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Research Article

The Matter of Inflammatory Responses in Endovenous Radiofrequency Ablation and Conventional Venous Stripping

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Abstract

Background: Varicose veins surgery was evolved in the past decade. Many studies showed that Endovenous Radiofrequency Ablation (EV-RFA), a novel method for varicose veins treatment, produced complications fewer than conventional venous stripping, particularly postoperative pain and ecchymosis. There were a lot of studies reported about inflammatory response but there was few studies compare inflammatory response between procedures. This study purpose compare preoperative and postoperative level of serum Interleukin 6 (IL-6) and C-Reactive protein (CRP) to determine the inflammatory response of EV-RFA and conventional venous strip- ping. This study also compares Visual Analogue Scale (VAS) and ecchymoses between these two procedures.

Methods: A prospective cohort study measuring IL-6 and CRP level at before and 24-hour after surgery in symptomatic varicose vein patients who underwent either EV-RFA or conventional venous stripping.

Results: Fifty-nine patients were included, 27 patients were treated by conventional venous stripping and 32 patients were treated by EV-RFA. There was no different in demographic characteristics among two groups. Twenty-four hour postoperative level of IL-6 and CRP significantly increased ($p < 0.001$ and < 0.001, respectively) in both EV-RFA group ($p < 0.001$ and < 0.001, respectively) and venous stripping group ($p = 0.043$ and < 0.001, respectively) compare to pre- operative level. Increasing in 24-hour postoperative level of IL-6 and CRP in EV-RFA group was significantly lower than in venous stripping group ($p < 0.001$ and $p = 0.045$, respectively). Post- operative VAS and ecchymosis were also significantly different between EV-RFA group and ve- nous stripping group. ($p < 0.001$ and $p < 0.001$, respectively).

Conclusion: EV-RFA produced inflammatory response, VAS and ecchymosis significantly lower than conventional venous stripping.

Introduction

Chronic Venous Insufficiency (CVI) is common lower extremity vascular pathologies with great medical and socioeconomic impact. It cost 1% - 2.5% of health care budgets in developed countries. It affects worldwide population with prevalence of 73% in female and 56% in male. It significantly decreases quality of life of affected patients [1]. It presents with wide spectrum of clinical manifestations from varicose veins, limb edema, hyper pigmentation of skin and finally the development of venous ulcer. It also includes deterioration in morphological and functional alterations of the venous system, occur with signs and symptoms varying in type and severity that categorized by the Clinical Etiological Anatomical Pathological (CEAP) classification [2].

Main pathophysiology mechanism of CVI is venous hypertension caused by shear stress and reflux from incompetent valves [3]. Venous hypertension cause venous dilatation, worsened valvular insufficiency and increased intravenous pressure. Changing in hemodynamics interfere microcirculation, Endothelial Cells (ECs) and vessel microenvironment, leading to venous microangiopathy and dilation and tortuosity of capillary beds [3]. The mechanosensors of endothelial cells are triggered by altered hemodynamics, transducer physical signals into harmful pathways resulting in ECs damages. Particularly these complex biological processes activated inflammatory and proteolytic cascades in vascular microenvironment including leukocyte adhesion, degranulation and releasing of cytoplasmic granules from neutrophils, macrophages, mastocytes, ECs and platelets [4]. All of these mechanisms lead into impairing of both microcirculatory and macro circulatory systems, cause remodeling of the venous walls and valves, venous hypertension, formation of varicosities, edema and leg ulceration [3,5].

Inflammations are an essential immune response to pathogens and damaged cells. In varicose veins, there are refluxes and incompetent valves and venous wall dilation resulting in increased venous pressure. Phenotypic modulation of Vascular Smooth Muscle Cells (VSMC) alters Extracellular Matrix (ECM) metabolisms. Angiogenesis are main mechanisms contributing morphological and functional modifications of varicose veins remodeling. Inflammatory cytokines and adhesion molecules included Transforming Growth Factor Beta (TGF-β), Interleukin 6 (IL-6), Interleukin 8 (IL-8) and Vascular Cell Adhesion Molecule 1 (VCAM-1) [6]. Increased ve- nous wall tension creates Matrix Metalloproteinases (MMPs) activities, which induce ECM degradation and affect structural integrity of the venous walls.

