Results of a Delphi Consensus Study of Geographic Atrophy (GA) Diagnosis and Current Management

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Disclosures

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Introduction

- Geographic atrophy (GA) is the advanced form of dry age-related macular degeneration (AMD) that results in progressive and irreversible disease and affects approximately 5 million people worldwide\textsuperscript{1,2}
- There are currently no approved medications for the treatment of GA\textsuperscript{3}
- In addition, there are no overall comprehensive guidelines for the diagnosis and monitoring of patients with GA
- This Delphi consensus development exercise was carried out to provide consensus guidance for the identification, monitoring, and management of patients with GA; and to determine the most important unmet needs in this disease

AMD=age-related macular degeneration; GA=geographic atrophy
Methods

A Delphi study is a widely used method to obtain input from a group of experts. The key features are anonymity among respondents with controlled feedback provided in a structured manner. Survey designers may then adjust their initial ratings based on feedback from the respondents over multiple subsequent iterations.1

Round 1

Initial set of 20 questions/statements developed by 8 expert retina specialists (the steering committee) focused on:
- Diagnosis and monitoring
- Management
- Unmet needs
- Education

Questions and statements sent to 175 randomly selected retina specialists worldwide

Round 2

A questionnaire for the second round of the Delphi exercise was designed on the basis of results from the first round. It consisted of 20 questions focused on:
- Diagnosis and monitoring
- Patient management
- Wet and dry AMD
- Future practice

Questions and statements sent to 125 retina specialists who participated in the first round

- Questions were open ended, multiple choice, rank order, and level of agreement (Likert scale)
- Results from each round were reviewed by the steering committee and consensus was achieved:
  - If they were selected by ≥75% of respondents (multiple choice questions)
  - If an option was ranked as 1 or 2 by ≥75% of respondents (ranking questions)
  - If response ratings were 6-9 for ≥75% of respondents (statements ranked with responses on a 9-point scale)

AMD=age-related macular degeneration.
Respondents (Round 1)

- Respondents specialized in the treatment of retinal disorders
- Experience:
  - Mean of 14.5 years practicing in specialty (standard deviation = 8.0 years, range = 3–42 years)
  - Practice setting:
    - Public sector: 46%
    - Private sector: 51%
    - Training/teaching/university hospital: 36%
  - Median number of patients with GA seen each month (50, interquartile range = 30–100)

Distribution by country:
- United States: 15%
- Germany: 15%
- United Kingdom: 14%
- France: 14%
- Australia: 14%
- Italy: 11%
- Spain: 11%
- Canada: 6%

GA=geographic atrophy.
Where consensus was achieved with ≥75% response
Consensus recommendations: Functional measures and imaging modalities

Which of the following functional measures or tests do you use in regular clinical practice?

- BCVA
- Amsler Grid

Which of the following imaging modalities do you use in regular clinical practice for GA?

- OCT
- FAF
- CFP

**OCT was viewed as the most important tool for diagnosing GA (82%)**

Other responses: Fundus fluorescein angiography, OCT angiography, Near-infrared / Near-infrared reflectance spectroscopy, Other

Other responses: Routine/habitual visual acuity, QoL questionnaires (e.g., VFQ-25), Microperimetry, Reading speed, LL BCVA, Digital applications (e.g., computer or smart phone); Dark adaptometry, Other

Consensus defined as selection or threshold ranking by ≥75% of respondents.

CFP=color fundus photography; FAF=fundus autofluorescence; GA=geographic atrophy; LL BCVA=low-luminance best-corrected visual acuity; OCT=ocular coherence tomography; QoL=quality of life; VFQ=Visual Function Questionnaire.
Consensus recommendations: Assessing patient symptoms and quality of life

What symptoms of GA do you look for/inquire about during the first visit?

- Reading difficulty: 93%
- Impaired ability to recognize faces: 84%

What are the most important topics to discuss with a patient newly diagnosed with GA?

- Impact on daily living: 89%
- Options for visual aids: 76%

Other responses: Reduced ability to text / type on a computer or mobile device; Inability to drive; Inability to watch television; Impaired night vision / functioning in dim light; Impaired / delayed dark adaptation; Glare symptoms; Other

Consensus defined as selection or threshold ranking by ≥75% of respondents. BCVA=best corrected visual acuity; GA=geographic atrophy.
Consensus recommendations: Establishing a prognosis and patient discussion

Rank order the importance of each variable for determining GA prognosis

Consensus defined as selection or threshold ranking by ≥75% of respondents. FAF=fundus autofluorescence; GA=geographic atrophy
Consensus recommendations: Patient monitoring (1)

Rank order the importance of each imaging modality when monitoring a patient with GA

<table>
<thead>
<tr>
<th></th>
<th>OCT</th>
<th>FAF</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>32</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Active wet AMD in either eye</th>
<th>Distorted vision on Amsler grid</th>
</tr>
</thead>
<tbody>
<tr>
<td>76</td>
<td>56</td>
<td></td>
</tr>
</tbody>
</table>

When only one option achieved consensus, the second highest choice is also shown.

Consensus defined as selection or threshold ranking by ≥75% of respondents.

