Asian Journal of Surgery (2015) xx, 1–6

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-asianjournalsurgery.com

ORIGINAL ARTICLE

Quality of life after great saphenous vein ablation in Thai patients with great saphenous vein reflux

Boonying Siribumrungwong [a,b,*], Pinit Noorit [c,*], Chumpon Wilasrusmee [d], Yot Teerawattananon [e], Ammarin Thakkinstian [f]

[a] *Department of Surgery, Faculty of Medicine, Thammasat University Hospital, Thammasat University, Pathum Thani, Thailand*
[b] *Center of Excellence in Applied Epidemiology, Faculty of Medicine, Thammasat University Hospital, Thammasat University, Pathum Thani, Thailand*
[c] *Department of Surgery, Chonburi Hospital, Chonburi, Thailand*
[d] *Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*
[e] *Health Intervention and Technology Assessment Program (HITAP), Department of Health, Ministry of Public Health, Nonthaburi, Thailand*
[f] *Section for Clinical Epidemiology and Biostatistics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*

Received 18 August 2015; received in revised form 21 September 2015; accepted 1 October 2015

KEYWORDS
endovenous procedures;
quality of life;
utility;
varicose vein

Summary *Background/Objective:* To determine the quality of life (QoL) in Thais after intervention for great saphenous vein (GSV) reflux.
Methods: Patients with Clinical Etiologic Anatomic Pathophysiologic classes 2 and 3 were enrolled in this study. QoL was measured using the EuroQol descriptive system (EQ-5D) questionnaire, and patients chose to receive either endovenous treatment or surgery after consulting with their surgeons. The QoL before the intervention, at 1 week, and at 1 month after the intervention were evaluated. Patients who reported "no problem" in each domain of the EQ-5D questionnaire before and 1 month after the intervention were compared. Utility gain was estimated from the questionnaire and compared between clinical classes. The proportion of worsening QoL at 1 week after the intervention was compared between patients receiving endovenous procedures and surgery.

Conflicts of interest: All contributing authors declare no conflicts of interest.

* Corresponding authors. Boonying Siribumrungwong, Department of Surgery, Faculty of Medicine, Thammasat University Hospital, Thammasat University, 95 Moo 8, Khlong Nueng, Khlong Luang, Pathum Thani 12120, Thailand; Pinit Noorit, Department of Surgery, Chonburi Hospital, Chonburi, Thailand.
E-mail address: boonying22@gmail.com (B. Siribumrungwong).

http://dx.doi.org/10.1016/j.asjsur.2015.10.004

Please cite this article in press as: Siribumrungwong B, et al., Quality of life after great saphenous vein ablation in Thai patients with great saphenous vein reflux, Asian Journal of Surgery (2015), http://dx.doi.org/10.1016/j.asjsur.2015.10.004

Results: A total of 83 patients—56 received endovenous procedures [23 received ultrasound-guided foam sclerotherapy (UGFS) and 33 received radiofrequency ablation (RFA)] and 27 received surgery—were enrolled. QoLs were significantly better in all domains after the intervention: pain/discomfort (58%), mobility (42%), anxiety/depression (38%), usual activities (19%), and self-care (9%). Utility gain was 0.255 (95% confidence interval: 0.197—0.313) and higher in class 3. At 1 week after the intervention, surgery had significantly higher patients with worse mobility scores. Among endovenous procedures, UGFS had higher patients with worse pain/discomfort scores than RFA at 1 week after the intervention (16% vs. 0%, $p = 0.025$).

Conclusion: GSV ablation for GSV reflux in Thai patients with CEAP C2 and C3 categories significantly improves both physical and mental QoL; patients who received endovenous procedures were found to have better early physical QoL.

