

# VITRECTOMY FOR THE TREATMENT OF SUBMACULAR HEMORRHAGES FROM MACULAR DEGENERATION: A COMPARISON OF SUBMACULAR HEMORRHAGE/MEMBRANE REMOVAL AND SUBMACULAR TISSUE PLASMINOGEN ACTIVATOR-ASSISTED PNEUMATIC DISPLACEMENT

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## ABSTRACT

*Purpose:* To evaluate two techniques for treatment of large submacular hemorrhages resulting from choroidal neovascularization associated with age-related macular degeneration.

*Methods:* Retrospective consecutive case series of 42 eyes of 42 patients who presented with submacular hemorrhages of at least 12 disc areas associated with visual loss of 3 months or less duration. One of two treatments was performed: (1) vitrectomy with removal of the submacular hemorrhage/neovascular membrane complex using subretinal forceps (SRH group), or (2) vitrectomy with injection of subretinal tissue plasminogen activator (TPA) followed by air-fluid exchange to achieve pneumatic displacement of the hemorrhage (TPA group).

*Results:* The mean visual acuity in the SRH group improved from 20/1000 -1 to 20/640 -2 at 3 months and 20/640 at 1 year and at the final examination at a mean of 2.92 years ( $P = .048$ ). The mean visual acuity in the TPA group remained stable initially with a visual acuity of 20/500 preoperatively and 20/640 +2 at 3 months. The visual acuity in the TPA group deteriorated to 20/1000 -2 at 1 year and 20/1000 +2 at the final examination at a mean of 2.3 years ( $P = .031$ ). Visual acuity improved by at least .3 logMAR units (3 lines) in 44% of the SRH group at 3 months and in 48% at 1 year and at the final examination compared with 20% of the TPA group at 3 months and 13% at 1 year and at the final examination ( $P = .042$  comparing SRH and TPA groups at 1 year and final examination).

*Conclusions:* Vitrectomy with removal of the subretinal neovascular membrane/hemorrhage complex resulted in better visual results than displacement of the subretinal hemorrhage primarily due to continuing declines in the TPA group.

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## INTRODUCTION

Optimal treatment of submacular hemorrhages arising from age-related macular degeneration remains controversial. Submacular hemorrhages most frequently develop spontaneously from choroidal neovascularization in elderly adults. Some patients are taking anticoagulants, which may increase the risk of subretinal bleeding. Small submacular hemorrhages (<12 disc areas) with thin layers of subretinal blood have better prognoses, and treatment is usually directed toward the associated choroidal neovascular membrane. If the choroidal neovascular membrane for small lesions is entirely obscured by hemorrhage, then these eyes are usually observed until the hemorrhage clears sufficiently to allow a treatable choroidal neovascularization subtype to be identified. Larger submacular hemorrhages ( $\geq 12$  disc areas) with a thick layer of subretinal blood do not have a clear treatment algorithm. Some of the treatments reported have included subretinal neovascular membrane and hemorrhage removal with forceps,<sup>1</sup> injection of gas without tissue plasminogen activator (TPA),<sup>2,3</sup> injection of intravitreal TPA alone,<sup>4</sup> injection of intravitreal TPA with gas,<sup>5-9</sup> injection of subretinal TPA with displacement by perfluorocarbon liquid,<sup>10</sup> injection of subretinal TPA followed by hemorrhage evacuation,<sup>11,12</sup> vitrectomy with intravitreal injection of TPA with an intraocular gas bubble to help displace the hemorrhage inferiorly,<sup>13</sup> and vitrectomy with injection of subretinal TPA combined with a gas bubble.<sup>14,15</sup> The recently reported Subretinal Surgery Trials (SST) for Group B<sup>16</sup> found that subretinal surgery with hemorrhage and membrane removal alone was not any better than natural history using a loss of eight or more letters as the primary visual acuity end point. In this trial, 36% of eyes had a neovascular membrane/hemorrhage complex of 12 disc diameters or less. Visual acuity was also relatively good, with 36% of eyes having a visual acuity of 20/100 to 20/160. The eyes in the current study represented the approximately two thirds of eyes in the SST B group that had larger, thicker subretinal hemorrhage and worse visual acuities. The purpose of the current study was to evaluate the results of submacular surgery for thick submacular hemorrhages that were at least 12 disc areas in size and to compare the results with those of an alternate technique of vitrectomy, consisting of injection of subretinal TPA to displace the subretinal hemorrhage without removal of the neovascular membrane.

## METHODS

This was a retrospective consecutive case series of 42 eyes of 42 patients who presented with submacular hemorrhage related to exudative macular degeneration and had surgery between 1994 and 2004. Only patients with relatively recent hemorrhages (<3 months) were treated.

