

Vitrectomy for Epiretinal Membrane: Does the Association with an Inflammatory Ocular Pathology Affect Outcomes?

Vitrectomia na Membrana Epiretiniana: A Associação com Patologia Ocular Inflamatória Afeta os Resultados da Cirurgia?

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ABSTRACT

INTRODUCTION: Epiretinal membrane (ERM) is a common complication in eyes with inflammatory ocular pathologies. This study aims to compare anatomical and functional outcomes following vitrectomy in patients with ERM, either idiopathic or secondary to an inflammatory ocular condition.

METHODS: This retrospective study was conducted in Centro Hospitalar Universitário de São João, Porto, Portugal. Medical records from the Immunopathology and Surgical Retina consultations (2013-2023) were reviewed. Two cohorts were established: Group A (idiopathic ERM) and Group B (ERM secondary to an inflammatory ocular pathology). Data collected included: demographic information, pre- and post-surgery best-corrected visual acuity (BCVA), surgical complications, intraocular pressure variation, and macular optical coherence tomography metrics.

RESULTS: Forty-two eyes from 42 patients were included, 21 in each group. No significant differences were observed between groups concerning the sex ($p=0.355$) or laterality of the affected eye ($p=0.212$). However, mean patient age at surgery was significantly lower in group B ($p<0.001$). The change in BCVA from pre-surgery to 6 months and 1 year post-surgery was not significantly different between the two groups ($p=0.493$ and $p=0.219$, respectively). Preoperative macular edema was significantly more frequent in Group B ($p<0.001$), while Group A exhibited a higher mean central macular thickness (CMT) ($p=0.030$). In Group A, the CMT decreased from $492.24\pm81.98\ \mu\text{m}$ pre-surgery to $415.71\pm43.12\ \mu\text{m}$ at 6 months and $407.71\pm42.66\ \mu\text{m}$ at 1-year post-surgery. Similarly, in Group B, the CMT reduced from $471.00\pm146.05\ \mu\text{m}$ pre-surgery to $351.38\pm102.06\ \mu\text{m}$ at 6 months and $345.63\pm104.88\ \mu\text{m}$ at 1-year post-surgery. No significant differences were observed between the CMT at 6 months and 1 year in either group. The rates of surgical complications and the presence of ocular hypertension after surgery were comparable between the groups ($p=0.707$ and $p=0.120$, respectively).

CONCLUSION: BCVA and CMT improvements following vitrectomy were comparable

between patients with idiopathic ERM and those with ERM secondary to inflammatory ocular pathology, with a similar safety profile observed in both groups.

KEYWORDS: Epiretinal Membrane; Macular Edema; Uveitis; Visual Acuity; Vitrectomy.

RESUMO

INTRODUÇÃO: A membrana epirretiniana (MER) é uma complicação comum associada a patologias oculares inflamatórias. Este estudo tem como objetivo comparar resultados anatómicos e funcionais após vitrectomia em pacientes com MER, com e sem associação com patologia ocular inflamatória.

MÉTODOS: Estudo retrospectivo realizado no Centro Hospitalar Universitário de São João, Porto, Portugal. Foi realizada uma revisão dos registos das consultas de Imunopatologia e Retina Cirúrgica (2013-2023) e foram criados dois grupos: Grupo A (MER idiopática) e Grupo B (MER secundária a patologia ocular inflamatória). Os dados avaliados incluíram: informações demográficas, melhor acuidade visual corrigida (MAVC) pré e pós-cirurgia, complicações cirúrgicas, variação da pressão intraocular e dados de tomografia de coerência óptica macular.

