Treatment of Primary Varicose Veins by Endovenous Obliteration with the VNUS Closure System: Results of a Prospective Multicentre Study

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Background. Radio frequency obliteration of the saphenous veins has been introduced as a less invasive alternative to traditional surgery for varicose veins.

Objective. To report the efficacy of obliteration and clinical outcomes following endovenous obliteration of the saphenous vein with limited follow-up to 3 years

Materials and methods. Radiofrequency obliteration (Closure® system, VNUS Medical Technologies, San Jose, CA) was performed in 330 limbs of 294 patients in a prospective worldwide multicentre study with 31 participating sites. Follow-up duplex ultrasound and clinical examinations were performed at annual intervals. The main outcome measures were the completeness of occlusion of the treated vein segment, presence of reflux and presence of signs and symptoms of venous disease.

Results. Before treatment 3.9% of limbs were categorised as CEAP clinical class zero or one. This improved to 82.9% at 1 year, 83.1% at 2 years and 86.8% at 3 years following treatment. Varicose vein free rates were 1 year: 90.1%, 2 years: 87.2%, 3 years: 88.2%. Duplex ultrasound demonstrated a reflux-free rate of about 88% over 3 years. Total occlusion (TO) of veins was 1 year: 81%, 2 years: 80.4% and 3 years: 75%. Partial occlusion (PO, <5 cm open segment) was 1 year: 6.3%, 2 years: 7.4% and 3 years: 17.6%. Incomplete occlusion (IO, >5 cm open segment) was 1 year: 12.7%, 2 years: 12.2% and 3 years: 7.4%. Partial occlusion did not result in any differences in the symptom severity score, the number of symptom free limbs, or the varicose vein absence rates at any follow-up time point when compared to the total occlusion group. The varicose vein absence rates were significantly lower in the IO group comparing to the TO and PO groups.

Conclusions. Radiofrequency saphenous vein obliteration improves the symptoms of varicose veins. The reflux-free rates in the treated veins remain constant over a 3 year follow-up period. There is no difference in clinical outcomes between the TO and the PO limbs, suggesting clinical effectiveness of the PO category. Greater than a 5 cm open segment in treated veins poses a risk of recurrence.

Keywords: Radiofrequency obliteration; Endovenous; Saphenous vein; Varicose veins.

Introduction

Surgery has been used for more than a century in the treatment of primary varicose veins of the lower limbs. Surgical treatments are classified into two distinct groups: resection surgery (e.g. saphenous vein stripping) and conservative surgery, which leaves the saphenous vein intact while eliminating the pathology. These techniques have been joined by less invasive endovascular techniques including radiofrequency obliteration. In the latter technique radiofrequency (RF) energy is used to heat the vein causing thermal destruction and vein shrinkage, with subsequent fibrotic vein occlusion.

Earlier articles analysed findings from 1 to 2 year clinical and duplex ultrasound follow-up.1-6 This report presents limited 3 year results of endovenous radiofrequency obliteration of saphenous vein reflux and aims to examine the haemodynamic factors influencing the clinical outcome.

Materials and Methods

This multicentre study was conducted in both university and state hospitals as well as in private practices. The study was undertaken principally in Europe but
also included centres in the United States and Australia. The study was submitted to ethics committees and, where applicable, to the local health service authorities for approval. Patients who gave informed written consent were included in the study. Common ethics committee requirements are in force in most of the countries involved.