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ECs injury also triggers inflammation by leukocytes infiltration and activation, resulting in further venous wall damage and fibrosis, leading to progressive venous insufficiency and varicose veins formation. Monocytes and macrophages migrate into venous wall and valve turning patient into venous insufficiency. Venous stasis cause inflammatory cytokines releasing by monocyte and macrophage including Interleukin-1b (IL-1b), IL-6 and Tumor Necrosis Factor Alpha (TNF-α). Refluxed vein activate ECs of luminal vein and vasa vasorum, indicate by up regulation of Intercellular Adhesion Molecule 1 (ICAM-1), Interleukin 1a (IL-1a) and TNF-α [7].

Treatments of varicose veins are conventional surgery and endovenous treatment. Conventional surgical treatment is high ligation and stripping. Modern endovenous treatments are defined such as Endovenous Radiofrequency Ablation (EV-RFA), Endovenous Laser Ablation (EVLA), sclerotherapy, mechanochemical endovenous ablation, N-butyl-2-cyanoacrylate injection. High Ligation and Venous Stripping (HL/VS) is traditional treatment that cause unsatisfactory cosmetic outcome for concerning patients due to multiple incisions. However, HL/VS still indicate in some situations including superficial saphenous tributary adherent closely to skin less than 1 cm, tortuous superficial veins and aneurysmal venous segment larger than 2.5 cm, chronic thrombophlebitis and acute superficial thrombosis [8]. Endovenous treatments are the alternative treatment giving better cosmetic result and faster recovery. Rasmussen et al reported results of four-arm RCT and concluded that postoperative pain was higher in HL/VS and EVLA, although efficacy of four modalities was not significantly different [9]. In past decade, most of patients with varicose veins in our institute were treated by HL/VS and EV-RFA. We questioned in difference of inflammatory reaction between our both varicose veins treatment options. Study of inflammatory responses and clinical outcomes was designed. IL-6 secretes by T-cell and macrophage responds to tissue trauma. Smooth muscle cells produce IL-6 as a proinflammatory cytokine induced activities of B-lymphocyte and cytotoxic T-lymphocyte. C-Reactive Protein (CRP) is acute-phased reactant protein produced by inflammation and tissue trauma response of hepatocyte. CRP level start increasing in 6 to 10 hours and peaked at 36-50 hours after inflammation or trauma. It returned to normal level within 1-2 weeks [10].

This study was designed to compare the difference of preoperative and 24-hour postoperative inflammatory response from tissue trauma after HL/VS and EV-RFA, identified by serum level of IL-6 and CRP.

Materials and Methods

Institutional review board of royal thai army medical department approved this prospective study. All patients gave inform consent to this protocol. A prospective cohort study was performed in patients who were diagnosed symptomatic varicose veins with reflux underwent operation from September 1st, 2013 to August 31st, 2015 in Phramongkutklao hospital. Included patients got symptomatic varicose vein with reflux in Great Saphenous Vein (GSV). All of patients were 18 years of age or older, and were ask to consent to enroll in study. The patients with connective tissue disease, autoimmune disease, cirrhosis, end stage real disease and hematologic disease were excluded from study. Patients who presented with venous ulcer or elsewhere infection were also excluded. Patients with history of recent trauma were not enrolled in study.

Fifty-nine patients were enrolled, 32 patients were in EV-RFA group and 27 patients were in HL/ VS group. We were performed either EV-RFA or traditional venous stripping for these patient and selected operation by patient preference.

Data collection

Demographic data including age, sex, clinical symptom, professional, underlying conditions, diameter of superficial vein and GSV. Preoperative and postoperative serum level of IL-6 and CRP were noted. Postoperative visual analogue scales and ecchymosis were evaluated. Serum level of IL-6 and CRP were compared preoperatively and 24-hour postoperatively.

