EXTENDED REPORT

Partial Tenon’s capsule resection with adjunctive mitomycin C in Ahmed glaucoma valve implant surgery

R Susanna Jr and the Latin American Glaucoma Society (SLAG) Investigators*

Aim: To verify if partial intraoperative Tenon’s capsule resection (PTCR) with adjunctive mitomycin C is effective in developing thin, avascular blebs in eyes undergoing Ahmed glaucoma valve insertion, and to assess the efficacy and safety of this procedure.

Methods: A multicentre, prospective, alternating case assignment, investigator unmasked, parallel group, comparative interventional study was conducted in four Latin American countries (Argentina, Brazil, Colombia, and Peru). Ahmed glaucoma valve implantation with PTCR (group A) and without PTCR (group B) was performed in neovascular glaucomatous eyes without previous surgery. Adjunctive mitomycin C (MMC) was used in both groups. Patients were examined 1 day, 10 days, 1 month, 2 months, 3 months, 6 months, and 1 year following the surgery. Intraocular pressure (IOP) and the appearance of the bleb were evaluated at each examination. Appearance of the bleb was classified at both the 1 month mark and last examinations into one of three groups: flat and vascularised; elevated avascular; or elevated and not avascular.

Results: 92 eyes from 92 patients were included in the study. The preoperative mean IOP was 50.0 (SD 10.5) mm Hg in group A and 48.4 (11.7) mm Hg in group B (p>0.05). Statistically significant IOP reductions were observed at all periods of follow up. 12 months after surgery, the mean IOP was 17.2 (5.0) mm Hg in group A and 18.3 (8.7) mm Hg in group B (p>0.05). A hypertensive phase occurred in 40.0% in group A and 46.8% in group B (p>0.05). At the 1 month and the final follow up, the blebs in all eyes were considered elevated and not avascular. The success rate (IOP <21 mm Hg) at 1 year after surgery was 70.4% in group A and 77.7% in group B (p>0.05). Overall, 74.2% of the patients achieved an IOP ≤21 mm Hg and 55.2% an IOP ≤17 mm Hg, with or without additional medication administered to lower IOP. The incidence of complications was similar in both groups.

Conclusions: In eyes undergoing Ahmed valve implantation for neovascular glaucoma, PTCR with MMC augmentation showed no additional benefits or complications over MMC augmentation alone; no avascular bleb was obtained with this technique. The incidence of a hypertensive phase was lower than reported in previous studies.

Aqueous shunt surgery has been used for three decades as an alternative to standard perilimbal filtering surgery or cyclodestructive procedures in complicated glaucomas.1

Elevated intraocular pressure (IOP) can occur after the insertion of the anterior chamber tube in the two stage Molteno procedure or after the opening of the tube in the one stage Molteno, Schocket, or Baerveldt procedures by releasing or removing the occluding suture.

This elevation of pressure, called a hypertensive phase (HP), is usually transient and probably resolves as the aqueous humour divulses the encapsulation surrounding the episcleral plate, with the creation of a bleb.2

It has been reported that a hypertensive phase occurred in 82% of cases after Ahmed valve implantation, and a 28% intervention rate to stabilise the IOP. Consequently, as usually performed, Ahmed valve implantation may not be the procedure of choice in patients with advanced optic nerve damage in whom target pressures in the low teens would be preferable.3

The appearance of the bleb obtained with setons is quite different from that of the usual bleb obtained with trabeculectomy with the use of intraoperative mitomycin C (MMC). There are usually no microcystic conjunctival changes and the bleb wall is thicker and more vascular. So, we hypothesised that performing Ahmed glaucoma valve insertion with partial intraoperative Tenon’s capsule resection (PTCR) and allowing direct contact between MMC and the conjunctiva might result in thin, avascular blebs, increasing the success rate and also decreasing the incidence of HP.

To the best of our knowledge, this is the first study in which PTCR with setons has been evaluated.

