Viewpoint:
Management of subfoveal hemorrhage
Objectives

To provide an overview of the challenges posed by subfoveal hemorrhage and its management

To identify areas requiring guidance

To present the recommendations of the Vision Academy on this topic

The Vision Academy provides ophthalmic specialists with a forum to share existing skills and knowledge, build best practice, and lead the wider community in the drive towards optimized, compassionate patient care.

Through their collective expertise, the Vision Academy seeks to provide guidance for best clinical practice in the management of retinal disease, particularly in areas with insufficient conclusive evidence.

QUESTION

What are the challenges posed by subfoveal hemorrhage and its management?
Background
Subretinal, submacular, and subfoveal hemorrhage

- **Subretinal hemorrhage**
  - Often associated with nAMD, blood from the retinal or choroidal circulation accumulates between the RPE and the photoreceptor layers\(^1\)

- **Submacular hemorrhage**
  - A subretinal hemorrhage occurring in the macular region\(^1,2\)

- **Subfoveal hemorrhage**
  - A subretinal hemorrhage that extends under the center of the foveal avascular zone\(^3\)

Subretinal hemorrhage causes severe visual impairment when the fovea is involved\(^1\)

The Vision Academy Viewpoint addresses the management of subfoveal hemorrhage

nAMD, neovascular age-related macular degeneration; RPE, retinal pigment epithelium.
Subfoveal hemorrhage: When does it occur?

Frequently described as a secondary condition to AMD:

Subretinal hemorrhage frequently results from a CNVM secondary to AMD

Subfoveal hemorrhage occurs in approximately 5.8% of patients with exudative AMD

As a result of CNVM conditions:

Other conditions associated with CNVMs, including:
- myopia
- trauma
- ocular histoplasmosis
- angioid streaks
- macroaneurysms
These conditions may occur in parallel with subfoveal hemorrhage

Increased risk due to certain medications and medical conditions:

Anticoagulant or antiplatelet medications were significantly associated with retinal/subretinal hemorrhages among patients with hypertension

AMD, age-related macular degeneration; CNVM, choroidal neovascular membrane.
### Mechanisms

Subretinal hemorrhage damages tissues through a variety of mechanisms\(^1\)

- Iron, hemosiderin, and fibrin in the blood have toxic effects on the overlaying photoreceptors
- Clot retraction can shear and damage photoreceptors
- Physical separation of the photoreceptors from the RPE can lead to atrophy and disciform scar formation

### Implications

- Patients with submacular / subfoveal hemorrhages experience progressive visual decline\(^{1,2}\)
- As the mechanisms of damage are time-dependent, early intervention is generally better,\(^1\) particularly with subfoveal hemorrhage

---

RPE, retinal pigment epithelium.

Classification of subretinal hemorrhage is critical for treatment choice and management

Subretinal hemorrhages are often classified by size:

- **Small**¹: At least 1DD but less than 4DDs
- **Medium**¹: At least 4DDs, but not extending beyond the temporal vascular arcades
- **Large**²: Extending beyond the arcades, but not beyond the equator

- Small hemorrhages can often undergo observation without intervention³
- Medium-sized hemorrhages that extend under the macula and obscure the underlying RPE can also cause significant vision loss; however they are often amenable to treatment³
- Large submacular hemorrhages often have a poor prognosis regardless of intervention³

---

DD, disc diameter; RPE, retinal pigment epithelium.
Prognostic factors for patients with subfoveal hemorrhage

Untreated subfoveal hemorrhages lead to worse visual prognoses, indicating that early intervention is critical\(^1\)

Prognostic factors include patient age, initial BCVA, and hemorrhage thickness, diameter, and duration\(^2,3\)

<table>
<thead>
<tr>
<th>Thickness: Thick (≥500 µm) subfoveal hemorrhage secondary to nAMD is a prognostic factor for dramatic vision loss(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organization: Hemorrhage reflectance quantified by OCT can indicate ease of hemorrhage displacement, as it might represent hemorrhage organization(^5)</td>
</tr>
<tr>
<td>Location: Hemorrhage location is also a good marker of treatment success, with hemorrhages located on the periphery of the fovea more likely to be displaced in response to treatment(^5)</td>
</tr>
</tbody>
</table>