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Most patients reported the abrupt onset of decreased acuity. The appearance of the subretinal hemorrhage was also evaluated to exclude eyes with white to yellow subretinal hemorrhages from denaturation of hemoglobin because the condition was presumably chronic and patients were less likely to benefit from removal. Patients were treated by one of two techniques. Patients who underwent surgery from 1994 through 2001 were offered only submacular surgery with removal of the neovascular membrane complex; they were designated the SRH group, meaning subretinal hemorrhage/membrane removal. The subretinal hemorrhage had to extend to at least the superotemporal or inferotemporal arcade (size >16 disc areas) to be offered surgery in the SRH group. A pars plana vitrectomy was performed with removal of the posterior hyaloid. A posterior vitreous detachment was created if the posterior hyaloid was not already detached. A retinotomy was made with a sharp pick or bent MVR blade adjacent to where the edge of the neovascular membrane was visualized or anticipated. The vitreous infusion pressure was elevated just prior to removal of the neovascular membrane. The neovascular membrane was then grasped by subretinal forceps and removed. Usually a majority of the subretinal hemorrhage was adherent to the neovascular membrane and was removed with the membrane. The infusion pressure was lowered gradually after 60 seconds. Care was taken to remove any residual subretinal blood around the retinotomy to allow laser endophotocoagulation to the retinal pigment epithelium around the edges of the retinotomy. The peripheral retina was checked for peripheral retinal breaks followed by a fluid-air exchange, filling the vitreous with air. Laser endophotocoagulation was used to surround the retinotomy, and the patient was instructed to remain prone for 3 days following surgery.

Patients who underwent surgery from 2001 through 2004 with smaller, less thick submacular hemorrhages were offered vitrectomy with injection of subretinal TPA to displace the hemorrhage (TPA group) or treatment with the SRH protocol. The SRH procedure was favored for eyes presenting with very large submacular hemorrhages outside of temporal arcades. The submacular hemorrhage had to be at least 12 disc areas to be treated with TPA but did not have to reach the temporal arcades. Vitrectomy was performed with removal of the posterior hyaloid. Then, approximately 0.1 to 0.2 mL of a 12.5 µg/0.1 mL TPA solution was injected into the subretinal space via a subretinal cannula immediately before the fluid-air exchange. No attempt was made to remove any hemorrhage or neovascular membrane from the subretinal space. The eye was filled about 75% with air, and the patient remained prone 50% of the time for 3 days to encourage displacement of the subretinal blood into the inferior periphery. Most eyes in the TPA group had displacement of a majority, but not all, of the subretinal hemorrhage into the inferior equatorial midperiphery.

Eyes were monitored postoperatively for complications and response to the surgery. Most eyes were examined at 1 day, 1.5 weeks, 6 weeks, 3 months, 6 months, 1 year, and at variable times thereafter. Nuclear sclerosis and posterior subcapsular cataracts were graded preoperatively and postoperatively by use of the Lens Opacity Classification System II (LOCS II) standard photographs, which were adapted for use in the Age-Related Eye Disease Study (AREDS).<sup>17,18</sup> Most eyes in the SRH group had geographic atrophy after the surgical procedure, corresponding to the area where the choroidal neovascular membrane was removed, so no additional treatment was required. Some eyes in the TPA group had postoperative treatment with photodynamic therapy if an appropriate lesion subtype was identified, but most did not have eligible lesions based on the recommendations for photodynamic therapy. Numerical variables were compared by using the *t* test for independent samples, and categorical data were compared by using Fisher's exact test.

## RESULTS

The baseline demographic features are summarized in the Table. Patients in the SRH group tended to be younger (78.5 versus 82.5 years), but the difference did not reach statistical significance ( $P = .06$ ). The duration of the subretinal hemorrhage and duration of follow-up were similar for the SRH and TPA groups. The time interval between the symptoms of abrupt decreased acuity from the hemorrhage and surgery varied from 1 day to 3 months, with 69% of eyes having symptoms of 1 month or less.

**TABLE. COMPARISON OF PREOPERATIVE DEMOGRAPHICS FOR PATIENTS UNDERGOING SUBRETINAL HEMORRHAGE/MEMBRANE REMOVAL (SRH GROUP) AND TISSUE PLASMINOGEN ACTIVATOR-ASSISTED PNEUMATIC HEMORRHAGE DISPLACEMENT (TPA GROUP)**

FEATURE	SRH GROUP n = 27	TPA GROUP n = 15	P VALUE
Mean age	78.8 ± 1.4	82.5 ± 1.5	.06
Sex	19/27 female (70.4%)	9/15 female (60%)	.52
Preoperative acuity	20/1000 -1 (20/70 -2 to HM)	20/500 (20/100 to 2/200)	.04
Fellow eye preoperative acuity	20/250 +2 (20/25 +1 to NLP)	20/100 +1 (20/25 to LP)	.10
Symptom duration	.87 ± .17 months	.96 ± .25 months	.74
Length of follow-up	2.92 ± .48 years	2.30 ± .25 years	.26

HM = hand motions; LP = light perception; NLP = no light perception.

Surgery was performed within a week of presentation in most patients who elected to have surgery, but patients often did not present to an ophthalmologist promptly following the acute onset of decreased acuity. Many of the eyes with subretinal hemorrhage had some

degree of decreased acuity prior to the hemorrhage due to previously diagnosed exudative macular degeneration. Ten eyes (23.8%) had prior photodynamic therapy before the development of the submacular hemorrhage. Preoperative visual acuity was significantly worse ( $P = .04$ ) in the SRH group, which was expected because the hemorrhages were larger and tended to be thicker than in the TPA group. The mean preoperative visual acuity was also worse in fellow eyes of the SRH group, although the difference was not statistically significant ( $P = .10$ ).

