

Chapter 18

Medical Follow-up of Celiac Patients

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Abstract

This chapter presents practical recommendations for the medical follow-up of patients with celiac disease. The gluten-free diet is currently the only available treatment for celiac disease. Patients with celiac disease require lifelong adherence to the gluten-free diet and medical follow-up. The benefits of strict adherence to the gluten-free diet including control of symptoms, seroconversion, and mucosal healing are discussed in detail. Despite extensive evidence of the benefits of the strict adherence to the gluten-free diet, rates of compliance and medical follow-up in clinical practice are less than optimal. The advantages and limitations of the four methods currently available for assessment of compliance to gluten-free diet (detailed dietary history, serology, histology and structured questionnaires) are summarized. Expert opinion and guidelines endorsed by several Medical Societies agree on the necessity of a medical follow-up; however, there is no universal consensus about how to perform said medical follow-up in daily practice. An algorithm for the medical follow-up of celiac disease patients is suggested based on available evidence and the author's institutional experience, which includes regular medical follow-up, annual serology measurement, evaluation of a detailed dietary history, assessment of clinical response and correction of nutritional deficiencies.

1. Initial Considerations

- The gluten-free diet is the only available treatment for celiac disease.
- Celiac patients require lifelong medical monitoring.
- There is no consensus regarding the most effective way to implement this medical monitoring.
- The basic objectives of medical monitoring are to facilitate adherence to the gluten-free diet and keep track of clinical response to treatment.

2. Introduction

The only currently available treatment for celiac disease is a strict adherence to the gluten-free diet, which involves removing all foods that contain wheat, barley and rye.¹ The benefits of a strict adherence to the gluten-free diet in celiac patients are considerable and include symptom control and prevention of complications.²

The percentage of people who achieve strict adherence to treatments involving a change in eating habits (59% on average) is among the lowest compared with other medical treatment modalities.³ *Compliance with medical treatment has a direct and objective influence in patient prognosis.* The basic goals of medical celiac disease follow-up are to facilitate monitoring the gluten-free diet and to monitor patient response to the treatment.⁴ Unfortunately, medical monitoring is deficient in most celiac patients and, in many cases, nonexistent.⁵ Therefore, it is not surprising that the percentage of adherence to the gluten-free diet is variable (42-91%).² Celiac patients require a medical monitoring plan and it is evident that establishing or confirming the diagnosis should not be the ultimate end of consultation with the gastroenterologist.⁶

Celiac disease is a chronic condition and, as such, requires lifelong medical follow-up.⁷ Although most experts recommend medical follow-up, there is no consensus on how and who should carry out medical monitoring in daily practice.⁸ There are few quality studies, based on evidence, on how to establish monitoring rules.

The objectives of this chapter are 1) to summarize the evidence on the benefits of strict adherence to a gluten-free diet and 2) to propose practical recommendations for the health monitoring of celiac disease patients based on available expertise and the author's institutional experience.

3. Benefits of Adherence to the Gluten-Free Diet

The gluten-free diet is a safe and effective treatment for controlling celiac disease symptoms and it may also decrease the risk of complications.⁹ A notable improvement in diarrhea may be observed as early as 7 days into the diet; it also improves in most of the patients (80%) within 60 days of strict adherence to the gluten-free diet.¹⁰

A strict gluten-free diet adherence is associated with a decrease in the absolute value of basal titers of anti-tissue transglutaminase antibodies (and other specific antibodies), which can be observed as early as 3 months into the gluten-free diet and tends to become more pronounced within the first year.¹¹ Antibody seroconversion (change of a test result from positive to negative) in relation to tissue transglutaminase was observed in 93% of the patients who submitted to an annual monitoring.¹²

Intestinal villi recovery is often incomplete and requires several years of strict adherence to the gluten-free diet in patients diagnosed as adults.^{13,16} In our experience, the recovery of intestinal villi in adult celiac patients was of 34% after 2 years and of 66% after 5 years of adhering to the gluten-free diet.¹⁴ On the other hand, the recovery of intestinal villi in children appears to happen much earlier, occurring in 95% of the cases within the first 2 years after starting the gluten-free diet, although the evidence is limited.¹⁵

Strict adherence to a gluten-free diet for at least 5 years appears to decrease the risk of developing lymphoma (relative risk was of 78% in patients without adherence to the diet and of 17% in patients who complied with the gluten-free diet).¹⁷ The risk of lymphoproliferative disease was null in celiac patients without villous atrophy¹⁸, which suggests that the good adhesion to the gluten-free diet with subsequent normalization of histology may be an aim to consider in medical monitoring.

