group not reported Could the conduct or interpretation of the index test have introduced bias?. NO Is there concern that the index test, its conduct, or interpretation differ from the review question? NO Could the reference standard, its conduct, or its interpretation have introduced bias? NO Is there concern that the target condition as defined by the reference standard does not match the review question? NO Could the patient flow have introduced bias? NO
Number of patients	50
Patient characteristics	Inclusion criteria: Diagnosis of CD based on the presence of flattened intestinal villi on duodenal biopsy. Exclusion criteria: None reported Age at diagnosis – mean (sd): mean not reported range 6 – 11 years Gender (M/F): 17/33 (67% female) Immunoglobulin A (IgA) deficiency: Not reported Time on gluten-free diet – 24 months
Intervention	.IgA tTG
Comparison	NA
Length of follow up	24 months
Location	Romania
Outcomes measures and effect size	Resolution of gastrointestinal and non-gastrointestinal symptoms Not reported

Bibliographic reference	**Laboratory Medicine** **2011 42 (8) PAGES 497-501** **Importance of the educational environment in the evolution of celiac disease** **Samasca, G., Iancu, M.et al.**
	number of people with negative test results <u>IgA tTG</u> at 3 months = 34/50 (68%) at 6 months = 34/50 (68%) at 9 months – not reported at 12 months = 41/50 (82%) at 24 months = 40/50 (80%) Growth in children and young people Not reported Complications of coeliac disease Not reported Dietary adherence Not reported Impact on carers Not reported Health-related quality of life Not reported
Source of funding	The authors report no conflicts of interest.
Comments	Study did not report on agreement or correlation between serology and biopsy

Bibliographic reference	**Laboratory Medicine** **2011 42 (8) PAGES 497-501** **Importance of the educational environment in the evolution of celiac disease** **Samasca, G., Iancu, M.et al.**

Bibliographic reference	**Autoimmune Diseases** **2014, Article ID 623514, 7 pages, 2014** **Celiac disease in adult patients: specific autoantibodies in the diagnosis, monitoring, and screening,** **Trigoni, E., Tsirogianni, A et al**
Study type	Cohort (Retrospective)
Study quality	Could the selection of patients have introduced bias? UNCLEAR not reported if a consecutive sample used Is there concern that the included patients do not match the review question? NO Could the conduct or interpretation of the index test have introduced bias?. NO Is there concern that the index test, its conduct, or interpretation differ from the review question? NO Could the reference standard, its conduct, or its interpretation have introduced bias? NO Is there concern that the target condition as defined by the reference standard does not match the review question? NO Could the patient flow have introduced bias? NO
Number of patients	70
Patient characteristics	Inclusion criteria: Newly diagnosed with CD Exclusion criteria: None reported Age at diagnosis – mean (sd): 39 years (11.1) Gender (M/F): 20/50 (71.4% female) Immunoglobulin A (IgA) deficiency: 0/70 (0%) Time on gluten-free diet – 36 months

Bibliographic reference	**Autoimmune Diseases** **2014, Article ID 623514, 7 pages, 2014** **Celiac disease in adult patients: specific autoantibodies in the diagnosis, monitoring, and screening,** **Trigoni, E., Tsirogianni, A et al**
	Assessed by: Not reported
Intervention	Anti-endomysium (EmA) which were determined semiquantitative by the technique of indirect immunofluorescence (IIF) using a commercial kit INOVA (NOVA Lite Monkey Oesophagus IFA Kit/Slides, USA) on a 5-μm-thin cryostat section of distal monkey oesophagus as antigen substrate. Patient samples were tested in dilutions ranging from 1 : 5 to 1 : 2560. The antibody titre was defined as the highest sample dilution yielding fluorescence. Titre below1 : 5 was considered negative. Anti-tissue transglutaminase class IgA (tTG-A) which were assayed using a commercial anti-tTG type IgA ELISA test kit (QUANTA LiteTM, INOVA Diagnostics, USA). The cut-off value provided was 25U. ELISA was performed in duplicate according to the manufacturer's instruction.
Comparison	NA
Length of follow up	36 months
Location	Greece
Outcomes measures and effect size	Resolution of gastrointestinal and non-gastrointestinal symptoms Not reported Growth in children and young people Not reported Response reported as number of people testing negative serology among those who were strictly compliant <u>IgA EMA</u> At 6 months = 20/51 (39.2%) At 12 months = 37/51 (72.5%) At 36 months = 48/51 (94.1%) <u>IgA tTG</u> At 6 months = 10/51 (19.6%)