AMD=age-related macular degeneration; GA=geographic atrophy; OCT=ocular coherence tomography
Consensus recommendations: Patient monitoring (2)

Rank order each GA biomarker (ranked on a scale of 3 from most important to least important)

<table>
<thead>
<tr>
<th>Lesion location with respect to the fovea</th>
<th>Total GA lesion size</th>
<th>Lesion location with respect to the fovea</th>
<th>Total GA lesion size</th>
</tr>
</thead>
<tbody>
<tr>
<td>How impactful its data are from clinical studies</td>
<td>How practical it is for clinical practice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent</td>
<td>25</td>
<td>33</td>
<td>75</td>
</tr>
<tr>
<td>Ranked first</td>
<td>50</td>
<td>31</td>
<td>61</td>
</tr>
<tr>
<td>Ranked second</td>
<td>25</td>
<td>61</td>
<td>43</td>
</tr>
</tbody>
</table>

Consensus defined as selection or threshold ranking by ≥75% of respondents.
When only one option achieved consensus, the second highest choice is also shown.
AMD=age-related macular degeneration; GA=geographic atrophy; OCT=ocular coherence tomography
Unmet needs

What are the most important unmet needs in GA?

- **Availability of treatment options that prevent atrophy or atrophy evolution**: 89%
- **Clinically relevant prognostic biomarkers**: 63%
- **Progression calculator (eg, predicting 5-year status of disease)**: 54%
- **Accuracy of GA diagnosis**: 29%
- **Informational/data gaps (eg, natural history of disease across racial groups)**: 14%
- **Access to care (eg, ability to see appropriate physician)**: 13%

Consensus defined as selection or threshold ranking by ≥75% of respondents.
GA=geographic atrophy.
Patients with CNV controlled by anti-VEGF therapy can continue to experience vision loss due to atrophic lesions.

Consensus defined as selection or threshold ranking by \( \geq 75 \% \) of respondents.

CNV=choroidal neovascularization; GA=geographic atrophy; VEGF=vascular endothelial growth factor.
Where consensus was not achieved
**Selected questions / statements: Diagnosis**

### Most frequent responses

<table>
<thead>
<tr>
<th>Feature of GA</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncorrectable reduction in visual acuity</td>
<td>56%</td>
</tr>
<tr>
<td>Risk of foveal involvement</td>
<td>51%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Condition to exclude when confirming the diagnosis of GA</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macular atrophy due to exudation and neovascularization</td>
<td>68%</td>
</tr>
<tr>
<td>Inherited retinal diseases (e.g., Stargardt disease, angioid streaks, Sorsby fundus dystrophy)</td>
<td>57%</td>
</tr>
</tbody>
</table>

GA = geographic atrophy.
## Selected questions / statements: Patient management

### At present, which of the following assessments are most useful for the management of GA?

- **62%**: foveal involvement
- **55%**: BCVA

### In general, how frequently do you have follow-up visits / consultations with GA patients?

- **52%**: once every 6 months
- **21%**: once every 12 months

### In general, how would you rate the awareness / uptake of imaging classifications?

- **35%**: medium
- **30%**: high

### In your opinion, which of the following are relevant biomarkers in GA?

- **69%**: total GA lesion size
- **53%**: lesion location

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BCVA=best correct visual acuity; GA=geographic atrophy.
In your clinical experience, what current practices in dry AMD / GA are most beneficial to patients?

<table>
<thead>
<tr>
<th>Rank</th>
<th>Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>68%: smoking cessation</td>
</tr>
<tr>
<td>2</td>
<td>60%: Low vision aids (e.g., magnifying device, text-to-audio technology)</td>
</tr>
</tbody>
</table>

Rank order each measure by how impactful its data are from clinical studies?\(^a\)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54%: quality of life questionnaires</td>
</tr>
<tr>
<td>2</td>
<td>40%: low luminance BCVA</td>
</tr>
</tbody>
</table>

\(^a\)Ranked first or second of six.

AMD=age-related macular degeneration; BCVA=best corrected visual acuity; GA=geographic atrophy.
### Most frequent responses

**For patients with CNV who develop atrophy within the same eye, which of the following is more common?**

1. **70%:** atrophy co-localized within areas of existing CNV
2. **30%:** atrophy outside areas of existing CNV

**In patients with wet AMD, which terminology would you use for an atrophic lesion that develops within areas of CNV?**

1. **41%:** macular atrophy
2. **38%:** RPE atrophy

**In patients with wet AMD, which terminology would you use for an atrophic lesion that develops outside areas of CNV?**

1. **50%:** GA
2. **30%:** RPE atrophy

**For patients with confirmed GA who develop CNV within the same eye, which of the following is more common?**

1. **71%:** CNV on the edge of existing atrophy
2. **16%:** CNV co-localized within areas of existing atrophy

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AMD=age-related macular degeneration; CNV=choroidal neovascularization; GA=geographic atrophy; RPE=retinal pigment epithelium.
Conclusions

• This study is the first exercise aimed at obtaining consensus among retina specialists on current practices in GA diagnosis and management
  – Treating physicians agreed on several aspects of GA diagnosis, including the use of imaging modalities and impact on QoL
  – Although foveal involvement and GA lesion size are important biomarkers in determining GA patient prognosis, identifying robust biomarkers was reported as a significant data gap
• Management routinely involved recommendations on smoking cessation and the use of low vision aids; however, experts agreed these were minimally effective as the current standard of care
• The need for treatment options was identified as the largest unmet need in GA, and could potentially trigger more frequent follow-ups and disease monitoring along with a better preservation of vision and improved QoL outcomes

GA=geographic atrophy; QoL=quality of life.