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Information about filaggrin genotype is valuable for adult atopic dermatitis patients

Editor

Loss-of-function mutations in filaggrin gene (*FLG*) represent the hitherto strongest genetic risk factor for AD.[1] *FLG* mutations have been associated with an early onset of dermatitis, a severe and persistent course, and in the context of dermatitis, an increased risk of asthma, rhinitis, hand eczema as well as irritant and allergic contact dermatitis.[2–7]

In 2009, a PCR-based *FLG* mutation analysis became available in our clinic.[8–10] Our physicians have since then been

Table 1 Clinical characteristics of the study population stratified by self-reported filaggrin genotype

	Filaggrin mutation status according to patient report (study population *n* = 115)*			
	Self-reported filaggrin mutation carriers *n* = 35 % (*n*/ntotal)	**Self-reported wild-type carriers *n* = 27 % (*n*/ntotal)**	**Patients who did not remember their test result *n* = 18 % (*n*/ntotal)**	**No response to the question on filaggrin mutation status *n* = 35 % (*n*/ntotal)**
Mean age, years (range)	43.4 (18–73)	43.9 (18–79)	43.8 (19–88)	42.5 (18–92)
Male, gender	34.3 (12/35)	37.0 (10/27)	44.4 (8/18)	37.1 (13/35)
Medical history				
Hand eczema	74.3 (26/35)	63.0 (17/27)	94.4 (17/18)	61.8 (21/34)
Asthma	54.3 (19/35)	34.6 (9/26)	47.1 (8/17)	45.7 (16/35)
Food allergy	48.6 (17/35)	26.9 (7/26)	23.5 (4/17)	34.3 (12/35)
Rhinitis	74.3 (26/35)	50.0 (13/26)	58.8 (10/17)	31.4 (11/35)
History of atopic disease in the family	74.2 (23/31)	88.5 (23/26)	62.5 (10/16)	78.1 (25/32)
Age at onset of dermatitis <18 years	94.1 (32/34)	76.0 (19/25)	83.3 (15/18)	84.4 (27/32)
Consequence of atopic dermatitis				
Daily pruritus	74.3 (26/35)	70.4 (19/27)	82.4 (14/17)	85.3 (29/34)
Sleep disturbance	96.8 (30/31)	82.6 (19/23)	93.8 (15/16)	83.9 (26/31)
Absence from work or school due to dermatitis	38.2 (13/34)	48.1 (13/27)	41.2 (7/17)	60.0 (21/35)
Dermatitis influenced my choice of profession or education	48.6 (17/35)	48.1 (13/27)	50.0 (9/18)	45.7 (16/35)
Xerosis influenced my choice of profession or education	45.7 (16/35)	33.3 (9/27)	44.4 (8/18)	45.7 (16/35)
Dermatitis led to a change of profession or training	17.1 (6/35)	14.8 (4/27)	16.7 (3/18)	22.9 (8/35)
Dermatitis feels like a disability	67.6 (23/34)	51.9 (14/27)	66.7 (12/18)	74.3 (26/35)
Previous treatments				
Systemic corticosteroids	47.1 (16/34)	40.7 (11/27)	44.4 (8/18)	60.6 (20/33)
Azathioprine, methotrexate or cyclosporine	38.7 (12/31)	24.0 (6/25)	23.5 (4/17)	22.6 (7/31)
Phototherapy	65.7 (23/35)	55.6 (15/27)	66.7 (12/18)	58.8 (20/34)
Filaggrin information provided by physician				
Written information was received	48.5 (16/33)	43.5 (10/23)	7.7 (1/13)	50 (1/2)
Oral information was received	85.3 (29/34)	85.2 (23/27)	58.3 (7/12)	50 (1/2)
Information about filaggrin gene status is important in relation to:				
A positive personal value to the patient	69.7 (23/33)	59.3 (16/27)		
Understanding of dermatitis pathogenesis	65.7 (23/35)	19.2 (5/26)		
Treatment	42.9 (15/35)	19.2 (5/26)		