Venous blood sampling

Venous blood samples were manually drawn by direct puncture using 23-gauge needle from antecubital vein. Five cubic milliliters of venous blood was collected into citrated tube and sent to laboratory under dry ice in air courier. Supernatant plasma was manually separated and stored at 20°C for batch analysis. Both preoperative and 24-hour postoperative blood samples were collected in the same technique. Preoperative blood samples were collected at night before operation and 24-hour postoperative blood sample was collected at 24-hours after finishing operation.

Diagnostic of Great Saphenous Vein (GSV) reflux

Venous duplex ultrasonography was done for diagnosis of GSV reflux and evaluating anatomy of vein by radiologist. Deep Vein Thrombosis (DVT) was ruled out under standard venous duplex examination. Venous duplex reflux examination included B-mode and color-flow imaging of deep and superficial vein and pulsed doppler assessment of flow direction. Flow direction was evaluated with provocative maneuver either Valsalva maneuver or augmenting flow with distal limb compression. Reversal of flow in superficial veins lasting more than 0.5 second indicated valvular incompetence and reversal of flow in superficial veins lasting more than 1 second indicated deep system reflux. Diameter of GSV and superficial vein were collected [11].

High ligation with venous stripping

Operation was done under regional anesthesia. Oblique incision was done parallel to groin crease, or 1-2 cm below in obese patients. GSV was identified and its tributaries were ligated. High ligation was done closely to femoral vein. Proximal ligation was done with simple and suture ligation as double ligation. Transverse venotomy was done and stripper was passing distally until knee level. Small incision was done at area where stripper was palpated. GSV was stripped in either upward or downward direction. If cosmetic issue was concerned, stab avulsion was simultaneously performed.

Endovenous radiofrequency ablation

Operation was done under regional anesthesia. We used the Covidien ClosureFAST™ catheter that constructed with a 7-cm bipolar electrode affixed to distal end. Ablation of GSV was started below popliteal area. Patient was in reverse trendelenburg position. Access site was performed with percutaneous puncture by 21-gauge needle under ultrasound guidance. A 7-Fr, 10-cm sheath (Radiofocus® Introducer II standard kit-Introducer sheath; Terumo intervention system) was advanced over the wire and 7-Fr ClosureFAST™ catheter was inserted.

The catheter tip was advanced to optimal point at 2.0-2.5 cm from Saphenofemoral Junction (SFJ). Proper placement of the catheter tip was confirmed by ultrasound. Perivenous tumescent anesthesia was administered under ultrasound guidance along entire targeted venous segment creating a fluid layer around GSV. Sufficient tumescent anesthesia was injected until 10-mm diameter of fluid around GSV was created and forming a 10-mm distance between the targeted vein and skin. A representative mixture of 40 ml of 1% lidocaine with epinephrine in 450 ml of normal saline, neutralized by 10 ml of 7.5% sodium bicarbonate. After performing tumescent anesthetic, patient turned into trendelenburg position, making vein collapsed and exsanguinated. Location of catheter tip was confirmed with ultrasound before ablation. By segmental ablation technique of the ClosureFAST™ system, each 7-cm segment were treated independently for 20 seconds each interval. In each treatment cycle, temperature must be 120° C for 5 seconds after initiation of energy delivery. If proper temperature did not achieved, 20-second treatment cycle was repeated. Finally, duplex ultrasonography was performed to evaluate treated vein for absence of reflux and evidence of occlusion.

Postoperative evaluation and management

Postoperative pain was evaluated by visual analogue pain scale. The presence of ecchymosis and numbness were recorded at the morning after intervention. Postoperative compression with a 30 to 40 mm Hg graduated stocking was applied for at least 1 week. Patients were instructed to ambulate immediately after procedure. Follow-up evaluations were performed at 1 week.

Statistical analysis

Demographic data, patient's characteristics and clinical results were evaluated by Chi square test. Postoperative pain was defined by visual analogue scale. The presence of ecchymosis and numbness was compared by Chi square test. Preoperative and 24-hour postoperative serum level of IL-6 and CRP were analyzed by Mann-Whitney U test and Fisher's exact test. Difference in preoperative and postoperative serum level of IL-6 and CRP were compared between EV-RFA group and HL/VS group by Wilcoxon signed ranks test.