The Ahmed glaucoma valve implant model S-2 (New World Medical, Rancho Cucamonga CA, USA) appeared on the market in 1993.4 It consists of a silicone tube connected to a silicone sheet valve held in a polypropylene body. The inner diameter of the silicone tube is 0.317 mm and the outer diameter is 0.635 mm. The surface area of the polypropylene body is 185 mm². Its unidirectional valve mechanism is designed to open when the IOP is at 8 mm Hg. In a previous pilot study (unpublished data, Susanna, 1999) the implantation of this valve, combined with PTCR and MMC application (0.5 mg/ml for 3 minutes), resulted in four consecutive cases of flat anterior chamber and hypotony but no avascular blebs. To reduce these complications, a second type of Ahmed valve implant model S-2, also developed by New World Medical, with the same characteristics but with a higher resistance to flow (high pressure Ahmed valve implant, HPAV) was designed to open when the IOP is at 12 mm Hg.

This valve was inserted with PTCR and intraoperative MMC in 10 consecutive eyes (unpublished data, Susanna, 1999) and no cases of flat anterior chamber or hypotony occurred.

The outflow characteristics of the two kinds of Ahmed glaucoma valves are shown in Figure 1.

We then embarked upon the current randomised trial to verify whether partial intraoperative Tenon’s capsule removal with the use of adjunctive of MMC is effective in developing...
thin, avascular blebs in eyes undergoing Ahmed glaucoma valve insertion, and also to assess the efficacy and safety of this procedure.

This study was approved by the institutional review board of each participant country and institution.

PATIENTS AND METHODS

In this multicentre, prospective, alternating case assignment, non-masked, parallel comparative study conducted in four Latin American countries (Argentina, Brazil, Colombia, and Peru) a total of 92 eyes from 92 patients with neovascular glaucoma were enrolled from January to December 2000.

The standard Ahmed valve was inserted in non-PTCR eyes, and the high pressure valve was inserted in PTCR eyes. The same surgeon in each centre performed surgeries on both groups of patients.

Eyes that fulfilled all the inclusion criteria but none of the exclusion criteria were randomised and treated with the regular Ahmed valve implant and adjunctive MMC or with the HPAV and adjunctive MMC and PTCR.

In each centre the first patient was assigned to one group (determined by a coin flip), and the second consecutive patient to the other group, and so on.

The outline of the study is shown in Figure 2.

Inclusion criteria:
- Eyes with light perception or better
- Neovascular glaucoma with no previous surgery
- Neovascular glaucoma with underlying central retinal venous occlusion (CRVO) or diabetes.

Exclusion criteria:
- Eyes with no light perception
- Neovascular glaucoma with previous surgery
- Neovascular glaucoma not associated with CRVO or diabetes.

The following information was documented for each patient: age, sex, race, any underlying diseases—for example, CRVO or diabetes, date of surgery, preoperative visual acuity and IOP, final visit visual acuity, and the IOP on postoperative day 1, 10, and at 1 month, 2 months, 3 months, 6 months, and 1 year. Postoperative complications were reported. The appearance of the bleb was evaluated at 1 month and 12 months after the surgery.

The Ahmed glaucoma valve was inserted into the eye using a standard technique in the non-PTCR eyes. A fornix based conjunctival flap was created between two adjacent recti muscles in the superior-temporal quadrant of the eye. A Weck sponge (Edward Weck Co, Research Triangle Park, NC, USA) soaked in a 1 mg/ml MMC solution was placed for 3 minutes below the Tenon’s capsule where the polypropylene reservoir would later be inserted. This higher concentration of MMC was used in an attempt to produce avascular blebs as the use of MMC 0.5 µg/ml was not effective in promoting avascular blebs in a pilot study (unpublished, Susanna, 1999).

The sponge was removed and the location rinsed with 20 ml of balanced salt solution. In PTCR eyes, the Tenon’s capsule was removed between the same two adjacent recti muscles from its insertion near the corneoscleral limbus to 13 mm posterior to the limbus. Special care was taken in order not to make holes in the overlying conjunctiva.

The MMC was applied as previously described, but in these cases directly in contact with the conjunctiva. After 3 minutes, the sponge was removed and the conjunctiva and episclera were rinsed with 20 ml of saline solution.