RESULTADOS: Foram incluídos 42 olhos de 42 doentes, cada grupo composto por 21 olhos. Não houve diferenças entre os grupos quanto ao sexo ($p=0,355$) ou à lateralidade do olho afetado ($p=0,212$). No entanto, a média de idades no momento da cirurgia foi significativamente menor no grupo B ($p<0,001$). A variação MAVC entre o pré-operatório e após 6 meses e 1 ano da cirurgia não foi significativamente diferente entre os dois grupos ($p=0,493$ e $p=0,219$, respetivamente). Edema macular pré-operatório foi significativamente mais frequente no Grupo B ($p<0,001$), enquanto o Grupo A apresentou uma espessura macular central (EMC) média mais elevada ($p=0,030$). No Grupo A, a EMC diminuiu de $492,24\pm81,98$ μm pré-cirurgia para $415,71\pm3,12$ μm aos 6 meses e para $407,71\pm42,66$ μm passado 1 ano da cirurgia. Da mesma forma, no Grupo B, a EMC diminuiu de $471,00\pm146,05$ μm para $351,38\pm102,06$ μm aos 6 meses e para $345,63\pm104,88$ μm passado 1 ano da cirurgia. Não foram observadas diferenças estatisticamente significativas entre a EMC aos 6 meses e 1 ano após cirurgia em ambos os grupos. A taxa de complicações cirúrgicas e a presença de hipertensão ocular após a cirurgia foram semelhantes entre os dois grupos ($p=0,707$ e $p=0,120$ respetivamente).

CONCLUSÃO: A melhoria da MAVC e da EMC após vitrectomia foi semelhante entre doentes com MER idiopática e aqueles com MER secundária a uma patologia ocular inflamatória. A cirurgia foi igualmente segura em ambos os grupos.

PALAVRAS-CHAVE: Acuidade Visual; Edema Macular; Membrana Epiretiniana; Uveíte; Vitrectomia.

INTRODUCTION

An epiretinal membrane (ERM) is an abnormal layer at the vitreoretinal interface, resulting from the growth of myofibroblastic cells along with the extracellular matrix on the inner surface of the central retina, specifically along the inner limiting membrane (ILM). Due to its contractile properties, ERM can exert traction to the underlying retina, leading to notable visual impairment, such as reduced visual acuity (VA) and metamorphopsia.^{1,2}

This condition can result from various causes and underlying pathological mechanisms. ERMs are classified as idiopathic when not associated with ocular abnormalities or associated with a posterior vitreous detachment only. In contrast, secondary ERM develops in association with ocular conditions, such as vitrectomy, laser retinopathy,

cataract surgery, diabetic retinopathy, retinal vascular occlusive disease, or intraocular inflammation.^{1,2}

In many patients, ERM may be asymptomatic. The appearance of symptoms typically depends on factors such as the location, duration, severity, and type of ERM. Vision is usually impacted when there is retinal traction or edema. Common symptoms include reduced VA, blurred vision, metamorphopsia, and loss of stereopsis.²

Optical coherence tomography (OCT) is the most sensitive diagnostic tool for ERM, often revealing an irregular, hyper-reflective layer on the ILM, frequently associated with retinal wrinkling and hyporeflective spaces between the ERM and ILM. The main morphological difference in OCT between idiopathic and secondary ERM is that the latter are more likely to have focal points of adhesion to the retina and not a continuous adhesion as usually happens in idiopathic ERM.²

ERM is a frequent complication in eyes with inflammation (iERM), either with or without cystoid macular edema (CME).³⁻⁵

While the spontaneous resolution of iERM has been reported, the only treatment for ERM is surgical removal, and advancements in vitrectomy systems have facilitated less invasive procedures. Despite ongoing debates regarding various aspects of the surgical approach to iERM, including optimal timing, perioperative management, and prognosis,^{1,2,6} potential similarities or differences compared to vitrectomy in idiopathic ERM have not yet been explored. It is possible that in iERM, retinal anatomical improvements may be less pronounced, visual acuity gains may be more limited, and there may be a risk of reactivating the inflammatory process in the postoperative period.

This study aims to compare anatomical and functional outcomes following vitrectomy in patients with ERM, either idiopathic or secondary to an inflammatory ocular pathology.

METHODS

STUDY DESIGN, PARTICIPANTS AND SETTING

This retrospective, longitudinal cohort study was conducted at Centro Hospitalar Universitário de São João, Porto, Portugal. This study adhered to the tenets of the Declaration of Helsinki. Patient informed consent for participation in this study was waived due to its retrospective nature, and all patient data confidentiality was strictly maintained with no identifiable information disclosed. Nonetheless, all patients signed a surgical informed consent before their surgical procedures.