Two hundred and ninety-four patients were included in this study between December 1998 and November 1999. In all, 330 limbs were treated for primary varicose veins in this multicentre, non-randomised, non-blinded prospective study. Female patients formed 76.9% of the group and the overall mean age was 46.3 years (range 18–97). A standardised case report form (CRF) was used at all the participating centres, thereby ensuring uniformity of data reporting. Study guidelines and standard protocols were issued to achieve consistency between the contributing centres. Clinical examination was always done by the same investigator at each centre. When possible, only one ultrasonographer at each centre was involved. During the follow-up period, the investigators provided all ultrasonographers with guidelines for performing examinations. In cases of missing or incomplete data, clarification with investigators was obtained. Duplex ultrasonography was undertaken in all patients preoperatively to assess the extent of venous disease. The mean pre-operative maximum vein diameter was 7.7 mm (range 3–17.4 mm) in the supine position. Reflux was assessed by response to a Valsalva manoeuvre in a reverse Trendelenburg position or with manual limb compression and release with the patient in a standing position. The mean duration of reflux was 3.8 s (range 0.5–30 s). Limbs with significant saphenous vein tortuosity which would impede catheter advancement or with an aneurysmal vein segment were not enrolled in the study.

Among 330 limbs treated, 323 (97.9%) were great saphenous veins (GSV) and seven (2.1%) were small saphenous veins (SSV) or a saphenous tributary. For the GSV, the location of vein treatment was limited to the thigh and just below the knee in 268 (81.2%) limbs, below the knee only in eight (2.4%) limbs and the entire GSV in 47 (14.2%) limbs. The CEAP clinical classification was not recorded on the data collection form. The two limbs classified as C0 both had preoperative leg pain and fatigue. In one additional limb with leg fatigue and oedema, the pre-treatment CEAP clinical classification was not enrolled in the study.

Reflux was defined as any evidence of reverse flow for more than 0.5 s in any treated vein segment or at the level of SFJ or SPJ. Adjunctive procedures associated at the time of treatment included phlebectomy of the varicose veins in 60% of the cases and sclerotherapy in 7% of the cases.

Patients were treated using the Closure® system (VNUS Medical Technologies, San Jose, CA). The procedures usually were performed under general anaesthesia although local anaesthesia (tumescent or regional) was used in some instances. The Closure catheter was passed pro-grade through a sheath after percutaneous sheath insertion, or through a small skin cut-down. The saphenous vein was catheterised either in the ankle region or just below the knee. The catheter connected to a saline infusion and to a radiofrequency generator, was advanced as far as the proximal part of the vein segment to be treated. Expandable bipolar electrodes at the end of the catheter were deployed by the operator. Once the catheter position was confirmed (using ultrasound or fluoroscopy), a near bloodless field in the vein to be treated was created by wrapping the limb with an Esmarch bandage and placing the patient in the Trendelenburg position. Tumescent anaesthetic solution was not routinely injected around the saphenous vein before treatment in this series. Each centre adhered to its own standard treatment protocol. The RF generator was turned on and the temperature at the electrode/vein wall interface was maintained at 85 °C via a feedback loop. The catheter was gradually withdrawn at a pullback rate of approximately two to three cm/min over the entire length of the vein to be treated.

Colour duplex ultrasound scans and clinical examinations were performed before treatment and at regular intervals postoperatively including 1, 2 and 3 years.

Efficacy of vein obliteration was categorised as follows:

Totally occluded (TO) veins were defined as those with no evidence of flow.

Partially occluded (PO) veins were defined as less than or equal to 5 cm segment of flow within the SFJ or an otherwise occluded vein trunk.

Inefficiently occluded (IO) veins were defined as greater than 5 cm of flow in any treated vein segment.

Reflux was defined as any evidence of reverse flow for more than 0.5 s in any treated vein segment or at the level of SFJ or SPJ.

Clinical assessment included a symptom severity scoring classification and varicose vein assessment. Varicose veins were defined as any visible abnormally dilated, tortuous vein. For symptom severity scoring,
limb pain, fatigue and oedema were each ranked as absent (0), moderate (1), or severe (2). A limb’s total score ranged from zero (asymptomatic) to six (pain, fatigue and oedema all present and severe). The scores were established by the surgeon assessing the patient who recorded his findings in the clinical notes.

Data collection is ongoing and this paper includes follow-up data through September 2002, including late receipt of data not previously reported.

**Statistical Analysis**

Continuous variables are presented as mean and range. Statistical comparisons were performed using Fisher’s Exact Probability Test or Student’s t-test where appropriate. Differences were considered significant at the \( p<0.05 \) level.