In both groups the Ahmed valve was irrigated with a balanced salt solution to prime the valve mechanism. The implant’s polypropylene body was placed 8–10 mm posterior to the corneoscleral limbus and sutured to the sclera with a 9-0 Nylon suture.

The anterior chamber was entered at the corneoscleral limbus with a 23 gauge needle, with the needle track being anterior and parallel to the iris. The tube was trimmed so that the bevel faced the corneal endothelial surface and was inserted into the anterior chamber through the needle track. A human donor patch (sclera or dura mater patch graft) was placed over the tube, with the anterior edge adjacent to the limbus and attached to the sclera with a 10-0 Nylon suture. The conjunctiva was sutured to the limbus, and all eyes were given subconjunctival injections of steroids and antibiotics.

During follow up, antiglaucoma medications were introduced when the IOP was higher than 23 mm Hg. For the purpose of comparing our results with historical series, we considered successful IOP control to be an IOP >4 mm Hg and <22 mm Hg and at least 30% of an IOP reduction.

The final examination was conducted 12 months after surgery. However, any reoperation for glaucoma control or to

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean age (SD)</th>
<th>Sex</th>
<th>Race</th>
<th>Aetiology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Male</td>
<td>Female</td>
<td>White</td>
</tr>
<tr>
<td>Group A</td>
<td>60.6 (12.1)</td>
<td>55.6%</td>
<td>44.4%</td>
<td>80.0%</td>
</tr>
<tr>
<td>Group B</td>
<td>60.7 (12.2)</td>
<td>53.2%</td>
<td>46.8%</td>
<td>76.6%</td>
</tr>
</tbody>
</table>
repair either implant reservoir exposure or a retinal detachment was considered the end point for the efficacy analysis, as such operations could influence the surgical outcome. Only eyes with a minimum follow up of 3 months were included in the efficacy results of this study.

RESULTS

A total of 92 eyes from 92 patients were included in this study. After randomisation, 45 eyes (48.9%) were given Ahmed valve insertion with PTCR (group A) and 47 eyes (51.1%) without PTCR (group B).

There was no statistical difference between both groups in terms of age, sex, race, aetiology of neovascular glaucoma and previous panretinal photocoagulation (PRP). Table 1 summarises these data.

Table 2 shows the number of eyes and the IOP profile before the Ahmed valve insertion and at 1 day, 10 days, 1 month, 2 months, 3 months, 6 months, and 1 year after its insertion. The analysis of the data from the preoperative phase to the 90th postoperative day in the 92 eyes, comparing the mean IOP values of the two groups at each follow up visit, shows a significant difference only on the first postoperative day (unpaired t test; \( t = 2.38; p=0.02^* \)).

When considering only the 58 eyes that were followed up for 1 year (25 eyes of group A and 33 of group B), the mean preoperative IOP in group A was 50.3 (SD 11.1) mm Hg and in group B 48.4 (12.3) mm Hg. This difference was not statistically different (unpaired t test, \( p=0.51 \)).

Comparing the mean IOP values on postoperative days 1, 10, 30, 60, 90, 180, and 360 for groups A and B, the unpaired t test revealed a significant difference between groups only in the first postoperative day (mean IOP of 19.1 (12.1) mm Hg in group A and 13.3 (9.1) mm Hg in group B).

Figure 3 shows the mean IOP for the preoperative and all postoperative visits until the 12 month follow up.

The success rate at the 1 year follow up in PTCR eyes was 70.4% and for non-PTCR eyes 77.7%, both with and without any additional medication for lowering IOP. Forty four per cent of the patients in group A were receiving hypotensive ocular medication; 45.4% in group B. There was no statistical difference between the two groups (\( p>0.05, \chi^2 \text{ with Yates's continuity correction} \)).

Altogether, the success rate both with and without medication at 1 year was 74.2%.

A hypertensive phase (HP) occurred in 40.0% in group A and in 46.8% in group B. This difference was not statistically significant (\( p>0.05, \chi^2 \text{ with Yates's continuity correction} \)).

The overall incidence of HP was 43.5%.

Table 3 shows the postoperative complications in both groups. Overall, both groups had a similar incidence of complications.