A comprehensive review of patients' records from the Immunopathology and Surgical Retina consultations (2013-2023) was conducted. We included only patients with a minimum follow-up of one year and all subjects were followed pre- and postoperatively in our tertiary center. Two cohorts were established: Group A (idiopathic ERM) and Group B (ERM secondary to an inflammatory ocular pathology; iERM). Patients with idiopathic ERM were randomly selected to form group A until it reached the same size as group B.

In all cases, the indication for surgery was persistent visual acuity reduction associated with ERM with or without CME.

Patients were excluded from both groups if they had a history of pan-photocoagulation or other retinal laser (for example, due to a retinal tear), prior intravitreal injection, previous vitreoretinal surgery, high myopia and/or concomitant macular/lamellar hole.

DATA COLLECTION

Clinical data were extracted from medical records, including demographic, surgical, and OCT parameters. Demographic variables included sex and age at surgery. Surgery data included the affected eye, history of cataract surgery, type of surgery (associated or not with cataract

surgery), best-corrected visual acuity (BCVA) before surgery, and at 6 months and 1 year after surgery, presence of surgical complications, and intraocular pressure variation (before and during the first six months after surgery). For group B, inflammatory ocular pathology diagnosis, baseline topical therapy, and systemic immunosuppressive therapy were also recorded.

The presence of an ERM was determined based on spectral domain OCT (Heidelberg SPECTRALIS®) and was defined as a hyperreflective preretinal layer. The thickness of the 1 mm central macular ring was evaluated before surgery, and at 6 months and 1 year post-surgery. Additionally, the presence of CME before surgery, recurrence of ERM after 1 year, and the presence of ERM in the contralateral eye were also assessed.

CME was identified in OCT exams as low-reflective intraretinal spaces, clearly defined and separated by thin, high-reflective retinal tissue.⁷

VA measurements recorded on the Snellen scale were converted to the logMAR scale for statistical analysis (counting fingers vision was converted to +2.00, and hand motion vision to +3.00).⁸

SURGICAL DATA, TECHNIQUE AND PERIOPERATIVE TREATMENT

All surgeries were performed under sub-Tenon's, peribulbar, or general anesthesia, according to the surgeon's preference and considerations regarding the patient's collaboration, and anticipated duration and difficulty of the surgery.

All patients underwent transconjunctival small-gauge three-port pars plana vitrectomy (23 or 25 gauge) by four experienced vitreoretinal surgeons. Phakic patients underwent combined phacoemulsification with intraocular lens implantation when indicated by their age.

ILM peeling was performed in all cases following ERM removal. Any retinal breaks found during surgery were treated with endolaser retinopexy. Fluid-air exchange was performed and, in some patients, according to the surgeon's preference, sulfur hexafluoride (SF6) tamponade was done.

Postoperative treatment was prescribed, including dexamethasone phosphate 1mg/mL, flurbiprofen sodium 3 mg/mL, and levofloxacin 5 mg/mL 5 times per day with a variable tapering, according to postoperative evaluation.

Intra and postoperative complications were evaluated.

STATISTICAL ANALYSIS

Kolmogorov-Smirnov was used to assess whether each variable followed a normal distribution. Continuous variables with normal distribution are presented as mean $\pm$ standard deviation (SD), while non-normally distributed data are reported as median and interquartile range (IQR). The continuous variables were compared between the two groups using the Student's t-test if they followed a normal distribution and the Mann-Whitney test if they did not. Chi-square test was used to compare categorical variables.

Statistical analysis was performed using the IBM® SPSS® Statistics software (version 29.0 for Windows; SPSS Inc., Chicago, IL, USA). The level of significance was established at a p -value of <0.05 .

RESULTS

BASELINE CHARACTERISTICS

Between 2013 and 2023, a total of 1239 patients were followed in the Immunopathology consultation at our hospital. Out of 105 eyes with uveitis that underwent vitrectomy, 24 were operated on for an ERM (1.94%). Three patients were excluded from the final analysis of group B because post-surgery OCT at 6 months and/or at 1 year were unavailable.

Both groups A and B comprised 21 patients each. In group A, 12 (57%) patients were male and 9 (43%) were female, whereas in group B, 12 (57%) were female and 9 (43%) were male. No significant differences were found between groups in terms of sex ($p=0.355$) and laterality of the affected eye ($p=0.212$).