Result

Fifty-nine patients were enrolled, 32 patients were in EV-RFA group and 27 patients were in HL/VS group. Mean age of patients were 56 and 52 years old in EV-RFA and HL/VS groups respectively. Male was 31.3% in EV-RFA group and 48.1% in HL/VS group. Most of patient's professional were housewife, teacher and government officer. Three major underlying medical comorbidity were hypertension, diabetes mellitus and dyslipidemia. Most common clinical presentation was heaviness in legs for both groups. Average size of superficial vein and GSV was 3-5 mm and 5-10 mm respectively for both groups (Tables 1 and 2).

Mean VAS was significantly lower in EV-RFA group compare to HL/VS (1.41±1.1 vs 3.89±1.53, $p < 0.001$). Postoperative ecchymosis was also significantly lower in EV-RFA (9.4% vs 59.3%, $p < 0.001$). Numbness was not significantly among two groups (3.1% vs 7.4%, $p = 0.456$). There was no significant difference of median baseline level of IL-6 between EV-RFA and HL/VS group ($p = 0.05$), however, there was significant difference of median baseline level of CRP among two groups. ($p = 0.045$). Both IL-6 and CRP level increased significantly from preoperative to 24-hour postoperative in both EV-RFA ($p < 0.001$ and $p = 0.043$, respectively) and HL/VS ($p < 0.001$ and $p = 0.001$, respectively) group. Rising of IL-6 and CRP level were lower in EV-RFA group compare to HL/VS group ($p < 0.001$ and $p = 0.045$, respectively) (Tables 3-5) (Figure 1).

Characteristics	EV-RFA (32) n (%)	HL/VS (27) n (%)	P-value
Age (years) mean (SD)	56.03 (14.46)	51.89 (10.77)	0.235
Sex 0.185			
male	10 (31.3)	13 (48.1)	
female	22 (68.8)	14 (51.9)	
Underlying disease			
DM	8 (25)	2 (7.4)	0.073
HT	10 (31.3)	8 (29.6)	0.893
DLP	3 (9.4)	4 (14.8)	0.520
Career			
Farmer	1	1	
Government officer	6	4	
Housewife	6	7	
Teacher	9	8	
Soldier	4	4	
Shopkeeper	4	3	
Symptom			
Aching	16 (50)	14 (51.9)	0.887
Heaviness	17 (53.1)	16 (59.3)	0.636
Cramping	6 (18.8)	8 (29.6)	0.328
Edema	9 (28.1)	6 (22.2)	0.604
Hyper pigmentation	5 (15.6)	2 (7.4)	0.331
Superficial vein			0.780
1-3 mm	7 (21.9)	4 (14.8)	
3-5 mm	21 (65.6)	19 (70.4)	
>5 mm	4 (12.5)	4 (14.8)	
GSV			0.513
<5 mm	0 (0)	1 (3.7)	
5-10 mm	27 (84.4)	21 (77.8)	
>10 mm	5 (15.6)	5 (18.5)	

Table 1: Demographic data and patient characteristics (Total n=59).

Clinical	EV-RFA (32) n (%)	HL/VS (27) n (%)	P-value
Pain score			< 0.001*
Mean±SD	1.41±1.1	3.89±1.53	
Median (min-max)	1 (0-4)	4 (1-7)	
Ecchymosis			0.001*
no	29 (90.6)	11 (40.7)	
yes	3 (9.4)	16 (59.3)	
Numbness			0.456
no	31 (96.9)	25 (92.6)	
yes	1 (3.1)	2 (7.4)	

Table 2: Clinical results (Total n=59).