BCVA, best corrected visual acuity; nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography.
Imaging of subfoveal hemorrhage to determine hemorrhage size, thickness, and etiology

- **FA** may be of limited value in the acute phase because of the masking effect of subretinal blood
- **ICGA** utilizes infrared light to penetrate the RPE and blood, and may be more helpful than FA in detecting CNV or PCV lesions
- **OCT / OCT-A** helps to localize the hemorrhage within the retinal layers and can objectively quantify hemorrhage size
  - **EDI-OCT** provides further detailed imaging of the choroid

**Fundus photography**

**FA / ICGA**

**OCT-A**

**EDI-OCT**

Images courtesy of Professor Annabelle Okada

**CHALLENGE REQUIRING VISION ACADEMY GUIDANCE**

What imaging types are recommended in patients with subfoveal hemorrhage?

CNV, choroidal neovascularization; EDI-OCT, enhanced depth imaging OCT; FA, fluorescein angiography; ICGA, indocyanine green angiography; OCT, optical coherence tomography; OCT-A, OCT angiography; PCV, polypoidal choroidal vasculopathy; RPE, retinal pigment epithelium.

Treatment
Treatment challenges to be addressed

There is currently a lack of evidence-based research to inform the management of patients with subfoveal hemorrhage.

- Mixed evidence on the most appropriate treatments for subfoveal hemorrhage
- Mixed evidence on the criteria for initiating treatment of subfoveal hemorrhage
Treatment options

Potential treatments include:

Intravitreal tPA with pneumatic displacement
- tPA is a protease enzyme which can lyse the clot\(^1\)
- Pneumatic displacement (PD) involves shifting the hemorrhage from beneath the fovea using the buoyancy of the gas to avoid irreversible damage to the photoreceptors and RPE layers\(^2\)

With or without surgical intervention (e.g. pars plana vitrectomy)
- Removal of the vitreous, including the fluid containing the hemorrhage\(^1\)

Intravitreal anti-VEGF
- Antiangiogenic agents: ranibizumab, aflibercept
Tissue plasminogen activator with pneumatic displacement
Positive visual outcomes have been demonstrated after 6 months of treatment with vitrectomy in combination with subretinal tPA in combination with PD or vitrectomy.

Intravitreal or subretinal injection of tPA facilitates the removal of the dissolved clot when used in conjunction with intravitreal PD and/or surgical intervention.

- A number of studies have demonstrated positive visual outcomes with tPA in conjunction with either PD or surgical intervention.
- One study has demonstrated a lack of statistical significance between the two treatments, highlighting tPA with PD as a less invasive, less costly procedure than tPA with vitrectomy.

<table>
<thead>
<tr>
<th>logMAR VA</th>
<th>Initial vision</th>
<th>Month 1</th>
<th>Month 3</th>
<th>Month 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitrectomy with subretinal tPA</td>
<td>1.8 ± 0.53</td>
<td>1.1 ± 0.5</td>
<td>1.0 ± 0.7</td>
<td>0.9 ± 0.6</td>
</tr>
<tr>
<td>Intravitreal tPA with PD</td>
<td>1.5 ± 0.51</td>
<td>1.0 ± 0.4</td>
<td>0.9 ± 0.5</td>
<td>0.9 ± 0.4</td>
</tr>
<tr>
<td>Pneumatic displacement</td>
<td>1.5 ± 0.45</td>
<td>1.3 ± 0.5</td>
<td>1.6 ± 0.4</td>
<td>1.6 ± 0.5</td>
</tr>
</tbody>
</table>

Both ppV and PD in combination with tPA resulted in positive visual outcomes after 6 months of treatment.

