10th Conference on Health Care of the Chinese in North America

Retina Disease Among Asians: Is There A Difference?

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CLINICAL TRIALS OF TREATMENT FOR DIABETIC RETINOPATHY

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I. DIABETIC RETINOPATHY STUDY (DRS)

A. Major eligibility criteria

1. Visual acuity ≥ 20/100 in each eye
2. PDR in at least one eye or severe NPDR in both
3. Both eyes suitable for photocoagulation

B. Major design features

1. One eye of each patient was assigned randomly to photocoagulation [scatter (panretinal), local (direct confluent treatment of surface new vessels), and focal (for macular edema) as appropriate]. The other eye was assigned to follow-up without photocoagulation.
2. The treated eye was randomly assigned to argon laser or xenon arc.

C. Major conclusions

1. Photocoagulation reduced the risk of severe visual loss by 50% or more (SVL = VA < 5/200 at two consecutively completed 4-month follow-up visits.)
2. Photocoagulation was attended by modest risks of a decrease in visual acuity (usually only one line) and in visual field (risks greater with xenon than argon).
3. Treatment benefit outweighs risks for eyes with high-risk PDR. The 50% 5-year rate of SVL in such eyes without treatment was reduced to 20% by treatment.

II. EARLY TREATMENT DIABETIC RETINOPATHY STUDY (ETDRS)

A. Major eligibility criteria

1. Visual acuity ≥ 20/40 (≥ 20/400, if reduction caused by macular edema)
2. Mild NPDR to non high-risk PDR, with or without macular edema
3. Both eyes suitable for photocoagulation

B. Major design features

1. One eye of each patient was assigned randomly to early photocoagulation and the other to deferral (careful follow-up and photocoagulation if high-risk PDR develops)
2. Patients were assigned randomly to aspirin or placebo

C. Major conclusions

1. In eyes with clinically significant macular edema (CSME), focal photocoagulation (with or without grid) reduced the risk of moderate visual loss (doubling of the visual angle) by 50% or more (at 3 years from 30% in eyes assigned to deferral to less than 15% in eyes assigned to immediate focal treatment), and increased the chance of a small improvement in visual acuity.

2. Both early photocoagulation and deferral were followed by low rates of severe visual loss or vitrectomy, which were combined as a measure of serious adverse outcome. The 5-year rate in the deferral group was about 6%, compared to about 4% in the early photocoagulation group.

3. Focal photocoagulation should be considered for eyes with CSME.

4. Scatter photocoagulution is not indicated for mild to moderate NPDR, but should be considered as retinopathy approaches the high-risk stage, and usually should not be delayed when the high-risk stage is present.

III. DIABETIC RETINOPATHY VITRECTOMY STUDY (DRVS)

A. Group H - Recent severe vitreous hemorrhage

1. Major eligibility criteria

a. Visual acuity ≤ 5/200
b. Severe vitreous hemorrhage, consistent with VA, duration 1-6 months
c. Macula attached by ultrasound

2. Major design features

a. In most patients, only one eye is eligible

b. Eligible eye(s) assigned randomly to early vitrectomy or conventional management, which consisted of vitrectomy if the center of the macula detached or if vitreous hemorrhage persisted for 1 year. Photocoagulation was carried out as needed and as possible.

3. Major conclusions

a. The chance of recovery of VA ≥ 10/200 was increased by early vitrectomy, at least in patients with Type 1 diabetes, who were younger and had more severe PDR. In the most severe PDR group, VA was ≥ 10/200 at 4 years in 50% of the early vitrectomy group versus 12% in conventional management group

B. Group NR - Very severe PDR with useful vision

1. Major eligibility criteria

a. Visual acuity ≥ 10/200
b. Center of the macula attached
c. Extensive, active, neovascular or fibrovascular proliferations

2. Major design features

a. Same Group H, except conventional management included vitrectomy after a 6 month waiting period in eyes that developed severe vitreous hemorrhage

3. Major conclusions

a. Chance of VA ≥ 10/200 increased by early vitrectomy, at least for eyes with very severe new vessels

VISION LOSS IN DIABETES

I. PATHOGENESIS

A. It is generally agreed that the underlying abnormality in diabetic retinopathy is chronic hyperglycemia, although the pathogenetic mechanisms responsible for the natural history of this disorder are not completely understood.