Table 4 shows the percentage of patients who achieved a specific mean IOP reduction with or without medication at the 1 year follow up for each group.

At 1 month and 12 months after surgery, all blebs were elevated and not avascular.

DISCUSSION

This study was performed to verify whether partial intraoperative Tenon’s capsule resection with the use of adjunctive of mitomycin C is effective in developing thin, avascular blebs in

Table 2  IOP profile before and after Ahmed glaucoma surgery

<table>
<thead>
<tr>
<th>Group</th>
<th>No</th>
<th>Mean IOP (mm Hg)</th>
<th>SD</th>
<th>SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop</td>
<td>A</td>
<td>45</td>
<td>50.00</td>
<td>10.50</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>47</td>
<td>48.43</td>
<td>11.67</td>
</tr>
<tr>
<td>PO 1</td>
<td>A</td>
<td>45</td>
<td>17.36</td>
<td>11.36</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>47</td>
<td>12.51</td>
<td>7.97</td>
</tr>
<tr>
<td>PO 10</td>
<td>A</td>
<td>45</td>
<td>14.20</td>
<td>9.87</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>47</td>
<td>12.34</td>
<td>5.66</td>
</tr>
<tr>
<td>PO 30</td>
<td>A</td>
<td>45</td>
<td>16.20</td>
<td>10.13</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>47</td>
<td>13.19</td>
<td>7.83</td>
</tr>
<tr>
<td>PO 60</td>
<td>A</td>
<td>45</td>
<td>19.16</td>
<td>9.57</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>47</td>
<td>17.36</td>
<td>7.59</td>
</tr>
<tr>
<td>PO 90</td>
<td>A</td>
<td>45</td>
<td>18.58</td>
<td>9.01</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>47</td>
<td>18.40</td>
<td>7.91</td>
</tr>
<tr>
<td>PO 180</td>
<td>A</td>
<td>33</td>
<td>18.12</td>
<td>8.77</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>40</td>
<td>16.08</td>
<td>8.26</td>
</tr>
<tr>
<td>PO 360</td>
<td>A</td>
<td>25</td>
<td>17.20</td>
<td>5.05</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>33</td>
<td>18.33</td>
<td>8.68</td>
</tr>
</tbody>
</table>

PO = postoperative day.

Figure 3  Mean IOP from baseline to 12 months of follow up (n = 58).

Table 3  Postoperative complications

<table>
<thead>
<tr>
<th>Retinal detachment</th>
<th>Hypotony</th>
<th>Flat anterior chamber</th>
<th>Plate exposure</th>
<th>Tube exposure</th>
<th>Tube blockage</th>
<th>Serous choroidal detachment</th>
<th>Endoph</th>
<th>Vitreous haemorrhage</th>
<th>Hyph</th>
<th>Phthisis bulbi</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTCR eyes</td>
<td>1</td>
<td>5</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Non-PTCR eyes</td>
<td>.</td>
<td>7</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>.</td>
<td>.</td>
<td></td>
<td>.</td>
</tr>
<tr>
<td>Total</td>
<td>1</td>
<td>12</td>
<td>9</td>
<td>3</td>
<td>2</td>
<td>8</td>
<td>1</td>
<td>3</td>
<td>14</td>
<td>1</td>
</tr>
</tbody>
</table>

Endoph = endophthalmitis; Hyph = hyphaema.
elevated eyes undergoing Ahmed glaucoma valve insertion, and to assess the efficacy and safety of this procedure.

We hypothesised that performing Ahmed glaucoma valve insertion with PTCR and allowing direct contact between MMC and the conjunctiva may result in thin avascular blebs, increasing the success rate and also decreasing the incidence of HP. It is possible that the development of MMC trabeculectomy-like blebs over exoplants could result in an unacceptable extrusion rate for these devices. However, whether or not this would occur remains to be determined, as we were unable to produce this kind of bleb.

When applying 1 mg/mL of MMC for 3 minutes in direct contact with the conjunctiva, the presence of a thin avascular bleb was not observed during the 12 month follow up of this study. Why MMC is effective at reducing scar formation at the limbus and not away from the limbus is unknown. It may be because the conjunctiva and Tenon's capsule have different properties at the limbus from those away from it. Another possibility is that the aqueous humour that continually bathes the capsule, loaded with vasoproliferative factors, may prevent the development of thin capsules. Also, the presence of the implant plate may act as a potent stimulus for fibroblast proliferation.