CHALLENGE REQUIRING VISION ACADEMY GUIDANCE

When should tPA and PD be used? When should surgical intervention be considered?
Vitrectomy with subretinal tPA and PD has been shown to result in positive visual outcomes and complete displacement of the hemorrhage

- **Chang et al. (2014):** Retrospective interventional case series of 101 patients presenting with thick submacular hemorrhage secondary to nAMD

- Patients underwent displacement of the hemorrhage (ppV), plus subretinal tPA with PD
  - VA significantly improved from baseline to Month 12 (p=0.002)
  - In 83 eyes, the procedure resulted in complete displacement of the hemorrhage from the fovea

- Vitrectomy with subretinal tPA and PD has been shown to be an effective therapeutic option for thick submacular hemorrhage involving the fovea

**CHALLENGE REQUIRING VISION ACADEMY GUIDANCE**
When should surgical intervention in combination with tPA and PD be considered?

BCVA, best corrected visual acuity; logMAR, logarithm of the minimum angle of resolution; nAMD, neovascular age-related macular degeneration; PD, pneumatic displacement; ppV, pars plana vitrectomy; tPA, tissue plasminogen activator; VA, visual acuity.

Evidence has demonstrated favorable visual outcomes with intravitreal tPA plus PD (both with and without vitrectomy) compared with PD alone for the treatment of subfoveal hemorrhage. 

Limitations of data:
- Impact of hemorrhage size and location on choice of treatment combination still unknown
- tPA plus PD appears to offer a less invasive, less costly alternative to vitrectomy; however further studies are needed
- Clear guidance on treatment choice is still lacking, due to a lack of consensus among studies

CHALLENGE REQUIRING VISION ACADEMY GUIDANCE
When should tPA and PD be used alone? When should the addition of surgical intervention be considered?

PD, pneumatic displacement; tPA, tissue plasminogen activator.
Intravitreal anti-VEGF therapy

VEGF, vascular endothelial growth factor.
Intravitreal anti-VEGF monotherapy

• Antiangiogenic agents are the standard of care for nAMD
  - Anti-VEGF agents have been shown to help clear intravitreal hemorrhage in diabetic retinopathy

• Monotherapy may be particularly relevant for patients not suited for PD, tPA, or surgery
  - Patients unable to maintain prone positioning

Intravitreal anti-VEGF combination therapy

In combination, it is believed that anti-VEGF therapy can control the underlying cause of the disease (CNV), while treatments such as vitrectomy, tPA, and PD can be applied to clear the hemorrhage.
Intravitreal anti-VEGF monotherapy
A number of small studies have demonstrated positive visual outcomes with intravitreal anti-VEGF monotherapy

- A number of studies have reported positive visual outcomes with anti-VEGF monotherapy for the treatment of submacular hemorrhage, including subfoveal hemorrhage, secondary to nAMD
- However, small sample sizes and differences in baseline features and treatment regimens limit direct comparison of these results

*Bevacizumab is not licensed for the treatment of visual impairment due to nAMD. Table adapted from Shin et al. 2016.5 BCVA, best corrected visual acuity; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.

<table>
<thead>
<tr>
<th>Study country</th>
<th>Shienbaum et al. 2013¹</th>
<th>Kim et al. 2014²</th>
<th>Iacono et al. 2014³</th>
<th>Liu et al. 2017⁴ subfoveal specific</th>
<th>Shin et al. 2016⁵ subfoveal specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of eyes</td>
<td>15</td>
<td>71</td>
<td>23</td>
<td>47</td>
<td>25</td>
</tr>
<tr>
<td>Follow-up period, months</td>
<td>6</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Extent of baseline hemorrhage (range)</td>
<td>&gt;50% of lesion area (4.3–170.2 mm²)</td>
<td>&lt;50%–&gt;50% of lesion area (3–20 disc areas)</td>
<td>&gt;50% of lesion area</td>
<td>‘Large submacular hemorrhage’ (7.3–96.6 mm²)</td>
<td>&lt;50% of lesion area (2.7–25.6 mm²)</td>
</tr>
<tr>
<td>Anti-VEGF agent</td>
<td>Ranibizumab and/or bevacizumab*</td>
<td>Ranibizumab and/or bevacizumab*</td>
<td>Ranibizumab</td>
<td>Ranibizumab or bevacizumab*</td>
<td>Aflibercept</td>
</tr>
<tr>
<td>Change in BCVA from baseline:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gain of ≥3 lines / ≥15 letters, n (%)</td>
<td>9 (60.0)</td>
<td>46 (64.8)</td>
<td>8 (34.7)</td>
<td>27 (57.0)</td>
<td>11 (44.0)</td>
</tr>
<tr>
<td>Maintained stable vision, n (%)</td>
<td>6 (40.0)</td>
<td>21 (29.6)</td>
<td>2 (8.7)</td>
<td>14 (30.0)</td>
<td>13 (52.0)</td>
</tr>
<tr>
<td>Loss of ≥3 lines / ≥15 letters, n (%)</td>
<td>0</td>
<td>4 (5.6)</td>
<td>2 (8.7)</td>
<td>6 (13.0)</td>
<td>1 (4.0)</td>
</tr>
</tbody>
</table>