Bibliographic reference	**Autoimmune Diseases** **2014, Article ID 623514, 7 pages, 2014** **Celiac disease in adult patients: specific autoantibodies in the diagnosis, monitoring, and screening,** **Trigoni, E., Tsirogianni, A et al**
	At 12 months = 25/51 (49.0%) At 36 months = 41/51 (80.4%) Complications of coeliac disease Not reported Dietary adherence 19 were considered partially adherent while 51 were considered strictly adherent Impact on carers Not reported Health-related quality of life Not reported
Source of funding	No funding reported but conflicts of interest listed
Comments	Unable to calculate data for accuracy of detecting non-adherence Study did not report on agreement or correlation between serology and biopsy

Bibliographic reference	**Clinical chemistry** **2002 48 (6 Pt 1) PAGES 960-963** **Comparative evaluation of serologic tests for celiac disease diagnosis and follow-up** **Martini, Silvia, Mengozzi, Giulioet al**
Study type	Cohort (prospective)
Study quality	Could the selection of patients have introduced bias? NO Is there concern that the included patients do not match the review question? NO Could the conduct or interpretation of the index test have introduced bias?. NO Is there concern that the index test, its conduct, or interpretation differ from the review question? NO Could the reference standard, its conduct, or its interpretation have introduced bias? NO Is there concern that the target condition as defined by the reference standard does not match the review question? NO Could the patient flow have introduced bias? NO
Number of patients	101
Patient characteristics	Inclusion criteria: CD confirmed buy biopsy (Marsh 2 or March 3) and positive clinical response to GFD Exclusion criteria: None reported Age at diagnosis – median (range): 37 years (21 – 72) Gender (M/F): 22/79 (78.1% female) Immunoglobulin A (IgA) deficiency: (%) Time on gluten-free diet – 12 months Assessed by: Not reported
Intervention	Serum EmAs were detected by immunofluorescence, using commercial slides of monkey esophagus (The Binding Site Ltd., distributed by Alfa Biotech). Sera were tested, as indicated by the manufacturer, at a 1:10 initial dilution, with the inclusion of positive and negative controls in every batch of tests. CD EmA-negative sera were further tested at a 1:5 dilution, and no false-negative results were obtained. Used four commercially available sandwich ELISAs that use human recombinant antigen (h-tTG): h-tTG 1 (DRG Diagnostics, distributed by Pantec S.r.l.); h-tTG 2 (EU-tTG® IgA; Eurospital S.p.A); h-tTG 3 (Immunodiagnostik, distributed by Li StarFISH); and h-tTG 4 (CELIKEYTM; Pharmacia & Upjohn, which uses human recombinant antigen extracted from eukaryotic cells. The

Bibliographic reference	**Clinical chemistry** **2002 48 (6 Pt 1) PAGES 960-963** **Comparative evaluation of serologic tests for celiac disease diagnosis and follow-up** **Martini, Silvia, Mengozzi, Giulioet al**
	same evaluation was also carried out with a sandwich ELISA that uses guinea pig tTG antigen (gp-tTG; GENESIS Diagnostics, distributed by Pantec S.r.l Duodenal biopsy
Comparison	NA
Length of follow up	12 months
Location	Italy
Outcomes measures and effect size	Resolution of gastrointestinal and non-gastrointestinal symptoms Not reported Growth in children and young people Not reported Response reported as number of people normal duodenal biopsy at 12 months Normal (mucosal recovery) = 12/101 (12%) Improvement (Marsh grade I) = 51/101 (50%) no change (Marsh grade II or III) = 38/101 (38%) Complications of coeliac disease Not reported Dietary adherence NA Impact on carers Not reported

Bibliographic reference	**Clinical chemistry** **2002 48 (6 Pt 1) PAGES 960-963** **Comparative evaluation of serologic tests for celiac disease diagnosis and follow-up** **Martini, Silvia, Mengozzi, Giulioet al**
	Health-related quality of life Not reported
Source of funding	None reported
Comments	Mean percentage changes in anti-tTG values were 81% (range, 75–86%) for h-tTG 1, 51% (range, 43–60%) for h-tTG 2, 51% (range, 42–61%) for h-tTG 3, 77% (range, 69–85%) for h-tTG 4, and 75% (range, 67–82%) for gptTG. The concordances of the different assays in both positive (persistent histologic impairment and positive serologic markers) and negative (reconstituted mucosa and negative serologic markers) individuals vs histologic score were 29% for h-tTG 1, 65% for h-tTG 2, 14% for h-tTG 3, 16% for h-tTG 4, and 19% for gp-tTG, compared with 48% for EmA testing.

Bibliographic reference	**Dewar (2012): Celiac disease: management of persistent symptoms in patients on a gluten-free diet** **Reference ID:**
Study type and aim	Prospective cohort study to establish aetiology of continued symptoms on a gluten-free diet (GFD)
Study quality	1. Could the selection of patients have introduced bias? 2. Is there concern that the included patients do not match the review question? 3. Could the conduct or interpretation of the index test have introduced bias? 4. Is there concern that the index test, its conduct, or interpretation differ from the review question? 5. Could the reference standard, its conduct, or its interpretation have introduced bias? 6. Is there concern that the target condition as defined by the reference standard does not match the review question? 7. Could the patient flow have introduced bias?