The mean visual acuities for the SRH and TPA groups are compared in Figure 1. It is of interest that the SRH group showed a significant improvement in visual acuity ( $P = .048$ ), whereas the TPA group had a significant decline in visual acuity ( $P = .031$ )

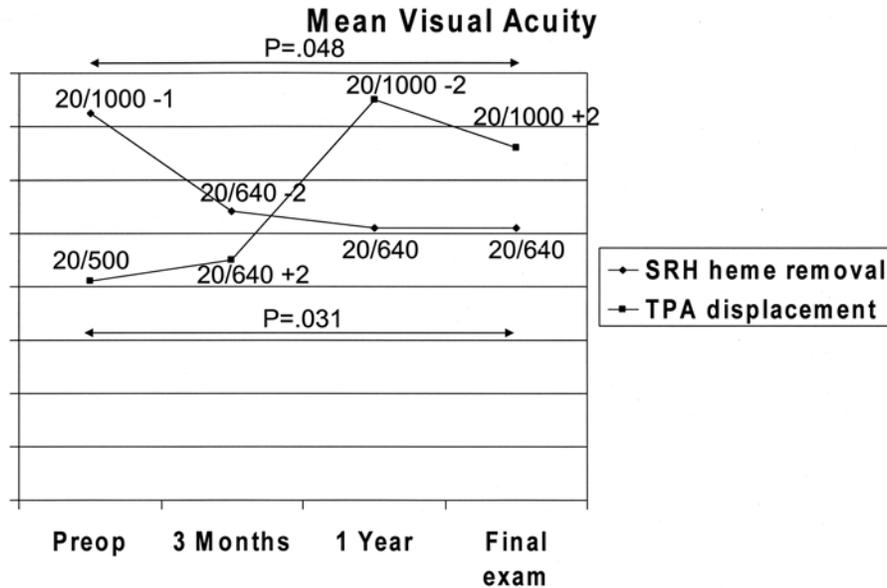


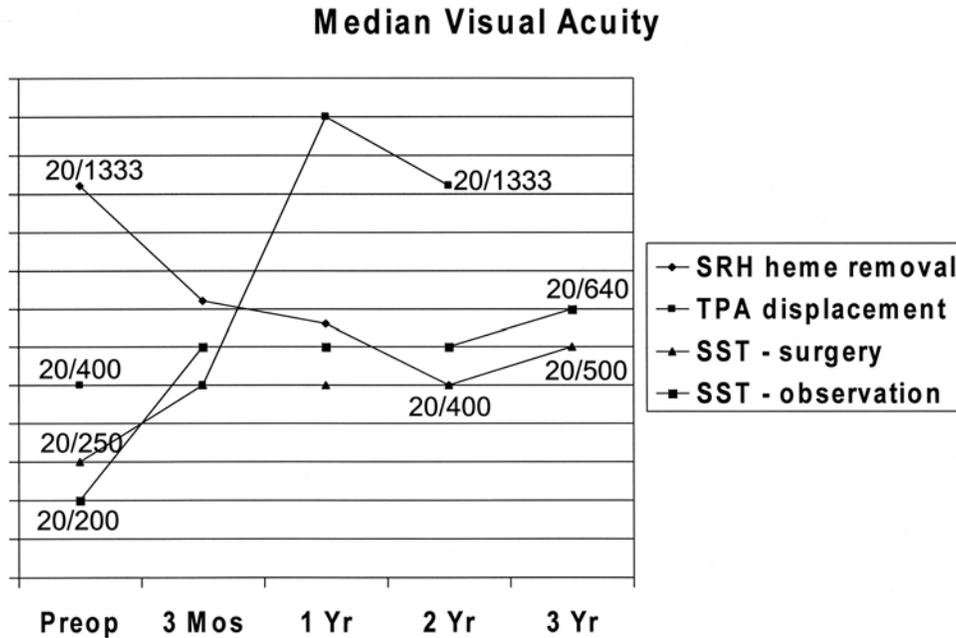
FIGURE 1

Mean visual acuity for the eyes that had removal of the subretinal neovascular membrane/subretinal hemorrhage (SRH group) and eyes that had displacement of the subretinal hemorrhage by tissue plasminogen activator (TPA group). The eyes in the SRH group had statistically significant improvements in visual acuity, and the eyes in the TPA group showed significant decreases in visual acuity.

