Exploring the Relationship Between Airway Attacks and Patient-Reported Outcomes in Hereditary Angioedema Attacks

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Rationale

- Hereditary angioedema (HAE) is a rare genetic condition characterized by painful, often debilitating swelling attacks that can affect multiple locations in the body.[1,2]
- The location of HAE attacks can implicate disease severity, with airway attacks associated with more severe disease.[3]
- Surveys of patients with HAE have shown inverse associations between disease severity or attack frequency and health status, work productivity, and health-related quality of life (HRQoL).[2,4]
- This analysis investigated the impact of attack location by airway vs non-airway attacks on patients experiencing HAE attacks:
  - Physician- vs patient-reported experience of an HAE attack
  - Use of on-demand medication and reasons not to treat an attack
  - Patient-reported outcomes describing HRQoL impacts and self-assessment of disease control

Methods

- Data were collected through the Adelphi HAE Wave II Disease Specific Programme™ (DSP™)* conducted between January 2023 and January 2024 in France, Germany, Italy, Japan, Spain, and the USA.
- DSPs are real-world, cross-sectional surveys with retrospective data collection.[5] A geographically representative sample of physicians was recruited to participate in the DSP.
- Recruited HAE-treating physicians utilized medical charts and their diagnostic and clinical judgment to provide data related to their consulting patients' most recent attack.
- Patients were recruited via their physician and were eligible for inclusion if the patient had a physician-confirmed diagnosis of HAE and provided informed consent.
- Patients with HAE voluntarily reported information on their attack severity, experience of fatigue and emotional distress, and on-demand treatment (ODT) use with their most recent attack. No operational definition for severity was provided as part of the HAE DSP.
- Patients assessed the impact of HAE on their work activity and HRQoL using self-report forms:
  - **Work Productivity and Activity Impairment Questionnaire - Specific Health Problem (WPAI-SHP)**[6]: higher scores indicate higher percent work impairment
  - **Angioedema QoL questionnaire (AE-QoL)**[7,8]: a tool validated for use in HAE that evaluates disease impact in 4 domains: "nutrition", "fatigue/mood", "fear/shame", and "functioning". Higher scores (0–100) indicate greater impairment
  - **Angioedema Control Test (AECT)**[9]: a questionnaire validated for use in AE to retrospectively assess disease control and make treatment decisions; scores <10 points correlate with poorly controlled disease.
- Institutional review board approval was obtained. Descriptive statistics were reported.

Results

- In this analysis, matched data are reported for 240 patients (52.9% female; mean ± SD age [years], 33.0 ± 12.8) from the patients' physicians (n=60) and the patients themselves on their most recent HAE attack, providing insight on physician and patient perspectives of the same medical events (**Table 1**).
- Of the most recent reported attacks, 42 (17.5%) were airway attacks, and 198 (82.5%) were non-airway attacks.
- Physicians reported that 172 (71.7%) patients were prescribed ODT (**Table 1**).

References

1. Busse PJ, et al. *N Engl J Med*. 2020;382:1136-48. **2.** Banerji A, et al. *Ann Allergy Asthma Immunol*. 2020;124:600-7. **3.** Bork K, et al. *Arch Intern Med*. 2003;163(10):1229–1235. **4.** Mendivil J, et al. *Orphanet J Rare Dis*. 2021;16(1):94. **5.** Anderson P, et al. *Curr Med Res Opin*. 2023;39:1707-15. **6.** Morrisroe K, et al. *Clin Exp Rheumatol*. 2017;35(suppl 106)4:130-7. **7.** Weller K, et al. *Allergy*. 2012;67:1289-98. **8.** Weller K, et al. *Allergy*. 2016;71:1203-9. **9.** Weller K, et al. *J Allergy Clin Immunol Pract*. 2020;8(6):2050-2057.e4.

Results (continued)

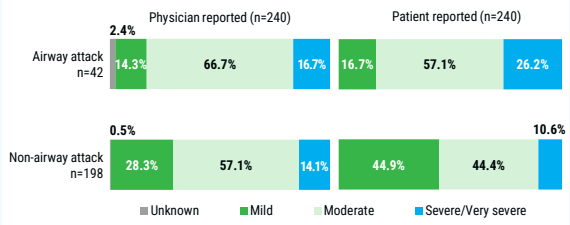
Table 1. Patient demographics and baseline characteristics (physician and patient reported)

	Physician reported (n=240)	Patient reported (n=240)
Age (years)[a], mean ± SD [range]	33.0 ± 12.8 [18–80]	33.1 ± 12.8 [18–80]
Female, n (%)	127 (52.9)	126[b] (52.7)
Patients in employment or education, n (%)	209 (87.1)	209 (87.1)
Number of comorbidities, mean ± SD	0.4 ± 0.8	NA
Time (years) since diagnosis, mean ± SD [range]	7.8 ± 7.9 [0.0–52.7] (n=226)	8.4 ± 8.4 [0.8–52.7] (n=206)
HAE type, n (%)		
Type 1	182 (75.8)	
Type 2	43 (17.9)	NA
HAE with normal C1-INH	9 (3.8)	
Unknown	6 (2.5)	
Receiving LTP, n (%)	133[c] (55.4)	142 (59.2)
Receiving ODT, n (%)	172 (71.7)	201 (83.8)
Number of HAE attacks in 12 months prior to data collection, mean ± SD [range]	2.5 ± 2.4 [0–12] (n=240)	2.7 ± 3.1 [0–24] (n=220)

C1-INH, C1-inhibitor; HAE, hereditary angioedema; LTP, long-term prophylactic treatment; NA, not assessed in patient surveys; ODT, on-demand treatment; SD, standard deviation.
[a]Age captured as binary number, not exact date. [b]One patient with missing data was excluded from the base. [c]One patient was receiving 2 different LTPs.