**Results**

Follow-up data were available on 252 limbs from 23 centres at 1 year, 148 limbs from 17 centres at 2 years, and 68 limbs from eight centres at 3 years (global cohort). Among the 68 limbs with assessment at 3 years, data was available on 65/68 limbs at 1-year follow-up and 58/68 limbs at 2-year follow-up (sub-cohort). This sub-group was analysed independently in addition to the global cohort to evaluate how representative this was of the global cohort results.

**Efficacy of obliteration**

Table 1 shows the assessments of efficacy of the global cohort and the sub-cohort. No significant differences were observed between the two cohorts \((P>0.05)\). In brief, the reflux free rates remained unchanged over the 3 years following endovenous RF obliteration.

Table 2 summarizes the occlusion categorizations of the global cohort at each yearly follow-up. In limbs with partially or inefficiently occluded veins, reflux was observed in eight PO limbs and 21 IO limbs at 1 year, 2 PO and 16 IO limbs at 2 years and five IO limbs at 3 years.

Statistical comparisons of each of the three groups between 1, 2 and 3 years demonstrated a significant increase in the PO rate at 1 and 3 years \((P<0.01)\) and between 2 and 3 years \((P<0.05)\).

As shown in Table 3, at 1 year the average length of the open segment was 2.6 and 23.8 cm for the PO and IO groups, respectively. At 3 years the average length of the open segment was 2.3 and 20 cm for the PO and IO groups, respectively. There was no clear change during the follow-up period.

The length of patent saphenous vein was analysed in the sub-group using identical criteria to those for the whole group. Table 4 summarises the results. The size of the PO group increased from 2 to 12 patients over the follow-up period, whereas the size of the IO group remained small and constant. The increase in numbers in the PO group was drawn from the TO group which decreased to 75% after 3 years. These changes reach statistical significance.

**Clinical assessment**

Fig. 1 shows the clinical assessment with regard to the presence of limb pain, fatigue or oedema during the follow-up period in comparison with the pre-operative status. In constructing this graph any limb with a score of more than zero was considered to have symptoms, irrespective of the size of the score. From this analysis the percentage of patients with each symptom was calculated for each time point. The graph does not reflect that far fewer patients were available for analysis at the later time points.

The maximum CEAP clinical class 0 or 1 (no sign of venous disease or spider veins) consisted of 3.9% of the limbs before treatment and improved to 82.9, 83.1 and 86.8% at 1, 2 and 3 years, respectively.

In order to examine the influence of partial occlusion on the clinical assessment results, the mean symptom severity score between the TO and PO groups was analysed. No statistically significant difference was found between the two groups at either 2 or 3 years. The mean symptom severity scores at 1 year were 0.06 for the TO and zero for the PO group \((P<0.05)\). There was also no significant difference between the TO and PO groups on the number of
symptom free limbs at 2 \((P = 1.0)\) and 3 \((P = 0.09)\) years by Fisher’s exact test. Comparisons at 2 and 3 years between the mean symptom severity scores of the combined TO and PO group versus the IO group demonstrated no statistically significant difference at either time interval. The results suggest that the occluded length of the treated vein does not predict the clinical symptom improvement (Table 5).

The physicians’ assessment of the presence of varicose veins at each visit is summarised in Table 6 with the results categorised according to completeness of vein occlusion at follow-up. Statistical comparison between groups demonstrated significant differences between the TO and the IO \((P < 0.0001)\) groups, and between the combined TO and PO cohort versus the IO group \((P < 0.0001)\), at 1 and 2 year follow-up. No statistical difference was found between the TO and PO groups at any time point.