CHALLENGE REQUIRING VISION ACADEMY GUIDANCE

When is anti-VEGF monotherapy recommended?

Ranibizumab has demonstrated effectiveness in patients with good baseline vision and shorter disease duration

- Iacono et al. (2014): Prospective interventional case series of 23 patients presenting with occult CNV with flat submacular hemorrhage, of whom six had foveal involvement
- Patients were treated with three monthly injections of intravitreal ranibizumab, with re-treatment given over a 12-month follow-up period on a PRN basis
- Mean BCVA significantly increased throughout the follow-up period from 0.82 ± 0.22 to 0.68 ± 0.41 (p=0.04)
- Subgroup analysis of baseline presence of blood in the foveal region disclosed a deterioration of BCVA from 0.96 ± 0.10 to 1.15 ± 0.23 at 12 months in eyes with foveal hemorrhages (p=0.03)
- Conversely, subjects with initial foveal sparing showed a significant improvement in BCVA, ranging from 0.77 ± 0.23 at baseline to 0.52 ± 0.33 at 12 months (p=0.01)

However, poor visual outcomes were seen in eyes with submacular hemorrhages involving the fovea

**CHALLENGE REQUIRING VISION ACADEMY GUIDANCE**

When should anti-VEGF monotherapy be used to treat subfoveal hemorrhage?
Aflibercept has been shown to increase VA and decrease hemorrhage size over 6 months of treatment

- **Shin et al. (2016):** Retrospective observational case series of 25 patients presenting with subfoveal hemorrhage secondary to nAMD
- Patients treated with three monthly injections of intravitreal aflibercept, with re-treatment given over a 6-month follow-up period on a PRN basis
- However, further studies are required to determine its effectiveness in treating eyes with subfoveal hemorrhage, and in cases where treatment is delayed

---

**Mean change in BCVA from baseline (ETDRS letters) during follow-up after aflibercept injection**

- **Baseline**
- **Month 3:** 9.0
- **Month 6:** 12.5
- *p* < 0.001

**Area of subfoveal hemorrhage (mm²) during follow-up after aflibercept injection**

- **Baseline**
- **Month 3:** 10.5
- **Month 6:** 3.9
- *p* < 0.001

**Vision significantly improved from baseline to Month 6 (p<0.001)**

**Hemorrhage size significantly decreased from baseline to Month 6 (p<0.001)**

---

**CHALLENGE REQUIRING VISION ACADEMY GUIDANCE**

When should anti-VEGF monotherapy be used in cases of delayed treatment or subfoveal hemorrhages?

---

BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; nAMD, neovascular age-related macular degeneration; PRN, pro re nata (as needed); VA, visual acuity.

Similar improvements in BCVA have been demonstrated with anti-VEGF monotherapy vs. combination treatment with vitrectomy, tPA and pneumatic displacement

- **Liu et al. (2017):** Retrospective study of 149 patients presenting with large subfoveal hemorrhage secondary to nAMD, receiving intravitreal anti-VEGF monotherapy or combined treatment of ppV with tPA and PD
- At baseline, patients in the surgical group had larger hemorrhages than those in the anti-VEGF monotherapy group (30.35 mm² vs. 14.47 mm²) and worse baseline vision (4.5 letters vs. 20.5 letters)
- Despite these baseline differences, the mean change in VA between the two study groups at the final visit was not statistically significant (p=0.36)

Although differences in the treatment groups make comparisons difficult, the two study groups show similar improvements in BCVA

**CHALLENGE REQUIRING VISION ACADEMY GUIDANCE**

When is anti-VEGF monotherapy preferred over surgical intervention?