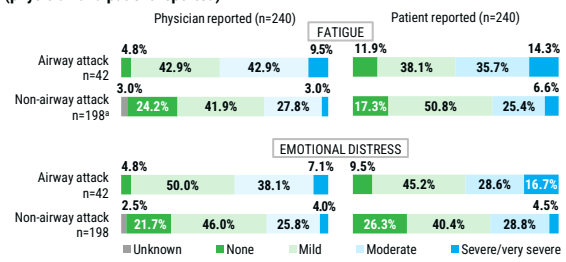
- Of patients who reported an airway attack, 35 (83.3%) described the attack severity as moderate to very severe (**Figure 1**). Severe/very severe attacks were reported by 11 (26.2%) patients but only by 7 (16.7%) matching physician reports.

Figure 1. Severity of most recent attack by location (physician and patient reported)



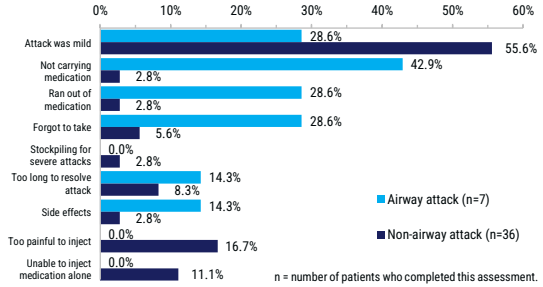
- Of patients who reported an airway attack, 21 (50.0%) reported moderate to severe fatigue and 19 (45.2%) experienced moderate to very severe emotional distress. The patient-reported incidences of severe/very severe fatigue and emotional distress were higher than those reported by their physicians (**Figure 2**).
- Of the 7/42 patients with an untreated airway attack, 42.9% were not carrying their medication, 28.6% ran out of medication, and 28.6% forgot to take it, whereas patients who did not treat a non-airway attack (36/198) most commonly cited mild attack severity as the reason not to treat (55.6%) (**Figure 3**).
- In total, 26/36 (72.2%) patients in the airway attack group and 109/164 (66.5%) patients in the non-airway attack group reported they often or always carry their ODT with them away from home.

Figure 2. Fatigue and emotional distress during most recent attack (physician and patient reported)



[a]One patient did not complete the fatigue assessment; n=197.

Figure 3. Reasons for not treating attacks (patient reported)



n = number of patients who completed this assessment.

- The mean percent overall work impairment was 24.4% for those with an airway attack (24 patient responses) and 11.2% for those with a non-airway attack (81 patient responses) (**Figure 4**).
- Among patients who experienced an airway attack, the mean total AE-QoL score was 27.9 vs 16.9 for those with a non-airway attack, demonstrating reduced HRQoL in the airway attack group (**Figure 5**).
- HAE was well controlled in both groups, but the mean AECT score was lower in patients with an airway attack (11.7, n=41) compared with those with a non-airway attack (13.8, n=196) (**Figure 6**).

Figure 4. WPAI-SHP (patient reported)

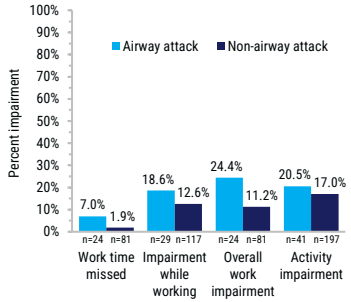


Figure 5. AE-QoL (patient reported)

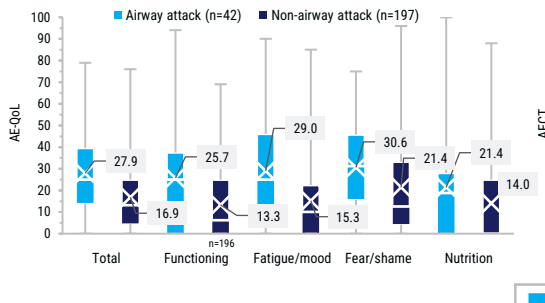
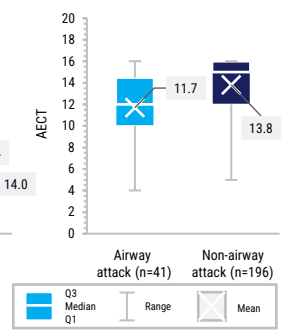


Figure 6. AECT (patient reported)



AECT; Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; WPAI-SHP, Work Productivity and Activity Impairment Questionnaire - Specific Health Problem.
n = number of patients with complete data for each assessment.

Conclusions

- **Most patients with an airway attack described the attack severity as moderate to very severe. Furthermore, about half of these patients experienced moderate to very severe fatigue and emotional distress with their attack. Notably, the matching physician-reported data indicated fewer perceived severe/very severe responses for all three measures.**
- **Compared with patients with non-airway attacks, patients who had most recently experienced an airway attack reported increased work and activity impairment and decreased HRQoL. Both groups of patients reported good disease control, but it was lower in patients with an airway attack.**
- **Despite the potential consequences, 3 out of 7 patients with untreated airway attacks did not have their medication with them and 2 out of 7 were out of medication, highlighting the importance of educating patients on the clinical guideline recommendation to always carry on-demand treatment and the need for convenient, portable therapies.**

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