Discussion

Demographic data, consisted of age, sex, professional, clinical presentation, superficial vein diameter and GSV diameter, was similar

in both EV-RFA and HL/VS group. EV-RFA group got ecchymosis and pain significantly lower than HL/VS group. In our study, we compared inflammatory mediator in symptomatic varicose veins patient between HL/VS and EV-RFA group. Patients presented with symptomatic varicose vein, which was the indication for varicose vein surgery, were included in study. All of patients were 18 years of age or older, and were ask to consent to enroll in study. The patients with connective tissue disease, autoimmune disease, cirrhosis, end stage real disease and hematologic disease were excluded from study. Level of IL-6 and CRP increased in these patients compared to their level in normal individuals. We excluded venous ulcer, infection and recent trauma that was able to interfere inflammatory response and cytokine levels. Chronic venous ulcer appeared relate to chronic inflammatory injury secondary to many causes such as sustained venous hypertension, and extravasation of macromolecules and iron-containing red blood cells from the microcirculation. Bacterial contaminations are thought to secondarily affect poor wound healing [8]. Chronic venous ulcer was excluded because there were multifactorial causes of inflammation. Although preoperative level of CRP was a little higher in HL/VS group but preoperative IL-6 was not difference among 2 groups. There were significant rising of 24-hour postoperative level of IL-6 and CRP in both groups especially IL-6. EV-RFA created thermal injury; however HL/VS created more tissue trauma and inflammatory responses.

	EV-RFA	Venous stripping	P-value
	Median	Median	
IL-6	2.10(1.5-9.39)	2.90(1.5-23.5)	0.05
CRP	0.98(0.0-7.13)	1.8(0.14-12.45)	0.045

Table 3: Baseline of preoperative level of IL-6 and CRP.

	Median	p-value
IL-6		
EV-RFA		< 0.001
Preoperative	2.10(1.5-9.39)	
Postoperative	3.45(2.0-16.91)	
HL/VS		0.043
Preoperative	2.90(1.5-23.5)	
Postoperative	11.50(3.5-179.6)	
CRP		
EV-RFA		< 0.001
Preoperative	0.98(0.0-7.13)	
Postoperative	1.08(0.19-13.12)	
HL/VS		0.001
Preoperative	1.8(0.14-12.45)	
Postoperative	4.34(0.17-93.46)	

Table 4: Pre-operative and post-operative level of IL-6 and CRP.

Rasmussen et al published four-arm RCT compared results of HL/VS, EVLA and EV-RFA and foam sclerotherapy. They found that postoperative pain was significantly lower and return to normal activity time was significantly shorter in EV-RFA and foam sclerotherapy group com- pared to HL/VS and EVLA group. However efficiency of treatment was not significantly difference among 4 modalities [9].

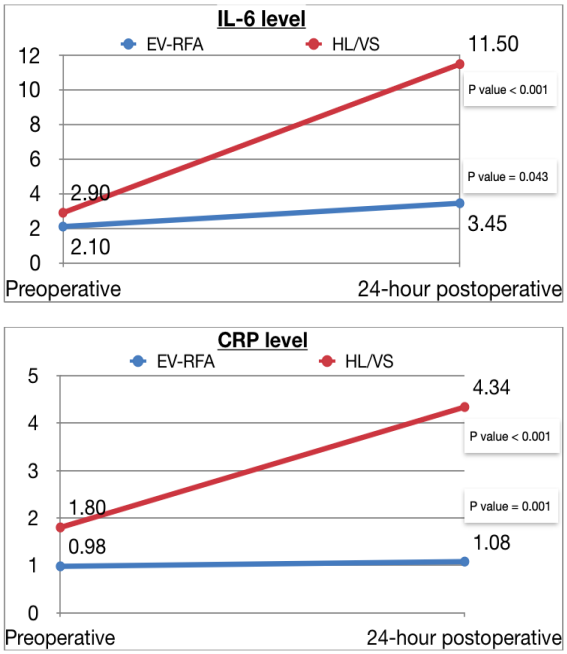

Figure 1: Pre-operative and post-operative level of IL-6 and CRP represented by line graph.

	EV-RFA	HL/VS	p-value
	Median	Median	
IL-6	1.15(-3.44-12.2)	8.61(-1.1-174.8)	<0.001
CRP	0.11(-1.11-11.25)	0.7(-3.49-86.98)	0.045

Table 5: Comparison of pre-operative and post-operative inflammatory response between EV-RFA and venous stripping.