The most frequent adjunctive procedure performed (either concurrent with the RF obliteration treatment or during the follow-up period) was stab avulsion of varices. Out of the 330 treated limbs, 201 limbs received avulsion phlebectomy at least once (including at the time of RF treatment). During follow-up no difference was found in the symptom severity score or in the number of asymptomatic limbs between those patients undergoing adjunctive phlebectomy and those who received no additional treatment. Neither did the age of the patient nor the diameter of the vein before treatment influence the outcome as assessed clinically or by duplex ultrasonography.

Complications which occurred following treatment and shortly afterward have been described elsewhere.\(^2\)\(^-\)\(^5\) Haematoma, infection, and superficial venous thrombosis were absent in all cases at 1, 2 and 3 year follow-up visits. Paraesthesia, described more appropriately as alteration of local sensitivity, was not observed in any of the limbs examined at the 3-year follow up. At 1 year, the incidence was 2.5% for limbs in which treatments were limited to the thigh and just below the knee (AK) and 7.4% for limbs with treatments extending to the ankle (BK). At 2 years, the incidence was 4.3% for AK treatments and 9.7% for BK treatments. At 3 years, paraesthesia was absent in both groups.

### Discussion

Primary superficial venous insufficiency has been treated traditionally by vein stripping with saphenofemoral ligation. Duplex ultrasound examination has shown persistence of reflux in the treated veins (either stable or progressive) in 9–29% of the cases at 1 year, in 13–40% at 2 years postoperatively\(^7\)\(^-\)\(^9\) and 15% of treated veins at 3 years.\(^10\)

In the present study, all the endovenous saphenous vein RF obliteration procedures were performed without saphenofemoral ligation. Venous reflux demonstrated by duplex ultrasonography was present in 11–12% of treated veins at each of the follow-up intervals. The patients who presented with IO at 1 year follow-up remained a small and constant number during the observation period. These probably reflect early treatment failures and do not arise later on. We can probably conclude from this that veins closed by RF ablation do not recanalise after 1 year. There was no statistically significant difference between the TO and

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**Table 2. Efficacy of obliteration outcomes at yearly intervals**

<table>
<thead>
<tr>
<th>Follow-up duration</th>
<th>1 year, (n = 252)</th>
<th>2 years, (n = 148)</th>
<th>3 years, (n = 68)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TO</td>
<td>204 (81.0%)</td>
<td>119 (80.4%)</td>
<td>51 (75%)</td>
</tr>
<tr>
<td>PO</td>
<td>16 (6.3%)</td>
<td>11 (7.4%)</td>
<td>12 (18%)</td>
</tr>
<tr>
<td>IO</td>
<td>32 (13%)</td>
<td>18 (12%)</td>
<td>5 (7.4%)</td>
</tr>
</tbody>
</table>

TO, totally occluded; PO, partially occluded; IO, inefficiently occluded.

**Table 3. Average length of the open segments (cm) at each yearly interval**

<table>
<thead>
<tr>
<th>Follow-up duration</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>TO</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PO</td>
<td>2.6 (1.0–5.0)</td>
<td>1.3 (0.1–4.0)</td>
<td>2.3 (0.5–5.0)</td>
</tr>
<tr>
<td>Reflux free</td>
<td>2.6 (1.0–5.0)</td>
<td>0.9 (0.1–2.0)</td>
<td>2.1 (0.5–5.0)</td>
</tr>
<tr>
<td>Reflux</td>
<td>2.7 (1.0–5.0)</td>
<td>3.5 (3.0–4.0)</td>
<td>2.7 (2.0–3.0)</td>
</tr>
<tr>
<td>IO</td>
<td>23.8 (5.5–80)</td>
<td>20.6 (6.0–55)</td>
<td>20 (20)</td>
</tr>
<tr>
<td>Reflux free</td>
<td>17.5 (5.5–40)</td>
<td>12.3 (9.5–15)</td>
<td>–</td>
</tr>
<tr>
<td>Reflux</td>
<td>28.1 (8.0–80)</td>
<td>21.8 (6.0–55)</td>
<td>20 (20)</td>
</tr>
</tbody>
</table>

TO, totally occluded; PO, partially occluded; IO, inefficiently occluded.