4. Adherence Monitoring Methods

There are four methods available to verify proper compliance with the gluten-free diet, such as: 1) Consultation with a dietitian, 2) Tracking of serology evolution, 3) Monitoring of bowel biopsy changes and 4) Use of structured questionnaires to assess adherence to the gluten-free diet.^{8,19}

Consultation with a dietitian is the “gold standard” to control adherence to the gluten-free diet.¹

Tissular anti-transglutaminase and anti-endomysium antibody titers greatly diminish and/or become normal in patients with good adherence to the gluten-free diet.^{11,20,21} In patients with a strict adherence to the gluten-free diet and who achieve seroconversion, anti-tissue transglutaminase and anti-endomysium antibodies rise when a gluten challenge test is performed.²⁰ These data suggest that the presence of positive anti-transglutaminase (or anti-endomysium) antibodies in the symptomatic patient after one year of follow-up requires further evaluation in order to detect the presence of accidental or intentional gluten contamination.²² Furthermore, negative antibodies can be observed in symptomatic patients who are exposed to accidental contamination with small amounts of gluten and in those who, while remaining asymptomatic, have follow-up biopsies with persistent atrophy.¹⁴ The absence of serum

antibodies in symptomatic patients (usually severe), with a strict adherence to a gluten-free diet is a feature of refractory celiac disease.²³

Intestinal biopsy is the only currently available method to definitively assess the recovery of the intestinal mucosa. The need for intestinal biopsy during follow-up is a highly controversial topic.²⁴ The video capsule is a new technique able to detect lesions suggesting intestinal mucosal atrophy (fissures, lack of folds, paving pattern) at the moment of clinical diagnosis and mucosal response after starting a gluten-free diet²⁵; however, it has not been systematically evaluated as a clinical follow-up method.

Finally, the use of a structured questionnaires to evaluate adherence to the gluten-free diet has been proposed.^{1,9,26,27} Generally, these questionnaires seem to correlate with the antibody level and/or the results of follow-up intestinal biopsies. The information obtained using the questionnaire developed in Boston (CDAT) appears to be superior to monitoring through the determination of tissular anti-transglutaminase antibodies.¹⁹ The questionnaire validated in Italy has the advantage that it can be administered by persons without any experience and that the average time for its completion is of one minute.²⁷ A limitation for the implementation of structured questionnaires in daily clinical practice is the need for their validation in clinical contexts and languages different from the one used where the questionnaire was initially created.

5. Medical Follow-up Recommendations

All medical societies and the opinion of international experts agree on the usefulness of performing a medical follow-up, but there is no unanimous consensus about what is the best way to do this.²⁸ The medical follow-up that patients obtain is generally based on local and/or personal practices.

The recommendations proposed by medical societies or expert opinions for monitoring are quite diverse.^{4,8,29} Most recommend periodic monitoring of symptoms, serology (anti-transglutaminase antibodies), consultation with an expert dietician and joining a local and/or regional support group. No consensus exists on the type of general laboratory studies needed to control the celiac patient's routine, on the need of regular bone densitometry tests and on intestinal biopsies during the follow-up.²⁸ The cost of follow-up visits can vary significantly according to the protocol used.²⁸ No study suggests that, regarding a long-term prognosis, one follow-up protocol is better than the other. The American Gastroenterological Association (AGA) recommends performing the following general laboratory studies in follow-up visits: complete blood count, folate, ferritin, calcium and alkaline phosphatase.⁴ By contrast, the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) recommends no routine general laboratory studies in celiac children during follow-up visits.²⁹

In the authors' clinical practice clinical monitoring of children and adults is performed 3-6 months into the gluten-free diet and then once every year (Figure 1).