Kheirelseid et al reported meta-analysis compared results between EV-RFA, EVLA, foam sclerotherapy and conventional HL/VS and found that there was no significant difference in recurrent rate, re-intervention, neovascularization, and GSV recanalization among 4 groups [12]. Rasmussen published a four arm RCT comparing HL/VS with EVLA, RFA, and foam sclerotherapy. The post-operative average pain scores at 10 days were significantly lower in the groups treated with EV-RFA and foam sclerotherapy compared with HL/VS and EVLA, with a shorter time to resumption of normal activities and work. The efficiency of the four modalities was not significantly different [9]. Common adverse effects including ecchymosis (5.8%), paresthesia (3.4%), hyperpigmentation (2.4%), erythema (2.0%), hematoma (1.4%) and phlebitis (1%). Most of complications subsided within the first week [13]. Recent studies reported incidence of thrombotic events after EV-RFA and EVLA, called Endovenous Heat-Induced Thrombosis (EHIT). Systematic review and meta-analysis reported by Healy at al, including 52 published studies, show that there was rate of DVT and Pulmonary Embolism (PE) was 0.3% and 0.1%, respectively [14]. Risk factors of EHIT were large vein size (11.0+/-4.3 mm) and concomitant sclerotherapy [15].

In this study, rate of numbness was comparable to other studies (3.1% VS 3.4%) al- though rate of ecchymosis was higher (9.4% VS

5.8%) [13]. However, rate of ecchymosis, and postoperative pain were lower in EV-RFA group compared to HL/VS group. There was no DVT and PE reported in our study.

CVI is a common condition with a wide spectrum of clinical presentations. Structural and functional alterations in healthy veins lead to symptoms and signs usually seen in CVI. There were published studies described pathophysiologies of CVI in last 2 decades, recently, many studies focused on the role of inflammation and subsequent localized endothelial activation and dysfunction. There was reducing in synthesis of anti-inflammatory agents, and enhancing the expression of proinflammatory and prothrombotic molecules [16-19]. Venous reflux was thought to be the cause of venous hypertension [20]. Its consequence was the reduction of shear stress, a key regulator of endothelial activation state [20,21], which promotes pathological change of venous wall and valve [7,22,23]. Shear stress reduces activation triggers of ECs and leukocytes, enhance expression of adhesion molecules and inflammatory cells infiltration into venous wall and leaflets. This established an environment promoted local inflammation [7,23]. Changing in normal signaling of ECs through different pathways induced production of proinflammatory mediators including IL-6, IL1, TNF-α, IFN, IL-8, MCP-1. On the other hand, endothelial cells promoted releasing of agents that stimulate thrombosis such as Von willebrand factor (Vwf) [24], plasminogen activator inhibitor-1 [25], and factor VIII [26], as well as inflammatory cytokine such as C Reactive Protein (CRP) [24] and Interleukin-6 (IL-6) [24]. These agents are biomarkers of endothelial dysfunction, and their levels correlated with a higher cardiovascular risk [27]. It was described that normal venous endothelium was able to become dysfunctional, and release prothrombotic and proinflammatory factors when exposed to increased endoluminal pressure [28]. Since CVI is a condition characterized by a sustained increasing in venous pressure, stasis or reversal of blood flow affected vessels; this may promote a prothrombotic state of endothelium. Recent study showed that releasing of prothrombotic agents from activated endothelium may explain correlation established between varicose veins and DVT [29].

This study focused on 2 inflammatory mediators, IL-6 and CRP. IL-6 was produced by monocyte, macrophages, helper T-cells, ECs, VSMCs, fibroblasts and stromal cells that effect to other cells in various functions. It effected to activate B-cell in transformation to plasma cell, and activated plasma cell in antibody secretion. It was a key role for acute phase of inflammatory response, and also effected to VSMC and endothelial cell in proliferation and proatherogenic effect [30].