1. Introduction

Varicose veins are common with prevalence rates of 10—15% in men and 20—25% in women[1] with an increasing prevalence with advancing age.[2] This has led to significant health spending.[3] The great saphenous vein (GSV) is the most common site of venous reflux and the standard treatment is ablation of this vein. Important outcomes after GSV ablation are anatomical occlusion, abolishment of reflux in the treated vein, good function, and good quality of life (QoL) for treated patients.[4]

Assessing patient's QoL is important in patient-centered approach because QoL measures patient's perceptions and concerns. QoL is also used for estimating utility scores, which are used to estimate quality-adjusted life years gained for health technology assessments to determine cost effectiveness of interventions.[5—7] Data from European countries have demonstrated improvement in patient's QoL using both generic[8,9] and disease-specific QoL questionnaires[10,11] after GSV ablation for GSV incompetence in patients with simple varicose veins and more severe disease such as lipodermatosclerosis and venous ulceration.

Recent guidelines recommend endovenous thermal ablation over open surgery because endovenous ablation is associated with less pain and morbidity with shorter times to recovery.[4] In terms of post-treatment QoL, a recent systematic review and meta-analysis[12] found better QoL at 1—2 weeks in favor of endovenous procedures over surgery but QoL thereafter was similar.

GSV-related QoL data in Asians are limited and there are no data from Thailand. Currently, all patients with GSV reflux treated by standard surgery and ultrasound-guided foam sclerotherapy (UGFS) are reimbursable by the Thai health care system irrespective of the Clinical Etiologic Anatomic Pathophysiologic (CEAP) clinical class and symptoms; however, those treated by radiofrequency ablation (RFA) are not eligible for reimbursement. A previous cost analysis for health economic evaluation in Thailand indicated that RFA had procedure-related costs of 26,417 Thai Baht, compared with 5556 Thai Baht and 5096 Thai Baht for UGFS and surgery, respectively.[13] Treatment for patients in CEAP clinical classes 4—6 clearly demonstrated significant QoL gain,[14] but treatment benefit in patients with less severe disease (clinical classes 2 or 3) was still questionable. Therefore, this study was conducted to determine QoL after intervention in CEAP clinical classes 2 and 3 patients with GSV reflux who seek medical attention in Thailand and also compared QoL after endovenous procedures and surgery.

2. Methods

The study was conducted at two university hospitals (Thammasat University Hospital, Pathum Thani, Thailand and Ramathibodi Hospital, Bangkok, Thailand) and one provincial hospital (Chonburi Hospital, Chonburi, Thailand) and was approved by the Ethics Committee Boards of all three study hospitals. All patients were informed and signed consents before the intervention. Patients were treated by a general and vascular surgeon who had experience working in this area for 5 years. Eligible patients were those with CEAP clinical classes 2 or 3 with a documented history of isolated unilateral GSV reflux, diagnosed by duplex scan, who underwent any one of the these procedures: RFA, UGFS, or surgery (high ligation and striping). The study was conducted between October 2011 and February 2013. Exclusion criteria were any one of the following: (1) history of deep vein thrombosis, (2) history of superficial thrombophlebitis, (3) peripheral arterial occlusive disease, and (4) pregnancy.

Consecutive patients who met the eligibility criteria and treated at the clinics of the participating surgeons were invited to participate in the study. The benefit and cost of each intervention was explained to the patients by the participating surgeons and then the patients were allowed to select an intervention method. RFA (Covidien ClosureFast, San Jose, CA, USA) was performed with tumescent anesthesia. The ablation was performed with incremental steps of 7 cm starting from 2—3 cm distal to the saphenofemoral junction to the knee level. The UGFS was performed concomitantly with saphenofemoral ligation by injecting foam sclerosant (Tessari's method; 1 cm^3 of 1% aethoxysklerol mixed with 3 cm^3 of air) of about 6—8 cm^3 to the GSV just below the knee level. Surgery was performed

Please cite this article in press as: Siribumrungwong B, et al., Quality of life after great saphenous vein ablation in Thai patients with great saphenous vein reflux, Asian Journal of Surgery (2015), http://dx.doi.org/10.1016/j.asjsur.2015.10.004

with saphenofemoral ligation with invagination stripping to the GSV just below the knee.