*P values for mean change in BCVA at final visit versus baseline.
BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; nAMD, neovascular age-related macular degeneration; PD, pneumatic displacement; ppV, pars plana vitrectomy; tPA, tissue plasminogen activator; VA, visual acuity; VEGF, vascular endothelial growth factor.
Anti-VEGF monotherapy has been shown to consistently improve VA for more than 2 years in patients with submacular hemorrhage due to PCV

- **Kim et al. (2015):** Retrospective observational study of 49 patients who initially presented with typical nAMD; 31 were later classified as having PCV
  - Patients were treated with either intravitreal bevacizumab† or intravitreal ranibizumab
  - In the PCV group, significant improvements in BCVA from baseline were seen at Month 12 (p<0.001) and at Month 24 (p=0.007)
  - Improvements in VA from baseline were seen for more than 2 years with anti-VEGF monotherapy
    - However, there was no common treatment protocol or follow-up examination schedule

**Anti-VEGF therapy resulted in significant improvements in BCVA from baseline in patients with PCV**

**CHALLENGE REQUIRING VISION ACADEMY GUIDANCE**

When should anti-VEGF monotherapy be used in patients with PCV?

---

* A definitive diagnosis was not possible in three patients. †Bevacizumab is not licensed for the treatment of retinal diseases. BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; nAMD, neovascular age-related macular degeneration; PCV, polypoidal choroidal vasculopathy; VA, visual acuity; VEGF, vascular endothelial growth factor.

Intravitreal anti-VEGF has been shown to increase VA from baseline to Month 12 in patients with PCV

- Cho et al. (2013): Retrospective interventional study of 27 patients presenting with subfoveal hemorrhage secondary to PCV
  - Patients treated with three initial monthly loading doses of intravitreal bevacizumab* or intravitreal ranibizumab, followed by re-treatment on a PRN basis
  - VA was significantly improved from baseline to Month 12 (p=0.02)
  - Intravitreal anti-VEGF therapy was shown to be a valuable therapeutic option

*Bevacizumab is not licensed for the treatment of visual impairment due to PCV.
ETDRS, Early Treatment Diabetic Retinopathy Study; PCV, polypoidal choroidal vasculopathy; PRN, pro re nata (as needed); VA, visual acuity; VEGF, vascular endothelial growth factor.
Studies have demonstrated that intravitreal anti-VEGF results in better visual outcomes in patients with better baseline vision and shorter hemorrhage duration.\(^1-3\)

This suggests that in patients with subfoveal hemorrhage and nAMD, intravitreal anti-VEGF treatment should be initiated promptly.

**CHALLENGE REQUIRING VISION ACADEMY GUIDANCE**

When should anti-VEGF treatment be initiated?

nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.

Intravitreal anti-VEGF combination therapy
Retrospective studies have examined the effectiveness of intravitreal anti-VEGF therapy in combination with tPA, PD, and ppV

- A number of retrospective case series have reported positive visual outcomes with different treatment combinations for subfoveal hemorrhage secondary to nAMD