Table 1 *Continued*

	Filaggrin mutation status according to patient report (study population *n* = 115)*			
	Self-reported filaggrin mutation carriers *n* = 35 % (*n*/ntotal)	**Self-reported wild-type carriers *n* = 27 % (*n*/ntotal)**	**Patients who did not remember their test result *n* = 18 % (*n*/ntotal)**	**No response to the question on filaggrin mutation status *n* = 35 % (*n*/ntotal)**
Knowing my filaggrin gene status has resulted in:				
Improvement of skin care habits	25.7 (9/35)	25.9 (7/27)		
Increased use of emollient	26.5 (9/34)	22.2 (6/27)		

*Patients were categorized as filaggrin mutation and wild-type carriers based on their response in a questionnaire study and not by PCR analysis.

recommended to routinely genotype patients with AD as it was assumed that AD patients would benefit from knowing their *FLG* mutation status.[2,4,5]

In 2014, a small survey was conducted to examine the potential patient benefit of knowing their *FLG* genotype. Briefly, a questionnaire was sent to 169 random adult patients who had been followed for AD at our department that year. All study participants had been categorized as having AD by the treating dermatologist and had also been genotyped for common mutations in *FLG*, i.e. R501X, 2282del4 and R2447X.[8] It was standard procedure to inform all patients about their genotype and physicians were expected to provide the patients with both oral and written information about the role of filaggrin and *FLG* mutations for the skin barrier and risk of dermatitis and comorbidities.

The questionnaire contained questions about AD and the possible benefit of knowing the *FLG* mutation status (Table 1). The Chi-square test, or where appropriate the Fisher exact test, was used to compare dichotomous variables. A two-sided *P*-value of <0.05 was considered statistically significant.

A total of 115 (68%) patients returned the questionnaires; 62 (53.9%) patients responded that they remembered their genotype, 18 (15.7%) that they did not remember their genotype and 35 (30.4%) did not respond at all to the question about their *FLG* mutation status (Fig. 1). Overall, among patients who remembered their genotype, most results were in accordance with PCR results.

The following analyses were based on the patient's self-reported genotype and *not* the PCR results, as the study aim was