B. Histologic findings include basement membrane thickening, endothelial proliferation, and pericyte loss.

C. Occlusion of retinal capillaries is thought to be secondary to abnormalities of the vessel wall.

1. Clotting disorders have been demonstrated and may contribute to capillary nonperfusion

a. In the Early Treatment Diabetic Retinopathy Study (ETDRS), a trial of aspirin (650 mg/day) vs placebo failed to demonstrate an effect on the incidence or progression of retinopathy in patients taking this antiplatelet aggregation medication.

II. STAGES OF DIABETIC RETINOPATHY

A. Nonproliferative (background) diabetic retinopathy

1. Two fundamental changes are responsible for the initial clinical abnormalities in diabetic retinopathy: capillary closure and increased vascular permeability or leakage

a. Increased retinal vascular permeability produces:

i. Dot-and-blot hemorrhages
ii. Retinal edema
iii. Fluorescein dye leakage
iv. Hard exudate formation

b. Focal intraretinal capillary closure leads to

i. Microaneurysms
ii. Retinal vascular loops
iii. Dilated capillaries
iv. Ischemic maculopathy

2. Treatment

a. Optimal control of the diabetes

i. The effect of blood sugar control on the progression of retinopathy remains controversial, but there is accumulating evidence that both the rate and severity of retinal changes are favorably influenced by control of blood glucose levels.

b. Control of systemic hypertension (if present)

c. The ETDRS recommends consideration of focal green-only argon laser for clinically significant macular edema (CSME),

which is defined as retinal thickening or adjacent hard exudate that involves or threatens the center of the macula. One or more of the following qualify an eye as having CSME.

i. Thickening within 500 μm of center, or
ii. Hard exudate within 500 μm of center (if adjacent to thickened retina), or
iii. An area of thickening at least 1 disc area in size, at least part of which is within 1 DD of the center

B. Preproliferative (severe nonproliferative) diabetic retinopathy

1. Widespread capillary closure causes retinal ischemia

2. The Diabetic Retinopathy Study (DRS) defined this stage as the presence of any three of the following:

a. Cotton-wool spots
b. Intraretinal microvascular abnormalities (IRMAs)
c. Venous beading
d. At least moderately severe retinal hemorrhages and/or microaneurysms

3. Treatment

a. Focal laser for CSME
b. Consideration of panretinal photocoagulation (PRP) for severe or very severe preproliferative diabetic retinopathy
c. Proliferative diabetic retinopathy

i. Neovascularization

a. May result from a disturbance of factors involved in homeostasis of the retinal vessels and not only from the production of one vasoproliferative factor

ii. Vitreous hemorrhage

a. Vitreous traction can lead to rapture of friable neovascular fronds with resultant hemorrhage
b. One study has indicated that limiting the activity of patients is not an effective method of preventing vitreous hemorrhage
c. The ETDRS demonstrated that aspirin therapy (650 mg/day) did not affect the incidence of vitreous hemorrhage

iii. Retinal detachment

a. Pars plans vitrectomy permits macular re-attachment through the elimination of fractional vitreoretinal adhesions

iv. Treatment

a. The Diabetic Ratinopathy Study demonstrated that the timely application of laser therapy reduces the incidence of severe visual loss by 56%

b. Panretinal (full scatter) laser therapy should be performed on eyes with high-risk characteristics

- Disc neovascularization (NVD) ≥ about 1/4 to 1/3 disc area as depicted in standard photo 10A with or without vitreous or preretinal hemorrhage, or