The median age at the time of surgery was 74.00 (7) years in group A and 53.00 (22) years in group B. Comparing the two groups, the mean patient age at surgery was significantly lower in group B ($p<0.001$). The age distribution of patients at surgery can be seen in Fig. 1.

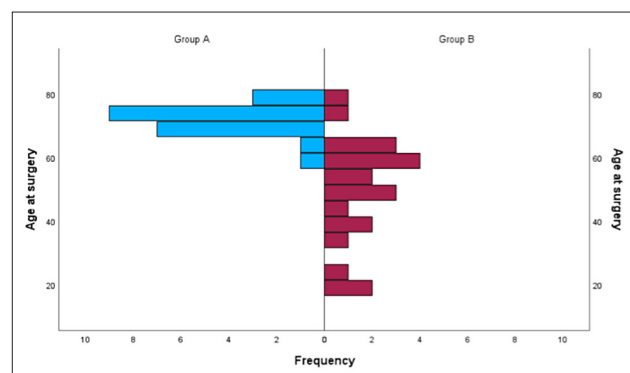


Figure 1. Distribution of patients' age at the time of surgery.

The frequency of cataract surgery before vitrectomy was similar between the two groups ($p=0.116$).

In group B, the most common ocular inflammatory diagnosis was idiopathic uveitis (33.3%; 7 eyes), followed by uveitis associated with sarcoidosis (19.0%; 4 eyes), inflammation associated with psoriasis (14.3%; 3 eyes), Behçet's disease (9.52%; 2 eyes) and Eales disease (9.52%; 2 eyes). The average time between the diagnosis of inflammatory ocular pathology and surgery was 5.86 ± 4.11 years. All patients had been clinically stable from an ocular standpoint for at least one year, and in 14 cases (66.7%) they were receiving immunomodulatory treatment at the time of surgery.

OCT ANALYSIS

The presence of macular edema before surgery differed significantly between the two groups, with 2 eyes (9.5%) in Group A and 13 eyes (61.9%) in Group B exhibiting edema ($p<0.001$).

The evolution of CMT (before surgery, after 6 months, and after 1 year) is presented in Fig. 2.

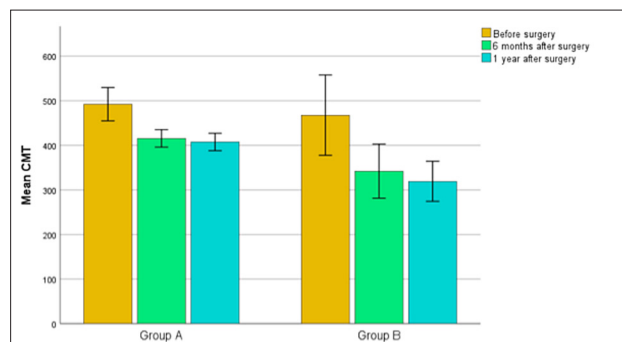


Figure 2. Central macular thickness (CMT) in OCT examinations before surgery, after 6 months, and after 1 year in groups A and B. Mean CMT before surgery was 492.24 ± 81.98 µm in Group A and 471.00 ± 146.05 µm in Group B ($p=0.030$). Mean CMT 6 months after surgery was 415.71 ± 43.12 µm in Group A and 351.38 ± 102.06 µm in Group B ($p=0.029$). Mean CMT 1 year after surgery was 407.71 ± 42.66 µm in Group A and 345.63 ± 104.88 µm in Group B ($p=0.019$).

The variation of CMT (before surgery, after 6 months, and after 1 year) was also evaluated and the results are presented in Table 1.

Table 1. Variation of central macular thickness (CMT) before surgery (BS), 6 months after surgery (6M) and 1 year after surgery (1Y).

	<i>p</i> -Value
Group A	
CMT BS Vs 6M	<0.001
CMT BS Vs 1Y	<0.001
CMT 6M Vs 1Y	0.142
Group B	
CMT BS Vs 6M	0.034
CMT BS Vs 1Y	0.046
CMT 6M Vs 1Y	0.332

Recurrence of ERM after 1 year was observed in only one case (Group A), with no significant difference in recurrence rates between groups ($p=0.311$). Moreover, the presence of ERM in the contralateral eye was also similar between the two groups ($p=0.352$).