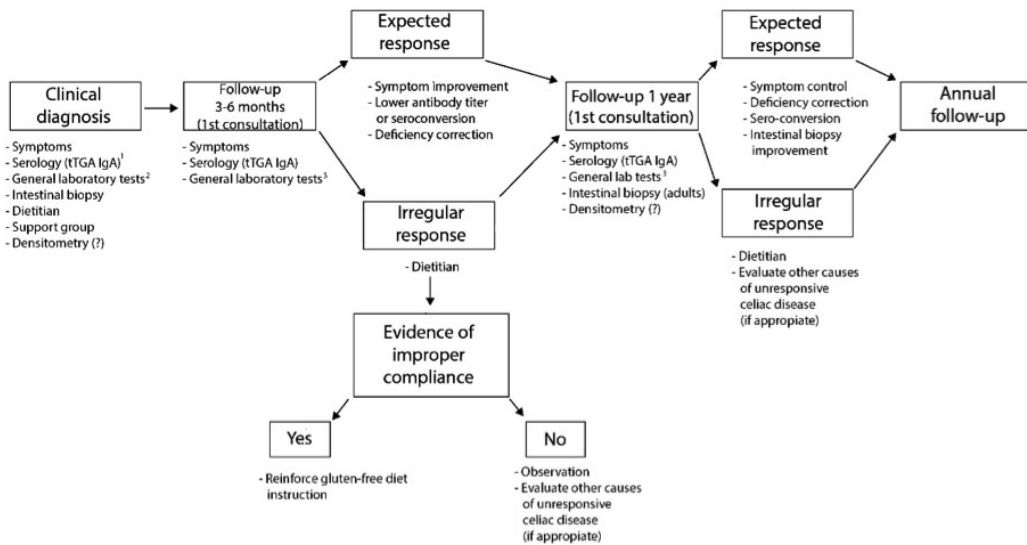


Figure 1. Clinical follow-up diagram for children and adults.¹ tTGA IgA (anti-tissue transglutaminase IgA antibody) is the serology of choice for the diagnosis and management of celiac patients.² General laboratory diagnoses include complete blood count, alanine aminotransferase (ALT), vitamins (A, D, E, and B12), copper, zinc, carotenoids, folate, ferritin, iron.³ General laboratory monitoring will only include only those studies that were abnormal at the time of diagnosis to verify their proper correction with the specific treatment.

The objectives of follow-up visits include:

- Documenting the improvement/disappearance of symptoms.
- Monitoring adherence to the gluten-free diet and to identify barriers to its successful implementation.
- Weight and height measurement (in children, complete growth assessment).
- Evaluating the response (titer decrease) of specific antibodies, relative to the baseline (the same antibody that was positive at diagnosis must be used and ideally, at the same laboratory).
- Confirming the correction of all nutritional deficiencies identified at diagnosis (for which monitoring laboratory tests should be individualized).

In the authors' institution consultation with the dietitian is performed at diagnosis and during the follow-up visit conducted within one year of initiating the gluten-free diet. Subsequent consultations with a nutrition specialist are evaluated in each individual case, taking into account the results obtained after the initial instruction and the presence of persistent or recurrent symptoms.³⁰ In routine clinical practice, consultation with the dietitian whenever possible is favored, although the authors' admit they work in a center specialized in celiac disease

management. A group of British celiac patients who answered a survey stated that their preferred follow-up method was consulting with a dietitian and having a doctor available if necessary.³¹ A common problem is that some centers lack access to dietitians experienced in gluten-free diet management. Additionally, no study shows that consulting with both a dietitian and a physician is better, in terms of prognosis, than consulting with only one of them. A Finnish study suggests that a high percentage of dietary adherence (>80%) can be achieved with a medical follow-up carried out in by the primary care physician.³²

3 to 6 months after the initial visit, the next one will take place one year after starting treatment with the following objectives:

- Documenting the total monitoring of symptoms.
- Checking anti-transglutaminase antibody seroconversion.
- Confirming the correction of general laboratory tests that were altered at the time of diagnosis.

There is sufficient evidence to indicate that regular monitoring including annual serology (anti-tissue transglutaminase) promotes adherence to the gluten-free diet.¹² Although it may seem questionable, the authors' include in their daily clinical practice an indication for repeat endoscopy with intestinal biopsies in the monitoring of adults in order to check histological response to treatment (usually after 1-2 years of proper adherence to gluten-free diet). The follow-up biopsy is particularly useful to evaluate histological response to the gluten-free diet in those patients who were diagnosed in the context of a specific negative serology and whose initial biopsy showed villous atrophy (in the authors' experience, 15-20% of the patients).³³ Intestinal biopsy monitoring is not considered necessary in children with good clinical response and anti-transglutaminase antibody seroconversion.

In all patients the authors' assess bone mineral density by densitometry at diagnosis or within one year of initiating a gluten-free diet, although this recommendation may seem questionable.

It is the authors' practice to recommend to all their patients to join a local and/or regional celiac patient support group. Participation in a support group or patients' association is one of the factors consistently associated with better adherence to the gluten-free diet.³⁴

In patients with good clinical response, subsequent follow-up visits are made each year (sometimes every 2 years) and include assessment of adherence to the gluten-free diet and serology. In a study conducted in Italy, which included a systematic and determined yearly anti-tissue transglutaminase antibodies for 5 years in a series of 2245 patients, it was demonstrated that 69% of the patients achieved permanent seroconversion; 1% did not achieve seroconversion and, in 30% of the cases, the results of serology monitoring oscillated between positive and negative values.

The goals of long-term medical follow-up of celiac disease patients in remission are to strengthen instruction on adherence to the gluten-free diet and avoid or facilitate early detection of associated diseases and/or complications.

6. Conclusions

Celiac patients require medical monitoring for life. There is no consensus on how to carry out monitoring. Generally, available recommendations are based on expert opinion. There is sufficient evidence to ensure that strict adherence to a gluten-free diet generates a positive impact in the short-to-long-term in celiac disease patients.

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