Bibliographic reference	Dewar (2012): Celiac disease: management of persistent symptoms in patients on a gluten-free diet Reference ID:
	Overall risk of bias:
Number of patients	Total N = 112
location	England
Patient characteristics	**Inclusion criteria:** Patients prospectively recruited who were referred with a diagnosis of non-responsive coeliac disease (NRCD) between 2002 and 2003. All patients had continued symptoms on a gluten free diet **Exclusion criteria**: none listed **Mean age**: 48.5 **Mean age at diagnosis**: 31 years **Mean years since diagnosis**: 3 years (1 – 12 years)
Signs and symptoms	Lethargy 43% Diarrhoea 65% Abdominal pain 37% Weight loss 23% Nausea and vomiting 10% Anemia 10% 2 symptoms = 49% 3 symptoms 20%
Investigations	Appraisal of CD diagnosis, history of symptoms, clinical exam, routine blood tests and assessment of diet and GFD compliance. 'Patients were then investigated according to usual clinical practice and subsequent findings'. Those who developed further symptoms were reinvestigated. Unless an obvious cause was immediately apparent, a further bowel biopsy was undertaken. Jumbo endoscopy forceps were used to obtain four samples that were carefully placed, mucosal surface upwards.
Length of follow up	All patients followed for a minimum of 2 years

Bibliographic reference	**Dewar (2012): Celiac disease: management of persistent symptoms in patients on a gluten-free diet** **Reference ID:**
Outcome	Cause of non-responsive CD
Results	Primary causes of NRCD: • Incorrect CD diagnosis: 12/112 (11%) • Gluten ingestion: 45/100 (45%) • Microscopic colitis: 11/100 (11%) • Bacterial overgrowth: 9/100 (9%) • Lactose intolerance: 7/100 (7%) • Inflammatory colitis 7/100 (7%) • IBS: 10/100 (10%) • RCD 9/100 (9%) Other causes: (all 1 - 2 %) • Anorexia • Pancreatic insufficiency • Diverticular disease • Medication-induced diahorrea • Combined variable immunodeficiency • Colorectal cancer • Anorectal dysfunction • Human immunodeficiency virus
Source of funding	Not stated
Comments	
Definition of NRCD: Failure of expected symptomatic response to GFD Total N CD = 100 (after removal of 12 non-CD)	

Bibliographic reference	Dewar (2012): Celiac disease: management of persistent symptoms in patients on a gluten-free diet Reference ID:
After 2 years 78% reported being symptom-free	

Bibliographic reference	Leffler (2007): Etiologies and predictors of diagnosis in nonresponsive celiac disease Reference ID:
Study type and aim	Cohort (retrospective) study to determine etiologies of NRCD
Study quality	1. Could the selection of patients have introduced bias? 2. Is there concern that the included patients do not match the review question? 3. Could the conduct or interpretation of the index test have introduced bias? 4. Is there concern that the index test, its conduct, or interpretation differ from the review question? 5. Could the reference standard, its conduct, or its interpretation have introduced bias? 6. Is there concern that the target condition as defined by the reference standard does not match the review question? 7. Could the patient flow have introduced bias? **Overall risk of bias:**
Number of patients	Total N = 113 consecutive patients identified as NRCD from a pool of 603 biopsy-confirmed CD patient
location	US
Patient characteristics	• **Inclusion criteria**: a database of all patients diagnosed with biopsy-proven CD between 2000 and 2006 was examined for cases of NRCD and RCD defined by criteria listed below. For analyses, RCD cases were grouped with ulcerative jejunitis (UJ) and enteropathy associated T-cell lymphoma (EATL). • **Exclusion criteria**: Individuals without definitive evidence of CD in the form of duodenal biopsy exam, or a skin biopsy in case of dermatitis herpetiformis were not included • **Mean age**: NA • **Mean age at diagnosis**: 42 years

Bibliographic reference	Leffler (2007): Etiologies and predictors of diagnosis in nonresponsive celiac disease Reference ID:
	• **Mean years since diagnosis**: NA • **Mean duration of symptoms**: NA
Signs and symptoms	• Diarrhoea: 54% • Lethargy: 5% • Abdominal pain: 55% • Weight loss : 20% • Nausea and vomiting : NA • Anaemia: NA
Investigations	Clinical notes, lab data, and diagnostic tests performed were investigated for each individual patient to identify evidence of NRCD. All entries were reviewed twice for accuracy Patients believed to be at high risk were evaluated for T-cell clonality and aberrant T-cell markers.
Length of follow up	Mean follow up = 20 months (2 – 126 months)
Outcome	Cause of non-responsive CD
Results	Primary causes of NRCD: • Incorrect CD diagnosis: 14/113 (12%) • Gluten ingestion: 36% • Microscopic colitis: 6% • Bacterial overgrowth (SIBO): 6% • Lactose intolerance: 8% • Inflammatory colitis:NA • IBS: 22% • RCD: 10% Other causes:

Bibliographic reference	Leffler (2007): Etiologies and predictors of diagnosis in nonresponsive celiac disease Reference ID:
	• Eating disorder • Peptic ulcer disease • Gastroparesis • Crohn's disease • Fod allergy • CVID • Duodenal adenoma
Source of funding	Not Stated
Comments	
Diagnostic criteria for NRCD: referral for evaluation of lack of response to a gluten free diet. Failure of clinical symptoms or lab abnormalities typical of CD to improve within 6 months after GFD. Recurrence of symptoms and/or lab abnormalities typical of CD while on GFD. Refractory CD definition: persistence of villous atrophy despite strict GFD and no evidence of another pathology, including overt lymphoma	

Bibliographic reference	Abdulkarim (2002): Etioloy of nonresponsive celiac disease: results of a systematic approach Reference ID:
Study type and aim	Cohort (retrospective) study to identify causes of persistent symptoms in patients with NRCD and characterise patients with RCD
Study quality	1. Could the selection of patients have introduced bias? 2. Is there concern that the included patients do not match the review question? 3. Could the conduct or interpretation of the index test have introduced bias? 4. Is there concern that the index test, its conduct, or interpretation differ from the review question? 5. Could the reference standard, its conduct, or its interpretation have introduced bias? 6. Is there concern that the target condition as defined by the reference standard does not match the review question? 7. Could the patient flow have introduced bias?

Bibliographic reference	**Abdulkarim (2002): Etioloy of nonresponsive celiac disease: results of a systematic approach** **Reference ID:**
	Overall risk of bias:
Number of patients	Total N = 55
location	US
Patient characteristics	• **Inclusion criteria**: patients who had been evaluated for NRCD between 1997 and 2001. Included in the study when a definite diagnosis of CD was secured based on the clinical picture, on biopsy findings compatible with CD, and on criteria met for diagnosis of NRCD or RCD (listed below). • **Exclusion criteria**: Patients excluded if the CD diagnosis was reversed based on absence of CD on biopsy and presence of other disease responsible for their symptoms • **Mean age NRCD**: 51.3 (21-80) • **Mean age RCD:** 66.1 (56-82) • **Mean age at diagnosis**: • **Mean years since diagnosis**:
Signs and symptoms	• Diarrhoea: 84% • Lethargy:37% • Abdominal pain: 52% • Weight loss :47% • Nausea and vomiting : 17% and 10%, respectively • Anaemia: 37%
Investigations	Patient records and small bowel biopsy results were reviewed. Patients underwent a systematic sequential evaluation including: • detailed dietary review, • serological testing for CD • repeat small intestinal and

Bibliographic reference	**Abdulkarim (2002): Etioloy of nonresponsive celiac disease: results of a systematic approach** **Reference ID:**
	• colonic biopsy, • small bowel aspirates for quantitative culture, • 72 hr stool fat measurement • small bowel radiographic studies • CT body imaging. All tests were not done in patients if an obvious case of symptoms was found which resulted in resolution of symptoms Dietary assessment involved 3 steps: 1. Physician review and direct questioning regarding patient's perspective of GFD 2. Direct and detailed evaluation by a dietician expert in celiac disease and the GFD 3. Serological tests, primarily endomysial antibodies (EMA) and gliadin antibodies (AGA)
Length of follow up	
Outcome	Cause of non-responsive CD
Results	Primary causes of NRCD: • Incorrect CD diagnosis: 6/55 (11%) (49 patients with CD) • Gluten ingestion: 25/49 (51%) • Microscopic colitis: 5/49 (10%) • Bacterial overgrowth: 7/49 (14%) • Lactose intolerance :NA • Inflammatory colitis :NA • IBS: 4/49 (8%) • RCD: 9/49: (18%) Other causes: • Pancreatic insufficiency 6/49 • Protein losing enteropathy

Bibliographic reference	**Abdulkarim (2002): Etioloy of nonresponsive celiac disease: results of a systematic approach** **Reference ID:**
	True RCD cases- further investigations: • T-cell receptor gene rearrangement: 6/9 tested for T-cell receptor gene rearrangement – 2/6 positive • Bone mineral density: 7/9 measured. 6/7 (85%) had osteoporosis. Prevalence of osteoporosis in RCD significantly higher than NRCD (10/28, 35%).
Source of funding	
Comments	
NRCD definition: persistence or recurrence of symptoms for up to 12 months, despite presumed GFD RCD: defined as persistence of symptoms and evidence for histological injury despite adhering to GFD for up to 12 months When original diagnosis of CD not made in authors institution (49 cases), original biopsy slides were retrieved if possible/ 32 original specimens retrieved and reviewed by same GI pathologist. Diagnosis in remaining cases based on original biopsy report, repeat biopsy, serological markers for CD, and response to GFD. Of those without CD, diagnosis was IBS (2/6), protein losing enteropathy (1/6|), malrotation of the gut (1/6), wheat allergy (1/6) Whipple disease (1/6).	