<table>
<thead>
<tr>
<th>Study country</th>
<th>Treatment</th>
<th>Number of eyes, n</th>
<th>Follow-up period, months</th>
<th>Mean change in BCVA from baseline to final follow-up visit, logMAR (ETDRS letters)</th>
<th>Any improvement in vision, n (%)</th>
<th>Maintained stable vision, n (%)</th>
<th>Any worsening of vision, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Korea</td>
<td>Ranibizumab + PD</td>
<td>93</td>
<td>12</td>
<td>-0.23 (+11.5) [p=0.007]</td>
<td>NA</td>
<td>16 (80.0)</td>
<td>16 (15.0)</td>
</tr>
<tr>
<td>Austria</td>
<td>Bevacizumab* / ranibizumab, tPA + PD</td>
<td>20</td>
<td>4</td>
<td>-0.54 (+27.0) [p=0.003]</td>
<td>16 (80.0)</td>
<td>1 (5.0)</td>
<td>1 (4.0)</td>
</tr>
<tr>
<td>UK</td>
<td>Bevacizumab* / ranibizumab, tPA + PD</td>
<td>8</td>
<td>12</td>
<td>-1.04 (+52.0) [p&lt;0.0001]</td>
<td>15 (60.0)</td>
<td>0</td>
<td>1 (4.0)</td>
</tr>
<tr>
<td>Korea</td>
<td>Bevacizumab* / ranibizumab, TNK + PD</td>
<td>25</td>
<td>12</td>
<td>-0.57 (+28.5) [p&lt;0.001]</td>
<td>33 (73.3)</td>
<td>9 (36.0)</td>
<td>1 (4.0)</td>
</tr>
<tr>
<td>UK</td>
<td>Vitrectomy, subretinal tPA + ranibizumab</td>
<td>45</td>
<td>12</td>
<td>-0.59 [p&lt;0.001]</td>
<td>10 (22.2)</td>
<td>NA</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Germany</td>
<td>ppV, tPA, PD + bevacizumab* / ranibizumab</td>
<td>41</td>
<td>12</td>
<td>-0.9 (+45.0) [p&lt;0.001]</td>
<td>96 (73.0)</td>
<td>NA</td>
<td>16 (12.0)</td>
</tr>
<tr>
<td>Germany</td>
<td>Bevacizumab* + PD</td>
<td>132</td>
<td>3</td>
<td>-0.67 (+30.0) [p&lt;0.0001]</td>
<td>20 (15.0)</td>
<td>4 (18.2)</td>
<td>NA</td>
</tr>
<tr>
<td>Japan</td>
<td>Bevacizumab* + PD</td>
<td>22</td>
<td>6</td>
<td>-0.32 (+20.6) [p&lt;0.01]</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Bevacizumab is not licensed for the treatment of visual impairment due to nAMD. †Reported as median change in BCVA from baseline at final follow-up.

BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; logMAR, logarithm of the minimum angle of resolution; NA, not available; nAMD, neovascular age-related macular degeneration; PD, pneumatic displacement; ppV, pars plana vitrectomy; TNK, tenecteplase; tPA, tissue plasminogen activator; VEGF, vascular endothelial growth factor.


**CHALLENGE REQUIRING VISION ACADEMY GUIDANCE**

When should anti-VEGF in combination with other treatments be used?
Combination of anti-VEGF therapy and PD has been shown to improve visual outcomes in patients with PCV

- Kitahashi et al. (2014): Retrospective case series of 32 patients presenting with massive subfoveal hemorrhage secondary to PCV
- 22 patients were treated with intravitreal bevacizumab* and PD; 10 were treated with PD alone
- BCVA in the combination group was significantly better than that in the PD group at Months 1, 3, and 6 after treatment (all p<0.01)
- Combination of an anti-VEGF agent and PD was shown to be an effective therapeutic option for eyes with massive subfoveal hemorrhage

*Bevacizumab is not licensed for the treatment of visual impairment due to PCV. †Bevacizumab + PD versus PD alone, p<0.01.

BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; PCV, polypoidal choroidal vasculopathy; PD, pneumatic displacement; VA, visual acuity; VEGF, vascular endothelial growth factor.


**CHALLENGE REQUIRING VISION ACADEMY GUIDANCE**

When should anti-VEGF in combination with PD be used?
Clinical challenges
Clinical challenges requiring guidance

**Imaging**
- Which imaging techniques should be used in patients with subfoveal hemorrhage to determine hemorrhage size?

**Intravitreal anti-VEGF treatment**
- Should intravitreal anti-VEGF treatment be administered? When should treatment be initiated?

**tPA and PD**
- When is treatment with tPA and PD appropriate?

**Surgical intervention**
- When should surgical intervention be considered?

PD, pneumatic displacement; tPA, tissue plasminogen activator; VEGF, vascular endothelial growth factor.
Vision Academy recommendations
Multimodal imaging with OCT is recommended

Important tools to distinguish between subretinal and sub-RPE blood, and for objectively quantifying hemorrhage size:\(^1\)

- Color fundus photography
- Fundus autofluorescence
- Spectral domain OCT (including use of the enhanced depth imaging mode)
- ICGA

These imaging tools can help determine hemorrhage size, thickness, location of blood (above or below the RPE) and etiology\(^2-5\)

Multimodal imaging with OCT should be used to determine several prognostic factors for subfoveal hemorrhage\(^2-5\)

ICGA, indocyanine green angiography; OCT, optical coherence tomography; RPE, retinal pigment epithelium.