The relationship of IL-6 and varicose vein had been studied by Christopher R. Lattimer [30] et al., compared serum inflammatory biomarker levels from varicose veins and antecubital vein of varicose veins patient and from leg vein and antecubital vein of healthy controls. They found that the most relevant inflammatory biomarkers in CVI were IL-6, IL-8, and MCP-1. IL-6 concentration was significantly greater in varicose vein compare to antecubital vein and healthy controls. This suggested that IL-6 released from the leg and diluted once it went to arm. Finding that IL-6 was elevated dominantly in the legs of varicose veins patients may explained that IL-6 was not directly related to systemic response CVI and may represent normal physiological response to higher venous pressures, typically in the gaiter region. This may reflected the higher sensitivity of IL-6 to local increased venous pressure contrast to IL-8 and MCP-1.

However, IL-8 and MCP-1 may be more specific for systemic inflammation in CVI. Age and disease severity were shown to correlate significantly with increases in IL-6 concentration [31].

CRP is one of the acute-phase proteins. CRP is predominantly secreted by the liver at 4- 6 hours after stimulation. It duplicates every 8 hours, and peaks within 36 to 50 hours. CRP has a plasma half-life of 19 hours, and even after a single stimulus, as in a trauma or surgery, it may take several days to return to the baselines [32]. There were 3 types of CRP assays consists of Conventional CRP, High sensitivity CRP (hsCRP) and Cardiac C-Reactive Protein (cCRP).

There were diversity of clinical use example hsCRP was detected lower level of CRP that bring to use for healthy individuals, cCRP was used for identify cardiovascular risk and conventional CRP assays were indicated for use for evaluation of infection, tissue injury, and inflammatory disorders. CRP assays provide information for the diagnosis, therapy, and monitoring of inflammatory diseases [33]. CRP is a more sensitive and more reliable indicator of acute inflammatory processes than the Erythrocyte Sedimentation Rate (ESR) and leukocyte count. Blood CRP levels rise more rapidly than ESR, and after the disease has subsided CRP values rapidly fall and reach the reference interval often days before ESR has returned to normal. Thus, CRP assays was applied to this study [34,35].

There is a correlation between increasing levels of IL-6 during inflammation and increasing levels of CRP [36], with IL-6 inducing the CRP gene [37]. CRP gene was protein from pentraxin family that encode to serum level of CRP , There were many studies that focus association of CRP gene variant to CRP level example that the minor alleles of rs1205 and rs1800947 are associated with lower CRP levels and that the minor allele of rs1130864 is associated with higher CRP levels, There were many studies that give priority association of variant type of CRP gene and many disease especially cardiovascular disease, stroke, hypertension and metabolic disease [38-40]. On the other hand, When CRP levels become elevated in atheroma, this leads to the induction of IL-6 by macrophages indicating that CRP may have a direct effect on IL-6 release [41].

CRP has half life of 19 hours and gets peak level at 36-50 hours [42], whereas IL-6 has half life of 2-3 hours and gets peak level at 12-18 hours [43]. Because half life of CRP is longer than IL-6, 24-hr postoperative level of CRP increased less than IL-6. However both CRP and IL- 6 level significantly increased 24 hour after surgery.

The inflammatory response (postoperative serum level - preoperative serum level of IL- 6 and CRP) between EV-RFA group and HL/VS group represented both of inflammatory cytokine could be predicted inflammatory response of both operation but significantly increasing in serum level of IL-6 due to shorter half life of this cytokine. In addition the little increasing of both inflammatory cytokine levels in EV-RFA group that implied minimal inflammatory response in this operation and hardly interfere inflammatory process in human.

Selection bias is main limitation of this study. There was no randomization of patients and no well control of postoperative program. Further well designed RCT need to confirm advantage of EV-RFA compare to other modalities in aspect of inflammatory response. However cost-effectiveness of each procedure is interesting issue to be concerned.

Conclusion

EV-RFA established lower postoperative pain and rate of ecchymosis compared to HL/VS. 24-hour postoperative level of CRP and IL-6 were also increased lower in EV-RFA group compared to HL/VS group. This result evidenced lower rate of tissue trauma after EV-RFA.

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