Bibliographic reference	**Hadithi (2007): The value of double-balloon enteroscopy in patients with refractory celiac diseae** **Refernce ID:**
Study type and aim	Prospective cohort study to assess value of double-balloon enteroscopy in patients with RCD
Study quality	1. Could the selection of patients have introduced bias? 2. Is there concern that the included patients do not match the review question? 3. Could the conduct or interpretation of the index test have introduced bias? 4. Is there concern that the index test, its conduct, or interpretation differ from the review question? 5. Could the reference standard, its conduct, or its interpretation have introduced bias?

Bibliographic reference	Hadithi (2007): The value of double-balloon enteroscopy in patients with refractory celiac diseae Refernce ID:
	6. Is there concern that the target condition as defined by the reference standard does not match the review question? 7. Could the patient flow have introduced bias? **Overall risk of bias:**
Number of patients	Total N = 21
location	Netherlands
Patient characteristics	**Inclusion criteria:** consecutive patients referred to specialist centre for DBE between 2004 and 2005 all patients were symptomatic on a strict GFD for a median period of 60 months and were suffering from persistent villous atrophy on duodenal histology. **Exclusion criteria**: None listed **Mean age**: 61 (41-89) **Mean age at diagnosis**: NA **Mean years since diagnosis**:5 (0.3 – 33)
Signs and symptoms	17/21 were symptomatic: Lethargy NA Diarrhea 11/21 (52%) Abdominal pain 3/21 (14%) Weight loss 3/21 (14%) Nausea and vomiting NA Anemia NA
Investigations	Primary: Double balloon enteroscopy (DBE) o Done within 4-6 weeks of initial duodenoscopy o Endoscope and flexible overtube both provided with soft latex balloons connected through built-in air route to a

Bibliographic reference	Hadithi (2007): The value of double-balloon enteroscopy in patients with refractory celiac diseae Refernce ID:
	controlled pump system. ○ Advancement or withdrawal of scope achieved by deflating or inflating balloons ○ Endoscope introduced orally in all patients ○ Length of visualized small bowel was estimated by calculating su of each sequential progressive extension of the scope through overtue ○ Patients prepared with Klean Prep bowel cleanse ○ Midazolam mean dose 10mg and mean dose 7.5 µg of fentanyl for conscious sedation ○ Small bowel assessed for a-priori defined low risk: reduction (≤ 3 per endoscopic field of view) or loss of folds, scalloping, nodularity or muscosa or mosaicism, visible vessels, after air insufflation. ○ Ulcerations at ;eat 5mm in diameter and stenosis were considered high risk lesions for their potential risk of harbouring malignancy ○ Endoscopic findings considered jejunal if were found in proximal 2-3 m of the calculated endoscopic insertion depth ○ Small bowel as visualized by DBE divided into proximal, distal, and middle, and 4 biopsies taken from each segment. Diagnostic workup prior to DBE: • IgA tTTG, IgA EMA CD antibodies • HLA DQ2/DQ8 genotyping • Eosophagogastroduodenoscopy • Abdominal CT (n=14) • Video capsule endoscopy (n=7)
Length of follow up	Median interval of 36 months
Outcome	Utility of DBE in examination of patients with RCD
Results	DBE findings: Jejunal ulcerations which revealed presence of EATL found in 5/21 (24%) of patients (95% CI: 10-45%) Ulcerative lesions in absence of histological evidence of EATL found in another 2 patients (9%; 95% CI: 2-28%). – histology of nonulcerative mucosa classified as Marsh 3 and therefore were considered to have ulcerative jejunitis In remaining 14 patients (66%), low risk features i.e. flattened villi, loss of folds, scalloping, and nodularity were