between the preoperative and final visit. Figure 2 compares the median visual acuity for the SRH and TPA groups as well as the SST surgery and control groups.<sup>16</sup> The SRH group showed improvement and the TPA group had a deterioration in median visual acuity, similar to the results with mean visual acuity. Both the surgery and control groups in the SST B group showed a modest decline in median visual acuity.<sup>16</sup> Figure 3 shows the mean change in visual acuity based on Snellen lines (which equal 0.1 logMAR unit) for the SRH and TPA groups. The mean visual acuities were not significantly different 3 months following surgery, but visual acuity improved significantly at the 1-year and final examination for the SRH group compared with decreased visual acuity in the TPA group. The mean visual acuity changes are compared with the SST B group in Figure 4. The mean change in visual acuity data for the TPA displacement group was similar overall to the SST surgery and control groups. The SRH eyes had improved visual acuity compared with the two SST groups. Visual acuity improved by 3 or more lines ( $\geq 3$  logMAR units) in 12 of 27 eyes (44.4%) of the SRH group compared with three of 15 eyes (20%) of the TPA group at 3 months ( $P = .18$ , Figure 5). These differences were statistically significant ( $P = .042$ ) at the 1-year and at the final examination (13 of 27 eyes, or 48%, versus two of 15 eyes, or 13%). Visual acuity deteriorated by 3 or more lines ( $\geq 3$  logMAR units) with moderate visual loss in three of 27 eyes (11%) in the SRH group compared with six of 15 eyes (40%) in the TPA group at 3 months ( $P = .048$ ) (Figure 6). These differences were statistically significant ( $P = .002$ ) at 1 year and at the final examination (4 of 27, or 14.8%, versus 10 of 15, or 66.7%). Severe visual acuity loss ( $\geq 6$  logMAR units) developed in one of 27 eyes (3.7%) of the SRH group compared with one of 15 eyes (6.7%) at 3 months ( $P = 1.00$ ). Severe vision loss occurred in one of 27 eyes (3.7%) in the SRH group and five of 15 eyes (33.3%) at 1 year ( $P = .016$ ). Severe vision loss was relatively infrequent in both groups at the final examination (one of 27 eyes, or 3.7%, in the SRH group versus two of 15 eyes, or 13.3%, in the TPA group;  $P = .287$ ).

**STATUS OF THE FELLOW EYES**

The mean visual acuity of the fellow eyes also decreased between the initial and final examinations, usually as a result of progression of macular degeneration in the fellow eye. Fellow eyes lost 1.6 lines in the SRH group and 0.3 lines in the TPA group. The mean final visual acuity was 20/320 -2 for SRH fellow eyes and 20/125 +2 for TPA fellow eyes. The fellow eyes had a worse visual acuity than the surgery eye in seven of 27 eyes (25.9%) in the SRH group compared with three of 15 eyes (20%) in the TPA group.



**FIGURE 2**

Median visual acuities for the two groups reported in this study (SRH and TPA groups) compared with the surgery and observation groups in the Subretinal Surgery Trials (SST). The SST eyes had better initial visual acuities, and both SST groups showed modest declines in visual acuity. Preoperative median visual acuity was worse in the eyes that had mechanical removal of large subretinal hemorrhages in the current study (SRH group). The SRH eyes had improved median visual acuity. Eyes in the TPA group had continued declines in visual acuity greater than those of either group in the SST study.

**SURGICAL COMPLICATIONS**

One eye in the SRH group (3.7%) developed a rhegmatogenous retinal detachment from the drainage retinotomy, which was repaired successfully with one additional surgery. The visual acuity in this eye was 1/200 prior to hemorrhage removal, and it improved to 20/400 by the final examination. This was an early eye in the series, and the author realized the importance of removing any residual subretinal blood around the drainage retinotomy to allow a good chorioretinal adhesion to form between the retina and retinal pigment epithelium surrounding the retinotomy site. There were no retinal detachments from peripheral retinal tears. One additional eye in the SRH group (3.7%) required an anterior chamber washout 1 week after surgery for increased intraocular pressure due to a hyphema. Two eyes (13.3%) in the TPA group required a second vitrectomy. The first was performed 2 weeks later for inadequate displacement of hemorrhage and included removal of the neovascular membrane/hemorrhage complex, effectively mimicking the SRH protocol. Visual acuity in this eye decreased from 2/200 preoperatively to hand motions at 1 foot at the final examination. The second patient developed a recurrent submacular hemorrhage 5 months following surgery. The TPA treatment was repeated successfully with displacement of hemorrhage. The visual acuity was 20/400 preoperatively and at the final examination. There were no cases of infectious endophthalmitis. Nuclear sclerotic cataracts increased in most phakic eyes, as would be expected following vitrectomy. The mean preoperative nuclear sclerosis score was .89 in 16 phakic eyes in the SRH group and .94 in the eight phakic eyes in the TPA group. None of the eyes in either group had preoperative posterior subcapsular cataracts. A similar percentage of eyes were aphakic (one eye) or pseudophakic preoperatively (11 of 27 eyes, or 40.7%, in SRH group versus seven of 15 eyes, or 46.7%, in TPA group). The mean final nuclear sclerosis score was 2.29 in the seven eyes that were still phakic at the final examination in the SRH group compared with 2.38 in four eyes that were still phakic at the final examination in the TPA group. There were no posterior subcapsular cataracts at the final examination in any phakic eyes. Hence, nuclear sclerotic cataracts likely contributed to decreased acuity in phakic

eyes in both groups, but the magnitude of the effect was similar and cataracts would not explain the poorer results in the TPA group compared with the SRH group.