In our study the removal of Tenon's capsule did not result in avascular blebs. So it is unlikely that Tenon's capsule was a major site for failure in trabeculectomies. The absence of avascular blebs even in early postoperative days (the first and 10th postoperative days) after applying a high concentration of MMC directly in contact with the conjunctiva suggests that neither continuous baths of the capsule with aqueous humour containing vasoproliferative factors nor the presence of the implant plate were major factors in preventing the appearance of avascular blebs. It is likely that different properties of the conjunctiva in the area away from the limbus and at the limbus are responsible for the different bleb appearance in these two sites.

The role of tenectomy without the use of adjunctive MMC in trabeculectomy is debatable. Tenon's capsule is an important site for failure in trabeculectomies. Some authors believed that tenectomy improves the success rate, although others did not. Tenonectomy should not be performed in trabeculectomy with the use of MMC, owing to the risk of severe complications, such as hypotony, maculopathy, endophthalmitis, bleb leakage, etc. In our study tenectomy with adjunctive MMC showed no additional benefit or complication over eyes without tenectomy.

It is interesting to note that the overall incidence of HP in our study was 43.5%. This incidence of a hypertensive phase is lower than the 82% reported by Ayyala, et al. They defined the hypertensive phase by the occurrence of an IOP >21 mm Hg in the first 6 postoperative months, while we defined it as occurring in the first 3 postoperative months. If we had treated the HP in their terms, the incidence of a hypertensive phase in our study would be 46.6%. This lower incidence of HP may be important in eyes with advanced optic nerve damage that are in urgent need of reaching a low IOP. In our study, as well as in the study by Ayyala et al, the gradual addition of glaucoma medication, however, made it difficult to distinguish between the resolution of the hypertensive phase and a medically assisted reduction to a stable IOP.

Our lower incidence of HP may be related to demographic differences between the studies, differences in study design (our study is prospective), or both. Also, the use of MMC may be responsible for the lower incidence of the hypertensive phase in our series. MMC has a transiently beneficial effect on bleb function after Baerveldt insertion in rabbits, which may also be the case in the present study. Most publications on the use of MMC in glaucoma implant surgery demonstrated no advantage of using MMC during the surgery, although in the study conducted by Perkins et al., intraoperative MMC offers an increased likelihood of a 2–3 year period of medication free IOP control in patients undergoing double plate Molteno implant compared to similar patients with no adjunctive antimetabolite therapy. However, to the best of our knowledge, there is no study comparing the effects of adjunctive MMC on the hypertensive phase of glaucoma after implant surgery.

It is not possible to establish if MMC is useful as adjunctive therapy in Ahmed valve insertion in neovascular glaucoma in the current study. It lacks the design necessary to address the efficacy of MMC in Ahmed glaucoma valve implantation.

A hypertensive phase after the insertion of a glaucoma drainage implant was described by Molteno and is thought to be a result of a temporary thickening of the capsule surrounding the plate, with restriction of aqueous humour diffusion through the capsule, followed by a gradual dilution of aqueous humour through the encapsulation, resulting in the formation of a bleb. Molteno described the changes that go together with the formation of the bleb as a hypotensive phase that lasts for the first 7–10 days after the operation, followed by a period of steady rising of IOP that lasts 3–6 months (HP), followed by a stable phase.

As in the series by Ayyala et al., the hypertensive phase in the non-PTCR eyes peaked at 1 month after surgery and in the PTCR eyes 1 month later (Fig 3). This late onset may be related to the PTCR procedure itself, which may delay the thickening of the capsule surrounding the plate.

There was no statistically significant difference between the mean IOP between groups at 1 month, 2 months, 3 months, 6 months, and 1 year after surgery (Table 2). However, there was a statistically significant difference between the groups at 1 day after surgery. The presence of cells, protein, and other inflammatory substances in the aqueous at the first postoperative day may be responsible for the higher IOP observed with the high pressure Ahmed valve (more resistant to aqueous outflow) than the standard Ahmed valve. However, at 10 days after the surgery the IOP difference between the groups was not statistically different.