- Vitreous or preretinal hemorrhage with any amount of new vessels, observed or assumed to be present but obscured by hemorrhage

c. Panretinal laser therapy should be performed for eyes with rubeosis iridis secondary to severe retinal ischemia

d. Panretinal laser therapy should be considered for eyes "approaching the high-risk stage"

ARMD

AGE-RELATED MACULAR DEGENERATION

Age-related macular degeneration (ARMD) is characterized by the presence of non-exudative macular abnormalities (drusen, macular RPE changes, geographic atrophy) and exudative macular abnormalities (subretinal neovascular membranes, serous and hemorrhagic detachments of the RPE and/or retina, disciform scarring) that result in central visual loss in elderly individuals. ARMD is the most common cause of irreversible legal blindness in individuals 52 years of age and older. The Framingham population-based study found fundoscopic evidence of ARMD and visual acuities of 20/30 or worse in 5.7% of 2631 individuals aged 52 years and older. The incidence of ARMD was strongly associated with age. ARMD was present in 1.6% of individuals between 52 and 64 years of age, 11% of individuals between 65 and 74 years of age and 27.9% of individuals 75 years

of age or older. Although non-exudative ARMD is approximately 10 times as common as exudative ARMD, the majority of individuals with severe permanent central visual loss have the exudative form of ARMD. In the Framingham study, 2.2% of individuals 65 years of age or older were blind in one or both eyes from ARMD. Approximately 80% of eyes with visual acuities of 20/200 or worse demonstrated the exudative form of ARMD.

NON-EXUDATIVE AGE-RELATED MACULAR DEGENERATION CLINICAL FEATURES

Patients with non-exudative ARMD typically present with gradual painless onset of blurred or distorted vision. Others may be asymptomatic with only a mild decrease in visual acuity when subtle macular abnormalities are discovered on routine ophthalmic examination. The earliest ophthalmoscopic signs of non-exudative ARMD are bilaterally symmetrical macular drusen and a subtle mottling of the macular pigmentation. Drusen are yellow deposits beneath the RPE and are usually most numerous in the region between the temporal vascular arcades, although they may also be located nasal to the disc or in the midperipheral retina. Drusen are best visualized with biomicroscopic retroillumination during which they appear as semitranslucent deep depositions. As the overlying RPE atrophies, the yellow color of the drusen is more easily appreciated. The various types of macular drusen that may be seen include hard drusen, soft drusen, semi-solid drusen and calcified drusen. Hard drusen are small, round, yellow-white deposits with well-defined borders that are often associated with hypopigmentation or hyperpigmentation of the adjacent RPE. Hard drusen are the most common type of drusen and are thought to represent nodular deposits formed by shedding of the basal cytoplasm of the RPE cells through their basement membrane into the subjacent space. Soft drusen are larger and have less well-defined borders compared with hard drusen. They gradually enlarge and may coalesce to form multiple irregular areas of localized RPE detachments. Semi-solid drusen are intermediate in funduscopic characteristics between hard and soft drusen. Finally, some drusen may acquire a glistening crystalline appearance over time, possibly caused by dystrophic calcification at which time they are referred to as calcified drusen.

Another form of drusen, named basal laminar or cuticular drusen, has been described by Gass and associates. Basal laminar drusen are small, well-defined, slightly raised, yellow, subretinal dots of uniform size that appear semitranslucent on biomicroscopic retroillumination. Basal laminar drusen are typically very numerous, distributed in a bilaterally symmetrical pattern, are most prominent in the posterior poles and tend to occur in younger individuals. These unusual drusen are often seen in association with other typical hard, soft or semi-solid drusen. Visual acuity is typically minimally affected despite the large number of these drusen. Thus, eyes with basal laminar drusen generally have a better visual prognosis, although small yellow exudative RPE detachments with a vitelliform appearance, geographic atrophy or subretinal neovascularization may develop. Histopathologically, basal laminar drusen correspond to focal areas of RPE attenuation overlying nodular thickenings of the RPE basement membrane. Basal laminar drusen may represent a nodular dystrophy of the RPE basement membrane and may, therefore, be a disease entity that is distinct from age-related macular degeneration.