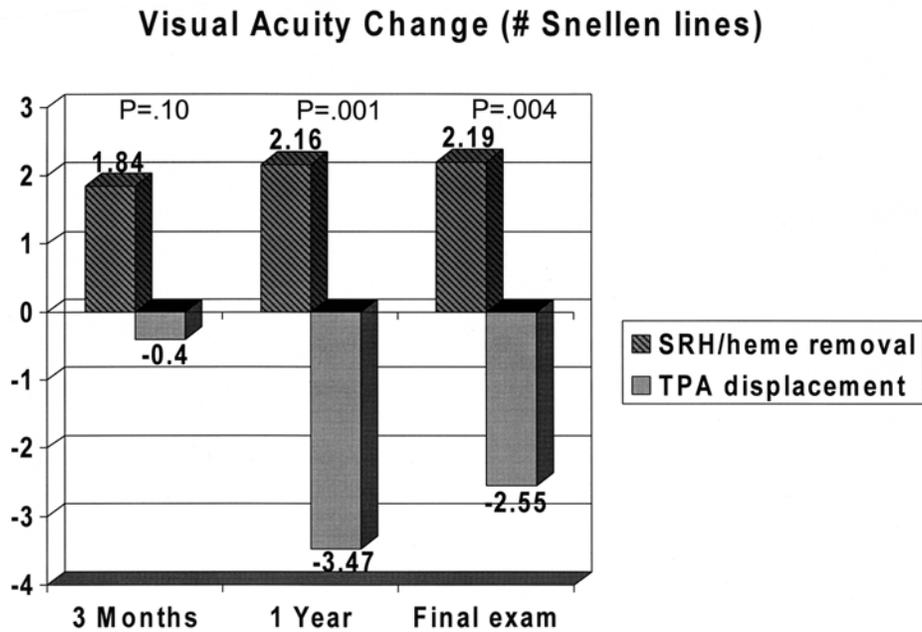


FIGURE 3

Comparison of mean visual acuity change in the SRH group and TPA group. The visual acuity changes were significantly better in the SRH group compared with the TPA group.

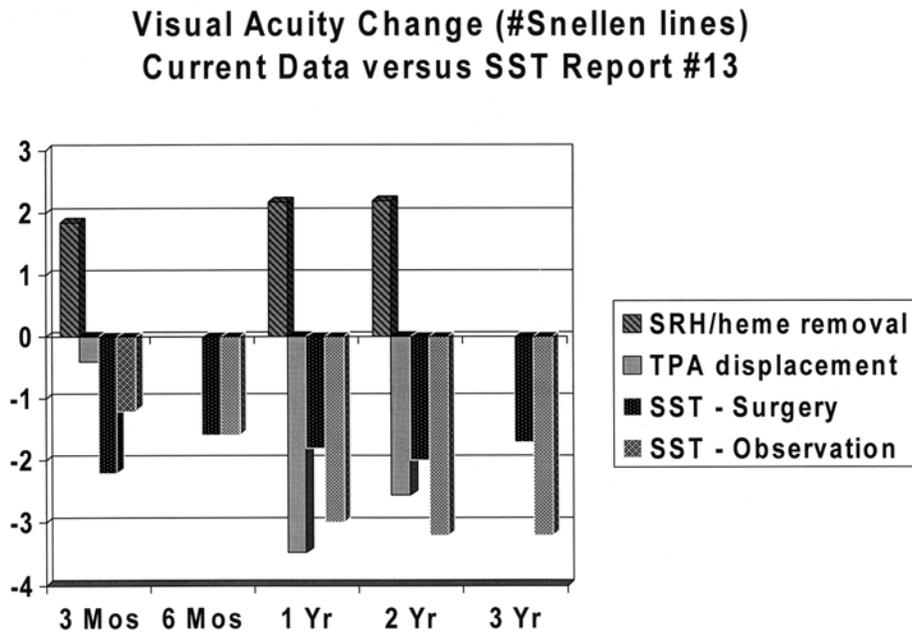


FIGURE 4

Comparison of mean visual acuity changes in the SRH and TPA groups and the Subretinal Surgery Trials (SST) data. The TPA group had absolute declines in visual acuity similar to those of the two SST B groups. Eyes with large subretinal hemorrhages in the current study showed improved visual acuities.

### Improved Acuity by 3+ Lines

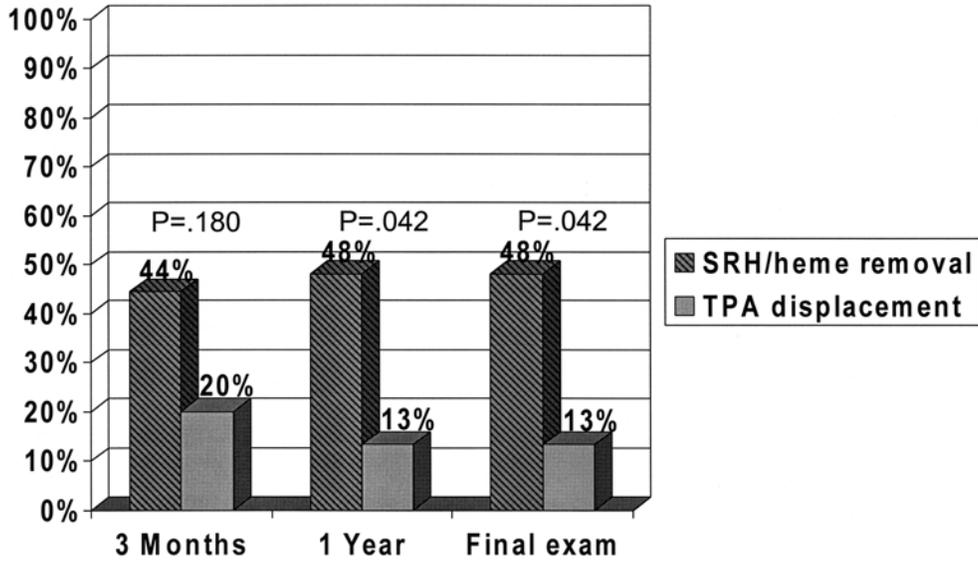


FIGURE 5

The percentage of eyes that improved by 0.3 logMAR units ( $\geq 3$  lines) was significantly greater in the SRH group compared with the TPA group at 1 year and the final examination.