\(^*\) \(n = 1\).
PO categories with respect to the symptom severity score, the number of symptom free limbs, or the varicose vein absence rates at any follow-up time point (with the exception that the mean symptom severity scores of 0.06 for the TO versus zero for the PO group at 1 year). These results suggest that PO (a 5 cm or less segment of open vein) does not result in the development of symptoms.

Varicose veins were present in 10–13% of the whole group at the three follow-up intervals. In comparison, Jones reported absence of varices in 85.5% of the cases at 1 year and 75% of the cases at 2 years after high ligation and GSV stripping. Varicose vein recurrence rates were associated with the IO status, confirming that technical failure of the treatment is an adverse factor affecting outcome as might be expected. However, we found no difference in outcome between the TO and the PO groups. Limbs with the outcome of partial occlusion commonly showed absence reflux on ultrasound. The remaining segment of vein did not reflux or contribute in any significant way to the recurrence of varices.

Neovascularisation, which is currently the subject of considerable discussion and a consensus statement, is for some authors the principal cause of post surgical recurrence, assuming that the basic procedure has been properly performed. Neovascularisation was identified by duplex ultrasound after 2 years in 45% (24 out of 53) of the cases following conventional saphenous ligation and stripping operations. One year data reported by De Maeseneer suggest that this process promotes the development of recurrent varicose veins. In our series, no evidence of neovascularisation was found, suggesting that this endovenous treatment may avoid this complication associated with groin incision and vein resection.

As the technique of RF obliteration of saphenous vein reflux became more widely adopted, an idea emerged suggesting that concurrent stab avulsion of varices need not be done. The rationale was that phlebectomies may not be needed at all in some cases. Once the truncal saphenous reflux has been abolished and venous hypertension removed, varices diminish greatly in size minimising their clinical significance. This strategy has not been evaluated in any clinical trial. In our study, comparisons of symptom scores, presence of symptoms and presence of visible varices were compared between the group of ‘no phlebectomy’ patients (no phlebectomies performed at the original treatment or at any point the follow-up) and the rest of the patients at 1, 2 and 3 years. No statistically significant differences were found.

Two further parameters, patient age and vein diameter prior to treatment, were evaluated to assess their effect on outcome. It might be expected that these might influence the results of treatment. Large veins may be less effectively treated by RF obliteration. In elderly patients possible alterations of the collagen fibrils’ response due to the age of the patient might limit the success of treatment. Neither patient age nor vein diameter was found to affect the clinical or ultrasound assessed outcome.

The authors acknowledge that only a limited group of patients underwent examination at the 3 year follow-up interval representing 27% of the original group. This may have led to patients with more troublesome veins presenting at the longer review intervals or perhaps those with recurrent veins attended other clinics for treatment. We accept that this allows for some uncertainty in our data. Long-term registry studies have to take into consideration the lack of follow-up data from some of the patients at each follow-up opportunity. In order to verify the

Table 4. Efficacy of saphenous obliteration in the sub-group

<table>
<thead>
<tr>
<th>Follow-up duration</th>
<th>1 year, n=65</th>
<th>2 years, n=58</th>
<th>3 years, n=68</th>
</tr>
</thead>
<tbody>
<tr>
<td>TO</td>
<td>59* (90.8%)</td>
<td>48</td>
<td>51* (75.0%)</td>
</tr>
<tr>
<td>PO</td>
<td>2† (3.1%)</td>
<td>6</td>
<td>12† (17.6%)</td>
</tr>
<tr>
<td>IO</td>
<td>4 (6.2%)</td>
<td>4</td>
<td>5 (7.4%)</td>
</tr>
</tbody>
</table>

TO, totally occluded; PO, partially occluded; IO, inefficiently occluded.
* p<0.05.
† p<0.01 (Fisher’s exact test).