The natural history of eyes with macular drusen is not welldefined. Most of the published studies are based on data collected in tertiary retinal referral centers which tend to attract more severely affected individuals. It is important to note that most, individuals with

macular drusen maintain good central vision throughout life. However, some patients may experience a severe loss of central vision, mostly due to the development of exudative changes. Gass followed 49 patients with bilateral macular drusen for an average of 4.9 years. Patients studied did not have exudative changes at the time of. enrollment. He noted that 18% of individuals had visual acuities of 20/200 or worse in at least one eye and 10% of individuals had visual acuities of 20/200 or worse in both eyes at the end of the study. The majority of patients who developed severe visual loss demonstrated exudative changes at the end of the study, although some demonstrated geographic atrophy. Smiddy and Fine, in a retrospective study of 71 individuals with bilateral drusen, estimated that the risk for developing exudative changes was 8% in 3 years. They noted that more drusen, larger confluent drusen and focal RPE hyperpigmentation were ophthalmoscopic characteristics that tended to be associated with a higher risk of developing exudative changes and severe visual loss.

Patients with geographic atrophy, the more severe form of non-exudative ARMD, also present with gradual painless blurring of vision. Geographic atrophy refers to one or several, well-defined areas of atrophy of the RPE and choriocapillaris that may be round, oval, annular or irregular in shape. Geographic atrophy is typically located within the temporal arcades and is bilateral in approximately half of affected individuals. When severe, atrophy of the sensory retina, RPE and choroid results in increased visualization of the larger choroidal vessels, which may appear to have thickened walls, within the zone of geographic atrophy. If the central fovea is involved, the visual acuity may be 20/100 or worse. Confluent or individual soft or semi-solid drusen, or serous RPE detachments, may develop into zones of geographic atrophy, although zones of geographic atrophy can also develop in areas of normal appearing RPE and retina. Zones of geographic atrophy expand gradually over a period of years, often become confluent, and may demonstrate a tendency to spare the central fovea until late in the course of the disease. Schatz and McDonald followed 50 eyes of 50 consecutive patients with ARMD and geographic atrophy for an average of 3.4 years. They found that geographic atrophy tended to follow the disappearance or flattening of soft drusen, RPE detachments or reticular mottling of the macular RPE. The average speed of expansion of zones of geographic atrophy was 139 microns per year and they noted a tendency towards formation of annular zones of geographic atrophy that surrounded, but spared, the cetral fovea. Subretinal neovascular membranes (SRNVMs) developed in 20% of eyes, were typically located at the edge of a zone of geographic atrophy, and tended to grow away from the atrophic area. A drop in visual acuity from 20/50 or better to 20/100 or worse occurred in 8% of eyes per year.

ANCILLARY STUDIES

Fluorescein angiography of hard drusen demonstrate typical RPE window defects with early hyperfluorescence that fades rapidly in later phases of the angiogram. More drusen may be seen on fluorescein angiography than is evident by ophthalmoscopy. However, some hard drusen may not demonstrate early hyperfluorescence, possibly due to lipid accumulation within the RPE cell or lack of RPE atrophy. In contrast with hard drusen, soft drusen demonstrate increasing hyperfluorescence on fluorescein angiography, but leakage beyond the borders of the drusen is absent. Semi-solid drusen also demonstrate similar late staining but tend to be less hyperfluorescent when compared with soft drusen. Basal laminar drusen demonstrate numerous well-defined dots of early hyperfluorescence that

result in a "starry-night" appearance that fades in later phases. Zones of geographic atrophy may demonstrate early hypofluorescence due to choriocapilaris atrophy, followed by progressive late hyperfluorescent staining.