### Decreased Acuity by 3+ Lines

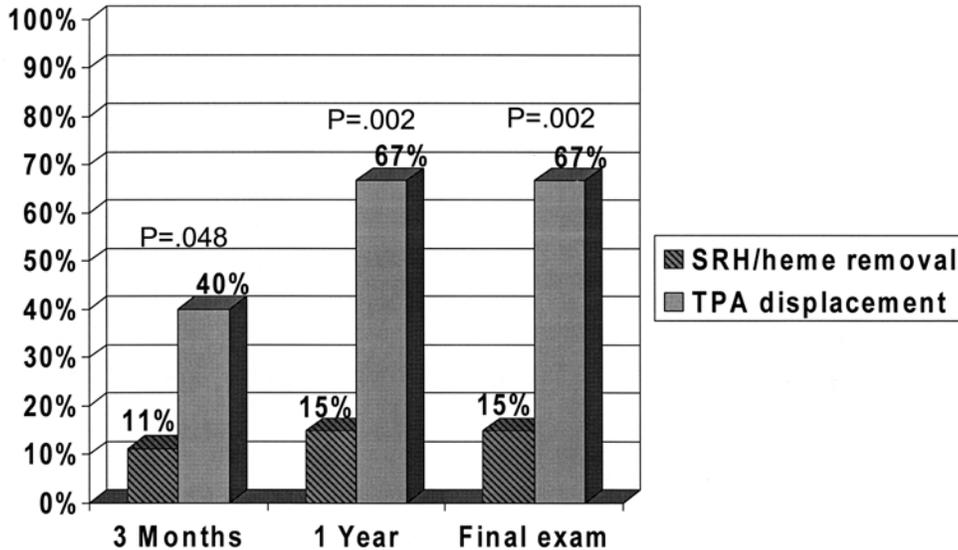


FIGURE 6

The percentage of eyes that had decreased acuity by 0.3 logMAR units ( $\geq 3$  lines) was significantly greater at all postoperative time points in eyes in the TPA group compared with eyes in the SRH group.

### Decreased Acuity by 6+ Lines

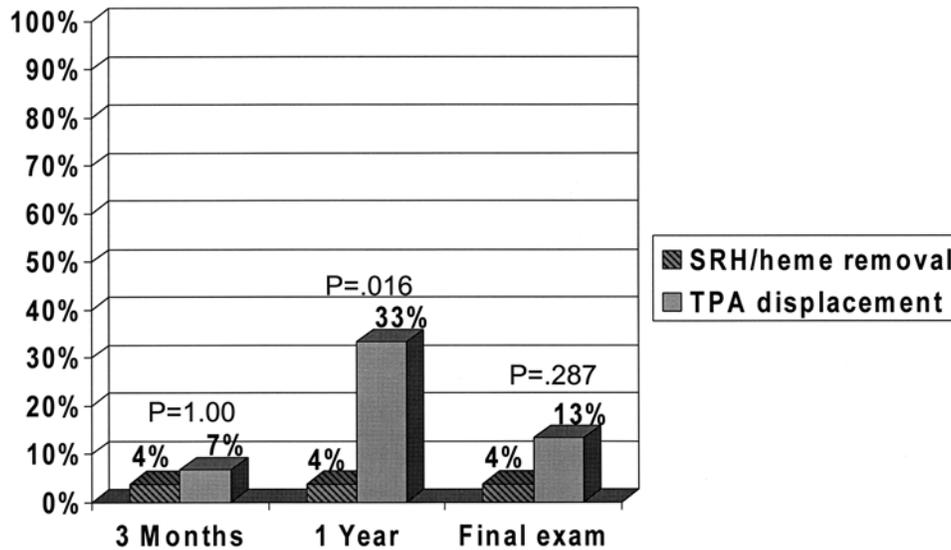


FIGURE 7

Analysis of the percentage of eyes with decreased acuity by 0.6 logMAR units ( $\geq 6$  lines) still favored the SRH group, but the differences were statistically significant only at 1 year.

## DISCUSSION

Eyes with large subretinal hemorrhages arising from exudative macular degeneration have a poor prognosis on account of progressive fibrosis and organization of the subretinal clot.<sup>19-21</sup> Scupola and associates<sup>19</sup> evaluated the natural history of eyes with a subretinal hemorrhage larger than 1 disc diameter and found that 80% of eyes deteriorated, with a mean final visual acuity of 20/1250. Berrocal and associates<sup>20</sup> reported on eyes with any amount of subretinal hemorrhage under the fovea (from small to large) and reported improvement in 40% of eyes, but found that the presence of subretinal neovascularization was associated with a poor visual outcome. Avery and associates<sup>21</sup> reported eyes with subretinal hemorrhage where greater than 50% of the neovascular membrane was composed of hemorrhage. After 3 years, a mean of 3.5 lines of visual acuity were lost and 44% of eyes lost 6 or more lines of visual acuity.