INTRA AND POST-SURGERY ANALYSIS

Cataract surgery combined with vitrectomy was more common in group A (15 eyes) compared to 4 eyes in group B ($p<0.001$). Notably, all phakic eyes in group A underwent

combined surgery, while 6 phakic eyes in group B did not undergo cataract surgery.

Surgical complications in group A included hyphema in one patient that required anterior chamber washout at the end of the surgery, and two patients needed photocoagulation laser due to iatrogenic retinal injury. In group B, three cases stood out: A case of three retinal re-detachments in a patient with a history of treated retinal vasculitis; one patient with granulomatous uveitis associated with Eales disease who intraoperatively presented a localized nasal choroidal detachment, which led to the early termination of the surgery and the need to postpone and re-operate later; and the third case, a patient with a history of idiopathic hypertensive uveitis who presented hypotonia and localized choroidal detachment in the postoperative period, that resolved without the need of further surgical intervention. The overall complication rate between the two groups was not significantly different ($p=0.707$).

Additionally, the use of adjuvant intravitreal injection of triamcinolone acetonide or 0.7 mg dexamethasone Intravitreal implant at the end of surgery was not different between the two groups ($p=0.078$) and the same happened concerning the chosen tamponade ($p=0.346$).

In group A, one patient had to initiate hypotensive topical treatment and in group B it happened in four patients. Nonetheless, the rate of ocular hypertension after surgery was comparable between the two groups ($p=0.120$).

In Group B, there were no cases of reactivation or worsening of inflammation associated with surgery, nor was there a need to increase the baseline anti-inflammatory treatment escalation during the one-year study period.

VISUAL OUTCOMES

LogMAR BCVA before surgery and one year after surgery were similar between the two groups ($p=0.718$ and $p=0.063$, respectively). Despite that, logMAR BCVA 6 months after surgery was better in group A (0.30 (0.20)), compared to group B (0.40 (0.30)) ($p=0.031$). The change in logMAR BCVA from pre-surgery to 6 months and 1 year post-surgery was not significantly different between the two groups ($p=0.493$ and $p=0.219$, respectively).

DISCUSSION

This retrospective study aimed to evaluate functional and anatomical outcomes following vitrectomy in patients with ERM secondary to inflammatory ocular pathology and to compare these results with those of patients with idiopathic ERM.

A few studies have already analyzed morphologic differences in idiopathic and secondary ERM using OCT.^{9,10} By contrast, the comparison between the two groups regarding functional and anatomic prognosis and safety of vitrectomy has not yet been well demonstrated.

In our hospital, of the 1239 patients that were followed in the Immunopathology consultation between 2013 and 2023, 24 were submitted to a vitrectomy for an ERM, thus

calculating a rate of 1.94%. Similarly, Yap A *et al* evaluated the long-term VA and morphometric progression in patients with uveitis and ERM, finding an operated ERM rate of 0.81% (44 out of 5450).¹¹

In our study, in terms of baseline characteristics, no significant differences were observed between groups concerning the sex ($p=0.355$) and laterality of the affected eye ($p=0.212$). However, the mean patient age at surgery was significantly lower in group B ($p<0.001$). On the one hand, it highlights the spectrum of ages affected by iERM, in contrast to the tendency of idiopathic ERM to affect older individuals. On the other hand, it calls attention to the importance of vitrectomy in rehabilitating patients with iERM, who are often still of working age.

In our investigation, OCT examination revealed that preoperative macular edema was significantly more frequent in eyes with iERM, occurring in 61.9% of cases ($p<0.001$). This finding aligns with the study of Cristescu IE *et al*, which reported a similar rate of concomitant CME of 66%, and with the study of Rao P *et al* that found a rate of 88.2% (15 of 17 eyes; considering thickening and/or intraretinal cysts).^{12,13} Also, Yap A *et al* found a CME rate of 31.9% (69/216 eyes) in eyes with ERM and 8.6% (449/5224 eyes) in those without ERM, indicating that eyes with ERM were significantly more likely to also have CME.¹¹ Therefore, when evaluating patients with uveitis, the presence of CME cannot be solely attributed to inflammation, as it is often caused by the presence of ERM.