Prompt initiation of anti-VEGF with careful monitoring is recommended as a first-line treatment for subfoveal hemorrhage in nAMD and PCV

- In patients with nAMD and subfoveal hemorrhage, anti-VEGF should be promptly initiated to minimize the risk of irreversible retinal damage.
- In eyes with good baseline vision and short hemorrhage duration, significant visual improvements were observed with anti-VEGF treatment.1-3

The importance of early detection and initiation of anti-VEGF treatment was demonstrated in studies showing significant visual improvements in eyes with good baseline vision and short hemorrhage duration.1

- Careful monitoring is important for the early detection of breakthrough hemorrhage to minimize the risk of complications.

Anti-VEGF treatment is recommended for patients able to attend regular follow-up appointments.

nAMD, neovascular age-related macular degeneration; PCV, polypoidal choroidal vasculopathy; VEGF, vascular endothelial growth factor.
Intravitreal tPA with PD is recommended for patients, depending on the thickness of the subfoveal hemorrhage


• Evidence has demonstrated favorable visual outcomes with intravitreal tPA plus PD (both with and without vitrectomy) compared with PD alone for the treatment of subretinal hemorrhage

Studies have demonstrated positive visual outcomes in patients treated with tPA in combination with PD or vitrectomy

• While a sub-RPE hemorrhage in association with a subretinal hemorrhage involving the fovea does not preclude the use of PD or vitrectomy, the location and size of the sub-RPE component may affect the decision to perform these procedures

Intravitreal tPA with PD and intravitreal anti-VEGF therapy is recommended for medium, large, or thick subfoveal hemorrhages in patients with poor baseline vision (<20/200), at the discretion of the physician

PD, pneumatic displacement; RPE, retinal pigment epithelium; tPA, tissue plasminogen activator.
Surgical intervention is recommended only for severe hemorrhages

- Evidence suggests that ppV in combination with subretinal tPA, PD, and intravitreal anti-VEGF therapy may offer a more effective option than anti-VEGF monotherapy for the treatment of patients with thick or large hemorrhages and poor baseline vision\(^1,2\)

- However, without adequate prospective studies, it is not possible to draw comparisons between surgery and other treatment modalities because of likely variation in surgical techniques between reports

The Vision Academy recommends surgical intervention only for severe subretinal hemorrhages, as determined by thickness and location

Surgical intervention may offer a more effective option than anti-VEGF monotherapy for the treatment of thick or large hemorrhage in eyes with poor baseline vision\(^1,2\) but additional studies are warranted

PD, pneumatic displacement; ppV, pars plana vitrectomy; tPA, tissue plasminogen activator; VEGF, vascular endothelial growth factor.

Vision Academy recommendations for the management of subfoveal hemorrhage

- Multimodal imaging with OCT is recommended to determine several prognostic factors for subfoveal hemorrhage, including hemorrhage, size, thickness, location and etiology, in order to drive treatment choice.

- Prompt initiation of anti-VEGF with careful monitoring is recommended as a first-line treatment for subfoveal hemorrhage in nAMD and PCV.

- Intravitreal tPA in conjunction with PD and anti-VEGF therapy is recommended for medium, large, or thick subfoveal hemorrhage in patients with poor baseline vision (<20/200).

- Surgical intervention with subretinal tPA is recommended only in severe cases, as determined by hemorrhage thickness and location.

The Viewpoint ‘Management of subfoveal hemorrhage’ can be downloaded from: https://www.visionacademy.org/resource-zone/treatment-best-practices
Additional larger studies are required to investigate the efficacy of anti-VEGF, as monotherapy or in combination with other treatment modalities, for the management of subfoveal hemorrhage in nAMD.

Treatment decisions may be affected by regional variations in reimbursement policies; however, the decision to treat should be based primarily on clinical experience and consideration of the available evidence.