## SUBRETINAL HEMORRHAGE TREATMENTS

Earlier surgical reports where the hemorrhage was drained without removal of the choroidal neovascular membrane reported mixed results. Vander and associates<sup>22</sup> reported improved visual acuity in 36% of 11 eyes, and results were better in eyes in which surgery was performed within 1 week of symptom onset. In the report by Wade and colleagues,<sup>23</sup> final visual acuity was 5/200 or worse in all of five eyes. Mandelcorn and Menezes<sup>24</sup> reported improvement in five of seven eyes, although three eyes also had removal of the choroidal neovascular membrane. Results again were more favorable if surgery was performed within 2 weeks of symptom onset.

Surgical removal of the neovascular membrane and hemorrhage improved visual acuity in 38.9% of 18 patients at 3 months in a study by Scheider and colleagues.<sup>1</sup>

The largest series of mechanical removal of the subretinal neovascular membrane and hemorrhage reported to date was the SST B group.<sup>16</sup> Visual acuity improved 2 or more lines in 19% of the surgery group compared with 17% of the observation group at 3 months. The results were similar at 36 months, with 20% of the surgery group compared with 18% of the observation group gaining 2 or more lines. Visual acuity decreased 2 or more lines in 56% of surgery eyes and 49% of the observation group at 3 months. Visual acuity decreased 2 or more lines in 51% of surgery eyes and 64% of observation eyes at 36 months. The primary analysis end point for the SST B group of loss of 2 lines or greater did not reach statistical significance. However, analysis of the subgroup of eyes with 6 or more lines of visual acuity loss showed statistically significant benefit of less visual acuity loss in the surgery group (20%) compared with the observation group (37%) at 24 months. The technique reported by Scheider<sup>1</sup> and the SST B group was similar to the technique used in the SRH eyes in the current study, except that TPA was not used (it was allowed in the SST at the discretion of the investigator).

TPA has been used as both a subretinal injection and an intravitreal injection as an adjunct to help facilitate liquefaction and removal of submacular hemorrhages.<sup>25,26</sup> TPA was initially used as a subretinal injection to help dissolve the subretinal blood. Favorable results with visual acuity improvement in 83% of eyes were reported by Lewis in eyes with hemorrhages less than 14 days

old.<sup>27</sup> A larger series, with and without TPA, which included a few eyes without exudative macular degeneration, found visual acuity improvement or stabilization in 57% to 92% of eyes.<sup>28</sup> The investigators concluded that the addition of TPA to help lyse the clot did not significantly improve visual outcome.<sup>28</sup> Another series of 18 eyes, which included two eyes without macular degeneration, found visual acuity improvement of 2 or more lines in 61% of eyes at the best postoperative visit but in only 28% of 18 eyes at the final examination.<sup>29</sup> Hauptert and colleagues<sup>15</sup> reported visual acuity improvement in 82% of 11 eyes with similar techniques. The techniques reported by Lewis,<sup>27</sup> Ibanez and associates,<sup>28</sup> Lim and coworkers,<sup>29</sup> and Hauptert and associates<sup>28</sup> are similar to the technique used for the TPA group in the current study. Perfluorocarbon liquids have been used to help displace blood into the vitreous after the submacular hemorrhage is liquefied by TPA with improved visual acuity in 82% of 22 eyes.<sup>10</sup> TPA has also been advocated prior to surgery to increase the duration of exposure of the subretinal clot to TPA with the goal of improving liquefaction of the clot prior to removal. Subretinal TPA injection in the office 24 hours prior to vitrectomy gave improved visual acuity in 80% of five eyes.<sup>4</sup> The current study did not find any long-term benefits to vitrectomy and pneumatic displacement of the subretinal hemorrhage alone. The short-term effects of displacing the hemorrhage with TPA seemed beneficial, but progressive visual loss related to the underlying choroidal neovascularization negated any benefit, such that the majority of TPA eyes lost visual acuity. Some investigators have treated only eyes with symptoms of the subretinal hemorrhage of less than 14 days.<sup>27</sup> This will likely give better visual results than in eyes with older subretinal hemorrhages, but we found that most patients with subretinal hemorrhages do not present within 14 days. There may have also been subtle differences in technique that caused the TPA eyes in the present study to fare more poorly compared with other reports. We found that anatomic appearance of the macula and visual results using the TPA technique were encouraging immediately following surgery, but visual acuity usually declined over the next 2 years despite additional treatment such as photodynamic therapy to the choroidal neovascular membranes.

Intravitreal TPA has also been used to help to liquefy subretinal hemorrhages without use of vitrectomy to allow treatment in an office setting. Hesse and colleagues<sup>9</sup> reported improved visual acuity in 45.5% of 11 patients treated with intravitreal TPA and an intraocular gas bubble without vitrectomy. A second series using a similar technique reported visual acuity improvement by 2 or more lines in 67% of 15 eyes at a mean of 10.5 months.<sup>30</sup> All but two eyes in this series had macular degeneration. Beneficial results with the same technique were reported in several subsequent small series.<sup>2,6-8,13</sup> Olivier and colleagues<sup>14</sup> reported visual acuity improvement by 2 or more lines in 61% of 28 eyes followed for 3 months. A larger series by Schulze and Hesse<sup>5</sup> found improved visual acuity in 76% of 47 eyes at 1 week, but 48% of eyes that improved showed deterioration during further follow-up. Steller and Gerke<sup>31</sup> reported a group of 25 eyes treated with the same TPA pneumatic displacement technique and found improvement in 40% of 25 eyes at a mean follow-up of 14.2 months. This technique was not tested in the current study, so no comparisons could be made to the SRH and TPA group results.