DIFFERENTIAL DIAGNOSIS

The distinction between familial drusen and the macular drusen seen in ARMD remains unclear. Familial drusen are thought to be more numerous, are present nasal to the optic disc, occur at an earlier age, and follow a dominant pattern of inheritance. Some authorities postulate that familial drusen represent a variant of ARMD. Indeed, many patients with ARMD demonstrate a positive family history of macular degeneration. The differential diagnosis of geographic atrophy includes central areolar choroidal dystrophy, Stargardt's disease, cone-rod dystrophy and chloroquine toxicity.

HISTOPATHOLOGY

Drusen are thought to represent the extruded contents of RPE cells that are a result of RPE cell metabolism and may be related to the degradation of shedded photoreceptor outer segments. Histopathologic examination of hard drusen reveals localized acuumulation of hyaline material between the inner and outer collagenous layers of Bruch's membrane. Soft drusen are caused by deposition of amorphous material between thickened basement membrane of the RPE and the outer collagenous layer of Bruch's membrane. Histopathologic examination of eyes with severe geographic atrophy reveals localized atrophy of RPE and choriocapillaris with secondary degeneration of the overlying photoreceptors.

TREATMENT

Despite extensive studies, the cause of ARMD and the factors responsible for the progression of visual loss in elderly patients with ARMD remain poorly understood. It is therefore not surprising that therapeutic options for this disease are currently limited. No therapeutic intervention has been conclusively proven to be useful in the prevention, reduction, or reversal, of visual loss secondary to non-exudative ARMD. Thus, the management of non-exudative ARMD is based on the early detection and management of the exudative changes that may develop, as described in the following section. Patients should be informed of the early symptoms of exudative ARMD (metamorphopsia, decreased vision, a new scotoma) and the importance of seeking appropriate medical care as soon as possible. Daily Amsler grid self-examination has been advocated as a means of allowing for earlier detection of macular dysfunction.

Therapeutic modalities that have been suggested for nonexudative ARMD include reducing exposure to light, nutritional supplementation, cessation of tobacco use and control of other systemic disease.

It has been suggested that excessive exposure to sunlight may result in acceleration of macular degenerative processes in individuals predisposed to ARMD, particularly those with fair complexion. Although epidemiologic evidence suggests that sunlight may play a role in cataract formation, evidence for a similar role in the progression of ARMD is not

convincing. However, it seems reasonable to recommend the use of sunglasses during exposure to bright sunlight such as when one is on a sunny beach. Sunglasses are a simple, effective and relatively inexpensive method of decreasing light exposure with minimal side-effects. Lenses that block ultraviolet light do not change color perception, but lenses that block blue light may distort color perception and may not be tolerated by some individuals. Some clinicians postulate that, since prolonged exposure to sunlight may have a cumulative effect, younger immediate relatives of patients with severe visual loss secondary to ARMD should be encouraged to wear sunglasses. However, conclusive scientific data for this recommendation is lacking.