The presence of the valve in Ahmed implants appears to be important in the early postoperative period in preventing hypotony and its attendant complications.

We found an incidence of hypotony of 11.1% in group A and 14.9% in group B. Overall, the incidence of hypotony was 13.0%. This is consistent with the 13% incidence of hypotony described by Coleman et al. and 9.4% described by Ayyala et al.

Table 3 shows the postoperative complications in the two groups. Overall, the incidence of complications was similar. Seven patients lost light perception after the Ahmed valve implantation. This may be related to the advanced stage of the glaucoma or to factors other than uncontrolled IOP, such as worsening of the underlying disease process—for example, CRVO, diabetes, retinal ischaemia, etc. In the study by Ayyala et al. four out of five patients who lost light perception had neovascular glaucoma.

**Table 4** Percentage of patients who achieved a specific mean IOP reduction with or without additional medication at 1 year follow up

<table>
<thead>
<tr>
<th>Mean IOP (mm Hg)</th>
<th>PTCR eyes (n = 25)</th>
<th>Non-PTCR eyes (n = 33)</th>
<th>Total = 58</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 15</td>
<td>29.6</td>
<td>31.6</td>
<td>30.6</td>
</tr>
<tr>
<td>16</td>
<td>40.7</td>
<td>48.6</td>
<td>45.1</td>
</tr>
<tr>
<td>17</td>
<td>48.1</td>
<td>54.3</td>
<td>51.6</td>
</tr>
<tr>
<td>18</td>
<td>51.8</td>
<td>62.8</td>
<td>58</td>
</tr>
<tr>
<td>21</td>
<td>70.4</td>
<td>77.1</td>
<td>74.2</td>
</tr>
<tr>
<td>25</td>
<td>92.6</td>
<td>82.8</td>
<td>87.1</td>
</tr>
<tr>
<td>≥ 30</td>
<td>92.6</td>
<td>94.3</td>
<td>91.8</td>
</tr>
</tbody>
</table>
Four patients died during this short period of follow up. The median age was 56 years (28–72 years). Two thirds of the patients in our study were diabetic and one third had CRVO. These patients had severe underlying systemic diseases, which may explain the high incidences of death.

Overall, the success rate at 1 year following the Ahmed valve insertion was 74.2%, which is almost identical to the 78% described by Coleman et al.18 and the 75% described by Ayyala et al.,19 and Kee.20

However, there are no studies using such a high concentration of MMC (1 mg/ml for 3 minutes) with glaucoma drainage devices.

The number of eyes that reached IOP values of at least 15 mm Hg and 17 mm Hg were similar in the groups (Table 4). Overall, 32.7% and 55.2% of eyes achieved an IOP value of at least 15 mm Hg and 17 mm Hg respectively. These results are impressive, considering that all eyes had neovascular glaucoma. It is likely that the results would be better if a greater number of eyes had demonstrated panretinal photocoagulation. Many eyes had cataract and retinal and corneal ablation alone; no avascular bleb was obtained with this technique. With the use of MMC, there may have been some blunting of the hypertension phase in the subjects studied compared with historical controls. The current study also lacks the design necessary to address the efficacy of MMC in Ahmed glaucoma valve implantation. In order to address these two issues, a randomised, prospective study, both with and without the use of MMC, in a homogeneous patient population would be required.

The authors have no financial interest in the matters described.

LATIN AMERICAN GLAUCOMA SOCIETY (SLAG) INVESTIGATORS

The team of surgeons were Daniel Grigera, MD, of Argentina; Susanna Remo Jr, MD, Ralph Cohen, MD, Geraldo V Almeida, MD, Paulo A A Mello, MD, PhD, Mara Fontes, MD, Riutiro Yamane, MD, of Brazil; Juan Camilo Parra, MD, Juan C Rueda, MD, Fernando G Goyeneche, MD, of Colombia; Henrique M Vargas, MD, Rodolfo Grosmen, MD, of Peru.

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