Bibliographic reference	Hadithi (2007): The value of double-balloon enteroscopy in patients with refractory celiac diseae Refernce ID:
	found by double balloon enteroscopy – these patients diagnosied wih RCD on basis of persistent villous atrophy despite GFD Esophagogastroduodenoscopy findings: Could detect low-risk lesions in duodenum Did not detect EATL nor ulcerative jejunitis in any patient CT findings: Abnormal in 4 patients with EATL Missed diagnosis of EATL in 1 patient Missed both ulcerative jejunitis patients Presence of EATL further suggested in 4/7 patients who had CT – after median 36month follow-up none of these patients developed lymphoma Author conclusions: complications of RCD like EATL and UJ can be efficiently detected or excluded by DBE
Source of funding	
Comments	
Duodenal and small bowel biopsies evaluated according to Marsh criteria Diagnosis of EATL: Established according to WHO classification based o histological and immunohistochemical features and TCR gene rearrangement studies. Immunohistochemical features are evidence of large or medium sized T-cell proliferation expressing CD3(+) CD8 (+-)and CD103(+) Standard esophagogastroduodenoscopy failed to diagnose 2 EATL patients due to limitations in introducing the endoscopy beyond ligament of Treitz Ulcers are more commonly located in the jejunum and ileum rather than duodenum and DBE more easily able to investigate these distal locations.	

Bibliographic reference	Van Weyenberg (2013): Video capsule endoscopy in patients with nonresponsive Celiac disease Reference ID:
Study type and aim	Retrospective cohort study to describe VCE findings in NRCD and identify VCE findings associated with poor prognosis

Bibliographic reference	**Van Weyenberg (2013): Video capsule endoscopy in patients with nonresponsive Celiac disease** **Reference ID:**
Study quality	1. Could the selection of patients have introduced bias? 2. Is there concern that the included patients do not match the review question? 3. Could the conduct or interpretation of the index test have introduced bias? 4. Is there concern that the index test, its conduct, or interpretation differ from the review question? 5. Could the reference standard, its conduct, or its interpretation have introduced bias? 6. Is there concern that the target condition as defined by the reference standard does not match the review question? 7. Could the patient flow have introduced bias? **Overall risk of bias:**
Number of patients	Total N = 48
location	Netherlands
Patient characteristics	**Inclusion criteria:** all adults who underwent VCE for evaluation of persisting symptoms despite GFD at specialist centre between 2005 and 2010. Patients divided into four classifications: Uncomplicated CD (n=22), RCD I (n=12), RCD II (n=11), EATL (n=3) **Exclusion criteria**: For EATL patients; patients were excluded if they had a diagnosis of primary EATL, with no diagnosis of CD prior to developing EATL. **Mean age**: • uncomplicated:49 (18.5) • RCD I: 62 (9.8) • RCD II: 63 (9.8) • EATL: 64 (1.7) **Mean age at diagnosis**: • uncomplicated:42 (18.6) • RCD I: 49 (13.4) • RCD II: 55 (15.5) • EATL: 60 (3.7)

Bibliographic reference	**Van Weyenberg (2013): Video capsule endoscopy in patients with nonresponsive Celiac disease** **Reference ID:**
	Mean years since diagnosis: NA
Signs and symptoms	• Lethargy - NA • Diarrhea – 24/48 (50%) • Abdominal pain – 8/48 (17%) • Weight loss – 12/48 (25%) • Nausea and vomiting - NA • Anemia - 2/48 (4%)

Investigations	• VCE
	  ○ Performed only in absence of signs suggestive of small-intestinal stenosis
	  ○ 2L polyethylene glycol bowel preparation
	  ○ Small intestine divided into proximal (first ¼) and a distal part (remaining ¾) based on small-bowel transit time (SBTT)
	  ○ When small bowel exam incomplete, used transit data from complete studies and defined proximal small intestine as part of visualized within 2 SD of mean ¼ of the SBBT of complete studies
	  ○ Proximal and distal part of all VCE studies were reviewed for signs derived from previous publications on VCE or conventional endoscopy in CD, inc:
	  ▪ Villous atrophy
	  ▪ Mosaic pattern
	  ▪ Scalloping of folds
	  ▪ Mucosal fissures
	  ▪ Erosions
	  ▪ Ulcers
	  ▪ Strictures
	  ▪ Masses
	  ○ Size of erosion and ulcers classified arbitrary as either small (≤5mm), intermediate (5-10 mm), or large

Bibliographic reference	Van Weyenberg (2013): Video capsule endoscopy in patients with nonresponsive Celiac disease Reference ID:

	(>10mm).
	• Small bowel biopsy
	  ○ Obtained during esophagogastroduodenoscopy and/or DBE within 2 months of VCE
	  ○ Graded according to Marsh classification
	• T-cell flowcytometry
	