The role of nutritional supplementation for non-exudative ARMD remains controversial. It has been suggested that radiant energy may cause free radical formation that can initiate lipid peroxidation of photoreceptor outer-segment membranes and disturb RPE cell metabolism in the absence of adequate protective mechanisms. Vitamins A, C and E, zinc, carotenoids, glutathione and various anti-oxidant enzymes are thought to prevent cellular damage by acting as free radical scavengers. Indeed, the Eye Disease Case-control Study Group compared serum levels of micronutrients with antioxidant capabilities in 421 patients with exudative ARMD with 615 controls and found that higher serum levels of carotenoids were associated with a significantly decreased risk of exudative ARMD. Although this might appear to be a plausible rationale for nutritional supplementation for non-exudative ARMD, conclusive evidence for efficacy of these substances in human clinical trials is still lacking. Interest in zinc supplementation for patients with ARMD has been stimulated by a prospective, randomized, double-masked controlled clinical trial involving 151 patients that was conducted by Newsome and associates. Zinc is a co-factor in many enzyme systems and the eye has the highest concentration of zinc in the body. Furthermore, zinc deficiency is prevalent in the elderly population, even in the United States. Newsome and associates, in their clinical trial involving 151 patients followed for 12 to 14 months, reported that only 14% of patients with non-exudative ARMD who were placed on 100 mg of oral zinc twice daily experienced loss of at least ten letters on the ETDRS eye chart, compared with 34% of untreated patients over a period of 12 to 14 months. Interestingly,the study did not demonstrate any significant correlation between serum zinc levels and visual acuity. Indeed, other studies have found an inverse: relationship between severity of ARMD and zinc levels, that is, higher serum zinc levels have been correlated with more severe macular degenerative changes. Furthermore, zinc supplementation may cause copper malabsorption and a hypochromic anemia, although this can be prevented with copper supplementation. In view of this potential side-effect, most commercialformulations of zinc supplementation for eye disease, such as Ocuvite or I-Caps, also contain copper. Zinc therapy may also cause other systemic side-effects, including gastric irritation. Thus, the role of nutritional supplementation for patients with ARMD remains unclear. The Age-Related Eye Disease Study, a multi-center controlled study sponsored by the National Eye Institute,should provide more scientific evidence for the role of nutritional supplementation in this disease.

Tobacco use, systemic hypertension and cardiovascular disease have been associated with a higher risk of visual loss due to ARMD. Although control of these factors have not been demonstrated to ameliorate the visual effects of ARMD, cessation of tobacco and optimal medical management of hypertension and cardiovascular disease is beneficial for the individual's general health and should be recommended for all patients with ARMD.

EXUDATIVE AGE-RELATED MACULAR DEGENERATION CLINICAL FEATURES

Patients with exudative ARMD typicaly present following the onset of metamorphopsia, central visual loss, or a new scotoma. Some patients report the presence of rapidly flickering or flashing lights. Occasionally, non-menacing formed hallucinations, such as faces or inanimate objects, may be perceived (Charles Bonnet syndrome). Fundus examination may reveal the presence of hemorrhage, hard exudates and retinal thickening associated with an oval or irregular, dirty, green-gray coloration which represents a subretinal neovascular membrane (SRNVM). The hemorrhage and exudation from the SRNVM are usually more evident than the membrane itself. Hemorrhage is typically subretinal, but it may also be located beneath the RPE, within the sensory retina, or in all three locations. Leakage of fluid from the SRNVM into the subretinal space, subRPE space and sensory retina results in exudative macular detachment, RPE detachment and macular edema respectively. Hard exudates, typically in a partial circinate pattern, are often present in a subretinal, subRPE or intraretinal location.

Serous RPE detachments are a less common cause of severe visual loss in patients with exudative ARMD. Serous RPE detachments appear as sharply demarcated, round or oval, yelloworange, blister-like mounds under the RPE. The detached RPE may become atrophic or may develop pigment figures in a hot cross bun or triradiate patterns. Funduscopic features suggestive of the presence of a SRNVM in eyes with RPE detachments include overlying detachment of sensory retina, cystoid macular edema, indentation of the margin of the, detached RPE (notch sign), presence of hemorrhage or hard exudates, uneven elevation of the detached RPE and RPE folds. A hemorrhagic RPE detachment has a characteristic greenish color due to accumulation of blood in a mound under the RPE and the overlying RPE pigmentation. Occasionally, it may even simulate a choriodal melanoma, although the associated signs of serous or lipid exudation and subretinal hemorrhage help to reveal its true nature.

Exudation or traction from a SRNUM under the RPE may occasionally create sufficient forces to cause a RPE tear. An RPE tear may also be precipitated by sudden thermal-induced shrinkage of a SRNVM that can occur during photocoagulation therapy. Fundus examination reveals the presence of a crescent-shaped zone of bared choroidal vessels. The outer arc of the crescent represents the torn edge of RPE and is typically located at one edge of the previous RPE detachment. The inner arc of the crescent appears darker and represents the retracted, scrolled-up sheet of RPE. If the central fovea is involved, visual loss is often dramatic, immediate, and permanent.