Fig. 1. Clinical assessment prior to treatment and at yearly intervals. Percentage of patients with any symptom at each follow-up interval.
representative ness of the most recent data, a lonti-
tudinal comparison at yearly intervals of haemo-
dynamic findings for a sub-group with the 3-year
follow-up data available was performed in this study.
The results from this sub-group were comparable to
those of the global cohort, confirming that the outcome
in the whole cohort reasonably reflected the outcome
of treatment.

In conclusion, following temperature controlled
radiofrequency saphenous vein obliteration, the reflux
free rates in the treated veins remained unchanged
over a 3 year follow-up period. There is no difference
in clinical outcomes between the TO and the PO limbs,
suggesting that clinical effectiveness of this technique
is maintained where a small segment of patent
saphenous vein persists. In the IO group with greater
than a 5 cm open segment in treated veins there is an
increased risk of recurrence and has to be monitored in
the long term follow-up.

Acknowledgements

The authors thank Michel Nuta, MD, from VNUS Medical
Technologies, for his assistance.

Table 5. Statistical significance of the symptom severity score between the sub-groups with total, partial and inefficiently occluded veins

<table>
<thead>
<tr>
<th></th>
<th>TO</th>
<th>PO</th>
<th>TO and PO</th>
<th>IO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity score-mean at 1 year</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Severity score-mean at 2 years</td>
<td>ns</td>
<td>ns</td>
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<td>ns</td>
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<tr>
<td>Severity score-mean at 3 years</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Symptom free limbs at 1 year</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Symptom free limbs at 2 years</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Symptom free limbs at 3 years</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
</tbody>
</table>

ns, not statistically significant (Fisher’s Exact Probability Test).

Table 6. Varicose veins assessment at each yearly follow-up interval

<table>
<thead>
<tr>
<th>Outcome</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Total</td>
<td>252</td>
<td>90.1</td>
<td>148</td>
</tr>
<tr>
<td>Varicose veins absent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TO</td>
<td>204</td>
<td>81.0</td>
<td>119</td>
</tr>
<tr>
<td>PO</td>
<td>193</td>
<td>94.6</td>
<td>112</td>
</tr>
<tr>
<td>Varicose veins absent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IO</td>
<td>32</td>
<td>12.7</td>
<td>18</td>
</tr>
<tr>
<td>Varicose veins absent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>227</td>
<td>90.1</td>
<td>129</td>
</tr>
</tbody>
</table>

TO, totally occluded; PO, partially occluded; IO, inefficiently occluded.

Appendix

Nigel Ackroyd, MD, Harbord, Australia; Henrick Åkesson, MD, Malmö, Sweden; Anders Alback, MD, Leena Laasonen, MD, and Tom Scheinin, MD, Helsinki, Finland; Thomas Bieber, MD, Peter Mulkens, MD, and Eberhard Rabe, MD, Bonn, Germany; Yolande Bullens, MD and HA. Martino Neumann, MD, PhD, Maastricht, The Netherlands; Stephano Camparini, MD and Gioacchino Coppi, MD, Modena, Italy; Jean-Marie Cardon, MD, Nimes, France; Denis Creton, MD, Nancy, France; Reinhard Fischer, Nikolaus Linde, and Claudio Duff, MD, St Gallen, Switzerland; Jean-Pierre Gobin, MD, Lyon, France; Mitchel P. Goldman, MD, LA Jolla, California; Jean-Jerome Guex, MD, Nice, France; Lowell S. Kabnick, MD, Morris-town, New Jersey; Robert L. Kistner, MD and Bo Eklof, Honolulu, Hawaii; Christian Lebard, MD and Francois Zucarelli, MD, Paris, France; Stefano Manfrini, MD, Vincenzo Gasbarro, MD, and Alberto Cataldi, MD, Ferrara, Italy; Robert F. Merchant, Jr, MD, Reno, NV; Kenneth A. Myers, MD, Richmond, Australia; Andrew Nicolaides, MD, FRCS, Andrew Lennox, MBBS, FRACS, and Zaki A. Zarka, MD, London, United Kingdom; Philippe Nicolini, MD, Decines, France;}

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