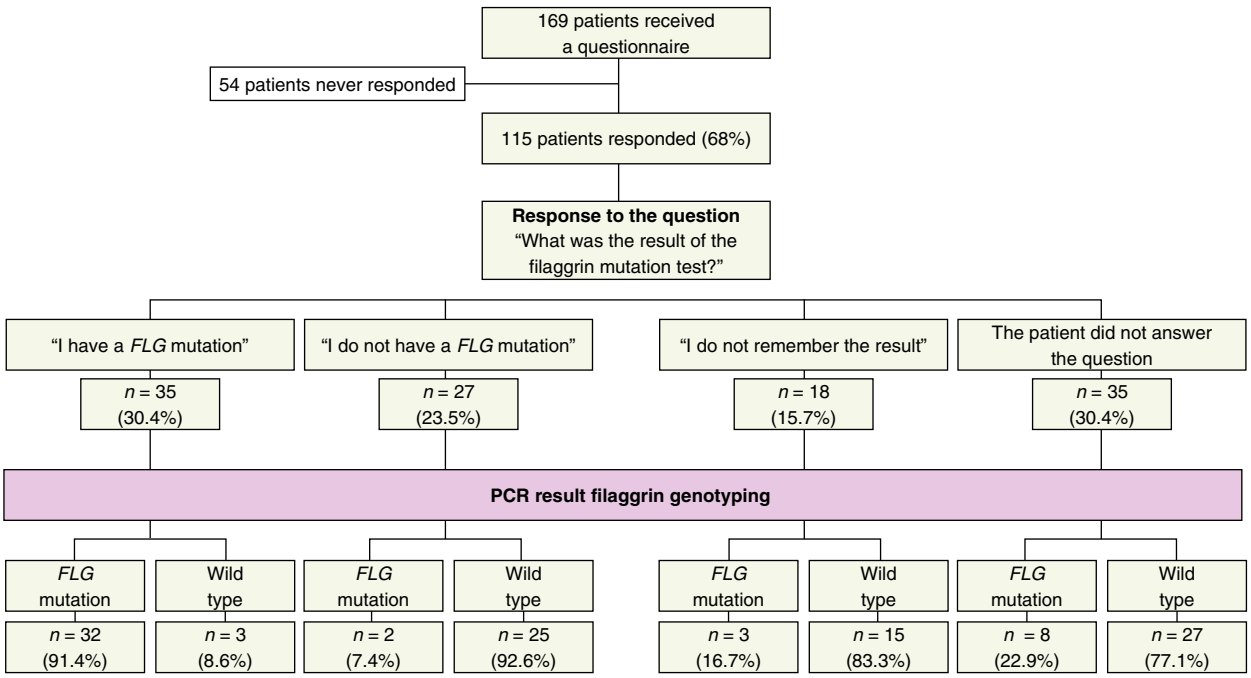

Figure 1 Flow chart of patients enrolled in this study.

to evaluate the personal value. Knowing their filaggrin genotype was considered of positive personal value for 23 (69.7%) self-reported *FLG* mutation carriers and 16 (59.3%) wild-type carriers ($P = 0.40$). Also, 23 (65.7%) of self-reported *FLG* mutation carriers reported that their understanding of AD pathogenesis had improved significantly from knowing their filaggrin genotype as compared to 5 (19.2%) of self-reported wild-type carriers ($P < 0.001$). The filaggrin genotype was of significant importance in relation to treatment of AD in 15 (42.9%) self-reported *FLG* mutations carriers compared to 5 (19.2%) self-reported wild-type group carriers ($P = 0.05$). However, surprisingly, improvement in skin care habits was similar in self-reported *FLG* mutation and wild-type carriers (9 (25.7%) vs. 7 (25.9%), $P = 0.99$). For example, only nine (26.5%) *FLG* mutation carriers vs. six (22.2%) wild-type carriers ($P = 0.70$) increased their use of emollient. We have no explanation for this discrepancy, but speculate that it is difficult to change treatment habits.

This study had limitations. The sample size was small, but reflected the patients who had been seen in the department at the time. The quality of the provided filaggrin information was unequal for all study patients, with a high flow of residents and interns through the clinic, but this setup is likely to reflect real life. To better assess the value of genotyping, a randomized controlled study is required.

In conclusion, although patients with self-reported *FLG* mutations had significantly better understanding of their AD pathogenesis compared to wild type carriers, surprisingly, this information did not result in an increased use of emollients or improvement in skin care habits.

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Fat removal using a new cryolipolysis device: a retrospective study of 418 procedures

Editor

The selective effect of cold on the hypodermis is a well-known medical phenomenon.[1,2] Cryolipolysis[3] induces selective apoptosis of the adipocytes using controlled exposure to intense cold. Its safety and efficacy has been reported in several studies[4,5] but was recently challenged.[6]

A retrospective, observational, monocentric post-marketing study was conducted. A single session of cryolipolysis was evaluated on subjects who consulted for fat removal. Subjects were included consecutively and paid for their treatment. Patients with medical history of cold disorders such as cryoglobulin or Raynaud's disease, visceral hernias, pregnancy, caesarean section within the last 6 months were excluded. The device used [Cristal™ cryolipolysis (Deleo, Saint Raphael, France)] benefits from the medical CE marking. It has two slightly curved handpieces that can be used simultaneously, with three different sizes. Thick protective epidermal membrane soaked with a cold-resistant gel was applied on the area. Cooling temperature was between −6 °C and −10 °C. Treatment duration was 60 min per area. A 5-min energetic massage was carried out immediately after treatment. A topical cream containing arnica extract (Cicabio Arnica+®, Laboratoire Bioderma, Lyon, France) which reduces bruising was prescribed in order to limit and treat secondary ecchymosis caused by suction.

A total of 418 areas in 147 subjects underwent the procedure. Areas were: abdomen (144), anterolateral flank (156),