The endstage of exudative ARMD is the disciform scar, which is a yellow-white disciform-lesion typically associated with detachment of the sensory retina, cystoid macular changes, hard exudates, hemorrhage and variable degrees of increased pigmentation. The RPE and sensory retina is typically distorted by the cicatrical changes and may demonstrate radial traction lines. Retinochoroidal vascular anastomoses may be seen. Occasionally, the serous and/or hemorrhagic process may be massive and result in detachment of large areas of RPE and retina and involve the fundus beyond the equator. Occasionally, subretinal blood may pass through the retina and cause severe loss of central and peripheral vision due to vitreous hemorrhage.

The visual prognosis for individuals with exudative age-related macular degeneration is poor. Klein and associates reported that eyes with well-defined SRNVMs demonstrate an average growth rate of 10 microns per day during the acute phase. However, some SRNVMs may grow up to 24 microns a day, indicating the importance of a recent fluorescein angiogram for defining the extent of a SRNVM. The visual prognosis is even poorer when the SRNVM lies close to the center of the fovea. The Macular Photocoagulation Study Group reported that the 62% of untreated eyes with well-defined extrafoveal SRNVMs experienced severe visual loss equivalent to at least quadrupling of the visual angle by 36 months. Almost 75% of SRNVMs grew into the central fovea during that period. The visual prognosis of eyes with juxtafoveal and subfoveal SRNVMs is even worse. Bressler and associates studied the natural history of 96 eyes with ARMD complicated by juxtafoveal or subfoveal SRNVMs. Of the 38 eyes with juxtafoveal SRNVMs (located 1 to 250 microns from the center of the foveal avascular zone), 92% had initial visual acuities of 20/100 or better. After an average follow-up of 21 months, 89% of eyes with juxtafoveal SRNVMs had lost two or more lines of Snellen visual acuity, and 71% had final visual acuities of 20/200 or worse. Subfoveal SRNVMs are associated with the worst visual prognosis. In the study conducted by Bressler and associates, 70% of 58 eyes with ARMD and subfoveal SRNVMs had final visual acuities of 20/200 or worse. Similarly, Guyer and associates reported that 77% of 22 patients with ARMD and subfoveal SRNVMs and an initial visual acuity of 20/100 or better lost at least four lines of vision without treatment after 24 months. The visual prognosis of poorly-defined SRNVMs is also poor and is only slightly better than that for well-defined SRNVMs.

The visual prognosis of eyes with ARMD and RPE detachments with evidence of SRNVMs demonstrable by fluorescein angiography is also poor, especially if the fovea is involved. Singerman and Stockfish found that 65% of eyes with ARMD and foveal RPE detachments with SRNVMs had visual acuities of less than 20/200 after one year. However, eyes with ARMD and serous RPE detachments without evidence of subretinal neovascularization have a much better visual prognosis, even if the subfoveal RPE is elevated. In addition, eyes with persistent RPE detachments tend to have better visual acuities than eyes with spontaneous collapse of the RPE detachment or eyes that develop RPE tears or subretinal neovascularization. Patients younger than 55 years of age with serous RPE detachments in the absence of foveal involvement or subretinal neovascularization have a much better visual prognosis, but this subgroup of patients may represent a variant of idiopathic central serous chorioretinopathy rather than exudative ARMD. Eyes with RPE tears often demonstrate poor vision, especially if the fovea is involved. The fellow eye is also at a higher risk of visual loss, usually from RPE detachments and/or RPE tears.

Eyes with vitreous hemorrhage due to breakthrough of hemorrhage from ARMD also have a poor visual prognosis. The vitreous hemorrhage typically clears over a period of months in approximately three quarters of affected eyes but the macula is typically destroyed by the exudative and cicatricial processes.