## STUDY LIMITATIONS

The current study was primarily limited by the lack of standardized visual acuities, which were utilized in the SST B group. The other studies cited used visual acuity measurement techniques similar to those used in the current study. The use of Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuities is more accurate at lower levels of visual acuity than use of Snellen measurements. This may have resulted in underestimation of the preoperative visual acuities in the current study, although the postoperative visual acuities were taken by using the same techniques and technical staff. This is one of two factors that explain why the baseline visual acuity was better in the SST B group than in the current study. The second factor is that the current study enrolled only eyes with larger subretinal hemorrhages, whereas the SST B study allowed a larger variation in subretinal hemorrhage size. One third of eyes in the SST B study had hemorrhages smaller than the minimum allowed in the current study. Another factor in the SST B surgery eyes that may have contributed to vision loss in the surgery group was the higher rate of retinal detachment (16%) with proliferative vitreoretinopathy in half of the eyes with retinal detachment. The one patient in the current study who developed a retinal detachment did relatively well with visual acuity improvement. The second limitation of the current study is that the long-term follow-up examinations could not be performed in all eyes. The SST B group reported follow-up data on 89% of eyes at 24 months and 51% of eyes at 36 months. In the current study, 78.6% eyes were observed for at least 1 year, 59.5% for 2 years, 38.1% for 3 years, and 23.4% for 4 or more years.

This study does not definitively answer the question about whether subretinal surgery with removal of the neovascular membrane and subretinal hemorrhage is beneficial for larger subretinal hemorrhages. The data do suggest that removal of hemorrhage and neovascular membrane may improve visual acuity in eyes that otherwise have a very poor visual prognosis. Other, newer treatment regimens, such as photodynamic therapy with verteporfin (Visudyne) and intravitreal angiogenesis inhibitors such as pegaptanib sodium (Macugen), have not been tested but are unlikely to be of much benefit in eyes with large submacular hemorrhages. Surgical removal of large subretinal hemorrhages with the SRH technique appears to be reasonably safe with a relatively low complication rate, apart from the development of nuclear sclerotic cataracts. Displacement of subretinal hemorrhages alone using the TPA pneumatic displacement technique was not beneficial and did not appear to give results as good as removal of the subretinal hemorrhage and neovascular membrane using the SRH technique. On the basis of the improved visual acuities and long-term stability, subretinal surgery using the SRH technique may still have a role in the treatment of large submacular hemorrhages arising from exudative macular degeneration.

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## PEER DISCUSSION

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DR WILLIAM F. MIELER. Dr. Thompson has presented a study of anatomic and visual outcomes from surgery for large submacular hemorrhage secondary to age-related macular degeneration, comparing results from conventional submacular surgery to those obtained with tissue plasminogen activator (tPA) assisted pneumatic displacement surgery.

As Dr Thompson indicated, the Submacular Surgery Trial (SST) recently reported the results from their study in late 2004. In the Group B (blood) group, there was no apparent benefit from surgery in comparison to observation at 36 months follow-up, in terms of visual gain or mild visual loss. While the visual endpoint was not reached in the SST, the only apparent benefit from surgery in the SST Group B patients was that there was a lessened rate of severe vision loss.

What can we take home from Dr Thompson's study? While the patients who underwent submacular surgery with removal of the neovascular complex fared better than those who had tPA assisted pneumatic retinopexy, it is truly difficult to compare the two groups. Standardized visual acuity was not employed, follow-up was limited in some cases, and the tPA pneumatic retinopexy assisted group actually had more favorable baseline findings. One could postulate that removal of the neovascular complex (along with the inadvertent removal of the RPE and choriocapillaris in most cases) is somewhat better than leaving the neovascular complex in place and subsequently treating it with other modalities. But is it truly better than natural history alone? Unfortunately, we cannot reach such a conclusion from this type of study.

We all strive to improve patient care and provide good anatomic and visual outcomes. We also readily recognize that many patients have features that differ from enrollment criteria utilized in prospective, controlled clinical trials. Many patients in Dr Thompson's current study would not have been eligible for participation in the SST. So what do we do with these patients?

So in summary, the key question that I would ask Dr Thompson is, in view of the currently published SST data, how does he manage a patient with a large subretinal hemorrhage from age-related macular degeneration at the present time?

DR JOHN T. THOMPSON. This study was undertaken because we do not have a good treatment for patients with a large submacular hemorrhage. These patients usually evolve to a large disciform scar, often with visual acuity of 5/200ths or less. They are certainly not appropriate for treatment with photodynamic therapy. There is no reason to believe that Macugen injection is likely to help this condition either, although this has not been specifically evaluated in a study. Submacular surgery in these cases is usually better than offering the patient no treatment option. I offer these patients the option of subretinal surgery, while at the same time explaining the risks of the surgery. The patient then decides whether they wish to proceed. I am encouraged by these results and think it is reasonable to perform this procedure based on the results presented in the study.