	• Double-balloon endoscopy

Length of follow up	For Uncomplicated and RCD patients, mean follow up 25 months. For EATL patients, 2 months.
Outcome	VCE, flowcytometry, findings in uncomplicated, RCD and EATL patients
Results	Other causes of NRCD found in 17 patients: • Gluten ingestion: 14 • Lactose intolerance: 2 • Inflammatory colitis: 1 VCE findings: No clear relationship between size and number of erosions or ulcers and final diagnosis. 2 patients (RCD I and uncomplicated CD) diagnosed with ulcerative jejunitis Most abnormalities encountered in proximal small bowel Comparison according to prognosis: low risk (uncomplicated RCD and RCD I) vs high risk (RCD II and EATL) Presence of proximal focal erythema associated with risk of poor prognosis (i.e. diagnosis of RCD II or EATL) Absence of progression of the capsule to the distal intestine was associated with increased risk of poor prognosis (i.e. diagnosis of RCD II or EATL). No patients without these features died at follow up 2/15 (13%) patients with one of these died at follow-up 4/5 (80%) patients with both of these features died at follow-up **Author conclusion**: VCE minimally invasive endoscopic modality that could be of use in identifying patients with NRCD who

Bibliographic reference	Van Weyenberg (2013): Video capsule endoscopy in patients with nonresponsive Celiac disease Reference ID:
	require urgent and intensive medical treatment
Source of funding	
Comments	

Definitions:

Uncomplicated CD: diagnosed if during follow-up clinical symptoms, villous atrophy, and positive serology improved without need for immunosuppression, or if an alternative reason for symptoms was established

RCD: defined by persistent or recurrent malabsorbtive symptoms and villous atrophy despite strict GFDfor at least 6 months in the absence of other causes.

RCD type I: characterised by normal, polyclonal immunophenptype of IEL's with favourable response to nutritional support and immunosuppressive therapy

RCD type II: characterised by presence of intraepithelial lymphocytes immunophenotype or by differences in clonality of the T-cell receptor (TCR) gene. Abnormal phenotype (>20% of the CD 103(=)/CD45(+) IEL's lacking surface CD3 on flowcytometry).

EATL: diagnosis based on international WHO criteria. Divided into primary and secondary. Primary excluded. Secondary is when patients were known to have CD prior to EATL diagnosis

Ulcerative jejunitis: defined as presence of ≥ 3 ulcers in the jejunum during enteroscopy

Bibliographic reference	Van Weyenberg (2011): MR enteroclysis in refractory celiac disease: proposal and validation of a severity scoring system Reference ID:
Study type and aim	Retrospective cohort study to determine MR enteroclysis findings in patients with uncomplicated CD, RCDI, and RCD II, and to determine diagnostic accuracy of MR enteroclysis to detect CD-related malignancies
Study quality	1. Could the selection of patients have introduced bias? 2. Is there concern that the included patients do not match the review question? 3. Could the conduct or interpretation of the index test have introduced bias? 4. Is there concern that the index test, its conduct, or interpretation differ from the review question?

Bibliographic reference	**Van Weyenberg (2011): MR enteroclysis in refractory celiac disease: proposal and validation of a severity scoring system** **Reference ID:**
	5. Could the reference standard, its conduct, or its interpretation have introduced bias? 6. Is there concern that the target condition as defined by the reference standard does not match the review question? 7. Could the patient flow have introduced bias? **Overall risk of bias:**
Number of patients	Total N=68
location	Netherlands
Patient characteristics	**Inclusion criteria:** From VU hospital MR database, authors identified 80 MR enteroclysis studies that were obtained between 2004 and 2009 in 72 patients who experienced symptoms despite being on a GFD. Consecutive studies obtained from Sept 2004 – Dec 2005 were included in the test group and used to construct a scoring system to predict RCD II. Consecutive studies obtained from January 2006 – July 2009 were included in the validation group and used to validate the scoring system. • Test group – n=28 • Validation group - n=40 **Exclusion criteria**: follow-up studies (n=12) obtained after chemotherapy and/or autologous hematopoietic stem cell transplantation for RCD or enteropathy-associated T-cell lymphoma were excluded **Mean age**: 56 (18-81) **Mean age at diagnosis**: NA **Mean years since diagnosis:** NA:
Signs and symptoms	Lethargy - NA Diarrhea – 5/68 (7%) Abdominal pain – 21/68 (31%) Weight loss – 34/68 (50%) Nausea and vomiting – 3/68 (4%) Anemia - NA

Bibliographic reference	**Van Weyenberg (2011): MR enteroclysis in refractory celiac disease: proposal and validation of a severity scoring system** **Reference ID:**