In this study, CMT was significantly higher in the idiopathic ERM group before surgery ($p=0.030$). Additionally, in both groups, preoperative CMT was significantly greater compared to CMT at both 6 months and 1 year post-surgery. However, no significant differences were observed between CMT at 6 months and 1 year in either group, indicating that the main improvement occurred within the first six months and remained stable up to 1 year. Extending the study period could be beneficial, as evidence suggests that retinal thickness may continue to improve after vitrectomy for a longer duration, even if not always statistically significant.^{14,15}

Regarding the use of intravitreal corticosteroids at the end of surgery, we did not find a significant difference between the two groups ($p=0.078$). However, a closer analysis showed that it was used in 1 eye in group A and 5 eyes in group B. In other words, while there was a difference, it was not statistically significant. Additionally, this aspect may not have been registered for all eyes in Group B, which can be attributed to inaccuracies in the surgical records—a limitation of retrospective studies.

In our study, the most common ocular inflammatory diagnoses associated with iERM were idiopathic uveitis, as well as inflammation related to sarcoidosis and psoriasis. Similarly, in Yap *et al*, idiopathic uveitis was the most frequent diagnosis, followed by sarcoidosis, HLA-B27-related uveitis, and toxoplasmosis. Additionally, Coassin M *et al* reported sarcoidosis panuveitis, presumed tuberculous uveitis, and Behcet's panuveitis as the most common diagnoses.^{11,16}

Regarding surgical safety, the rate of surgical complications between the two groups was not significantly dif-

ferent ($p=0.707$). Indeed, patients with iERM underwent surgery during periods of quiescent inflammation, with or without systemic immunosuppression. In the study of Cristescu IE *et al*, postoperative complications of patients with iERM included retinal detachment and hypotony, transient secondary ocular hypertension that was controlled with topical eyedrops, anterior capsular phimosis and posterior capsular opacification (5 out of 29).¹²

In the present study, the median BVCA before surgery was 0.5 (0.3) in group A and 0.5 (0.5) in group B, and the median BCVA six months after surgery was 0.30 (0.20) in group A and 0.40 (0.30) in group B. In Rao P *et al* the mean BCVA before surgery was 0.8 ± 0.6 in contrast to 0.6 ± 0.6 six months after surgery and in Cristescu IE *et al*, the mean BCVA improved from 0.73 ± 0.3 to 0.49 ± 0.36 in six months.^{12,13}

Moreover, when evaluating VA progression, we found that, at six months after surgery, BCVA was better in group A ($p=0.031$), but this difference disappeared by 1-year post-surgery ($p=0.063$). This difference may suggest that BCVA recovery may be faster in eyes with idiopathic ERM.

Our study's limitations include its retrospective nature, the small sample size of a single tertiary hospital, and the fact that the vitrectomy was performed by different surgeons. Additionally, previous cataract surgery was not considered an exclusion criterion, and poor prognostic OCT features for ERM surgery—such as a disrupted ellipsoid zone or the presence of an ectopic inner foveal layer—were not evaluated. However, to our knowledge, this is the first series to report anatomical and functional outcomes of the vitrectomy in patients with ERM and well-controlled uveitis of any type and compare them to a series of patients with idiopathic ERM.

CONCLUSION

To conclude, our findings indicate that functional and anatomical improvement following vitrectomy was similar between patients with idiopathic ERM and those with iERM and that the procedure is equally safe in both groups. Therefore, delaying vitrectomy in cases of ERM associated with inflammatory ocular diseases should only be considered if the underlying disease is not controlled. Otherwise, the procedure should proceed, as it often leads to significant improvement in visual function, often to patients who are still of working age.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

JSO: Data collection, literature review, writing, revision.
STC, MF, LF and ARS: Writing, revision.
All authors approved the final version to be published.

JSO: Recolha de dados, revisão da literatura, redação, revisão.

STC, MF, LF e ARS: Redação, revisão.

Todos os autores aprovaram a versão final a ser publicada.

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Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de Ética responsável e de acordo com a Declaração de Helsínquia revista em 2024 e da Associação Médica Mundial.

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