Investigations	MR enteroclysis
	• Overnight fast, 9-F nasojejunal tube positioned distal to duodenojejunal junction with fluoroscopic guidance
	• During MR imaging, a minimum of 2000mL of 0.5% methylce3llulose solution in water was infused through the tube, at a flow rate of 80-100mL/min using MR compatible pump system. No IV contrast used
	• Imaging ceased when optimal distension of the full small bowel and cecum was obtained
	• No antispadmodics administered
	• Number of jejunal folds and ileal folds per 5cm calculated by using maximum value of three measurements for each loop
	• Small bowl thickening was considered to be present when the wall thickness of a distended small-bowel loop was more than 3mm
	• Itaussception defined as a target mass or a complex layered mass within the bowl luman
	• Lymph nodes larger than 1cm in diameter in their shortest axis considered enlarged
	• Mesenteric fat infiltration defined as decrease in signal intensity of mesentry surrounding mesenteric vessels
	Study Pipeline:
	• Test group (n=28)
	  ○ Patients grouped into uncomplicated CD; RCD I or RCD II (see diagnostic criteria below)
	  ○ Comparison of diagnostic groups – NB this is exploratory only, no corrections for multiple comparisons were made.
	  ○ Identification of predictors for RCD II – Continuous MR enteroclysis features were dichotomized by using cut-off levels determined by identifying the point where the sensitivity and specificity to detect RCD II were equal on the ROC
	  ○ Construction of scoring system – by utilizing independent predictors of RCD II
	• Validation group (n=40)
	  ○ Validation of scoring system in second group of patients
	  ○ Analysis of inter observer variation
	• Whole-group analysis (n=68)
	  ○ Survival analysis in all patients

Bibliographic reference	**Van Weyenberg (2011): MR enteroclysis in refractory celiac disease: proposal and validation of a severity scoring system** **Reference ID:**
	○ Calculation of accuracy for detection of malignancy
Length of follow up	28 months
Outcome	MR enteroclysis findings and validation of scoring system
Results	MR enteroclysis findings: Patient group comparisons in test group • No MR parameter differed significantly between patients with uncomplicated CD or RCD I • Median jenunal folds per 5cm lower in RCD II vs RCD I or CD • Splenic volume lower in RCD II vs RCD I • Diffuse bowel thickening and jenunoileal fold pattern reversal more frequently observed in RCD II than in CD • Mesenteric fat infiltration more prevalent in RCD II than RCD I Scoring system construction • Multivariate analysis showed following parameters to be independently associated with RCD II: ○ Presence of less than 10 folds per 5cm jejunum ○ Diffuse bowel wall thickening ○ Mesenteric fat infiltration • At optimal cut-off from ROC analyses of 2, none of 10 patients with RCD II were missed anf absence of RCD correctly diagnosed in 15/18 patients without RCD II • Readers disagreed for 9/40 studies on one feature • 6/9 discrepancies occurred in patients with RCD II • Agreement on: ○ 37/40 wall thickening ○ 37/40 mesenteric fat infiltration ○ 37/40 on <10 jejunal folds **see below for proposed scoring system

Bibliographic reference	**Van Weyenberg (2011): MR enteroclysis in refractory celiac disease: proposal and validation of a severity scoring system** **Reference ID:**

Diagnostic accuracy of MR enteroclysis scoring system in test group
Sensitivity 100% (66 – 100), specificity 83% (58-96)

TP 10	FN 3
FP 0	TN 15

Diagnostic accuracy of MR enteroclysis scoring system in validation group
Sensitivity 87% (58 – 98), specificity 96% (78-100),

TP 13	FN 1
FP 2	TN 24

Survival analysis and detection of CD-related malignancy

- 14/68 patients died during follow-up
  - 2/41 with MR score of <2
  - 12/27 with MR score of ≥2
  - Diagnosis RCD II in 13/14 of those that died
  - Causes = EATL (n=8); sepsis (n=2); meningo-encephalitis (n=2); disseminated small-bowel carcinoma (n=1),

Bibliographic reference	**Van Weyenberg (2011): MR enteroclysis in refractory celiac disease: proposal and validation of a severity scoring system** **Reference ID:**
	malabsorption (n=1) • 5 year cumulative survival rate 95% in patients with MR score <2 compared with 56% in patients with an MR score ≥2
Source of funding	
Comments	
<u>Definintions</u>: **CD**: diagnosed based on the results of duodenal biopsies and positive serology for antihuman tTG and EMA in all patients Uncomplicated CD: diagnosed if during follow-up clinical symptoms and villous atrophy improved without the need for immunosuppressive therapy **RCD I:** diagnosed in case of persisting villous atrophy despite a GFD, but with normal phenotype of IEL's **RCD II**: diagnosed in case of persisting villous atrophy with abnormal phenotype IEL's **EATL** and adenocarcinoma: histological analysis of biopsy or resection specimens, and were established according to international consensus criteria Proposed scoring system: score calculated by adding total number of points • Number of jejunal folds per 5cm o ≥10 = 0 points o <10 = 1 point • Mesenteric fat infiltration o Present = 1 point o Absent = 0 point • Diffuse bowel wall thickening o Present = 1 point o Absent = 0 point Author conclusions: : MR enteroclysis can be used to investigate the presence of RCD II or malignancy in symptomatic patients with CD	