Baseline characteristics of patients including age, sex, CEAP clinical classification, and venous clinical severity scores (VCSSs) were collected on a standard case record form. The QoL used was the generic EuroQol descriptive system (EQ-5D) questionnaire. This self-administered questionnaire has five domains, namely, mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain was scored as follows: 1 (no problem), 2 (some problems), or 3 (severe problems). The questionnaire was administered to patients before the intervention, at 1 week, and at 1 month after the intervention. The translated (into Thai) version of the EQ-5D questionnaire has already been validated and widely used in Thailand.[5] The health state preferences measured by the EQ-5D questionnaire were then converted into utility scores using the preference weight for the Thai population by subtracting the relevant coefficients of results of each domain from 1.0.[5,15] A value close to 1.0 indicated "good health" whereas a value close to 0 implied "worst health condition."

Baseline continuous data were described using mean (SD) if they were normal distribution; otherwise, median [interquartile range (IQR)] was used. Frequency and percentage were used to describe categorical data.

Changes in QoL over time were assessed by comparing QoL score before and after the intervention. Changes were then graded as worsening if the preintervention score was higher than the postintervention score; otherwise, it was graded as equal/better improvement. The proportion of worsening QoL at 1 week after the intervention was then estimated and compared between the intervention groups. In addition, the proportion of patients reporting no problem before and 1 month after the intervention was also reported.

Changes in VCSS were calculated by subtracting preintervention scores from postintervention scores, whereas utility gain was calculated by subtracting postintervention scores from preintervention scores. Data were then reported using median (IQR).

Data were then compared between the intervention groups as follows: one-way analysis of variance was applied to compare means if data were normally distributed; otherwise, Kruskal–Wallis test was applied to compare medians. Chi-square or Fisher's exact test was used to compare proportions between the intervention groups. McNemar's Chi-square test was used to compare the proportion of patients reporting "no problem" before and after the intervention (using preintervention and postintervention scores). A p value <0.05 was considered to be statistically significant. Analysis was performed using STATA version 13.0 (StataCorp, College Station, TX, USA).

3. Results

Eighty-three patients were enrolled. All completed the preintervention questionnaires. Seventy-six (92%) and 64 (77%) completed postoperative questionnaires at 1 week and 1 month, respectively. Among the 83 patients, 56 (67%) had undergone endovenous procedures (i.e., 23 UGFS and 33 RFA) and 27 (33%) had received open surgery. Baseline characteristics of the patients were evaluated and they were not statistically different between the three groups, except income/mo, which was higher in the RFA group than in the other two groups (Table 1). The proportion of CEAP classification C3 was highest in the open surgery (81%) group, compared with the RFA (65%) and UGFS (53%) groups. The VCSS was not significantly different ($p = 0.442$) between the two groups with median values of 6, 5, and 6 for RFA, UGFS, and surgery, respectively. In addition, preintervention EQ-5D questionnaire responses were not significantly different between endovenous procedures and surgery (Table 2).

3.1. QoL changes

3.1.1. Preintervention versus 1-month postintervention changes

The proportion of all patients who reported "no problem" was significantly higher in all five domains after the intervention, compared with that before the intervention (Figure 1). Fifty-eight percent of patients had better QoL in the pain/discomfort domain, followed by mobility (42%), anxiety/depression (38%), usual activities (19%), and self-care (9%) after the intervention.

Table 1 Baseline characteristics between endovenous and surgery groups.

Variables	RFA	UGFS	Surgery	p
	$N = 33$	$N = 23$	$N = 27$	
Age (y)	55 (9.9)	49 (13.4)	52 (14.8)	0.25
Income/mo, Thai Baht	30,000 (20,000–41,000)	10,480 (8000–20,000)	10,000 (3500–15,000)	<0.001
GSV diameter (cm)	0.79 (0.14)	0.69 (0.22)	0.85 (0.36)	0.39
CEAP C classification				0.12
C2	11 (35)	9 (47)	5 (19)	
C3	20 (65)	10 (53)	22 (81)	
VCSS	6 (5–7)	5 (3–6)	6 (4–8)	0.44

Data are presented as n (%), mean (standard deviation), or median (interquartile range).
CEAP = Clinical Etiologic Anatomic Pathophysiologic; GSV = greater saphenous vein; RFA = radiofrequency ablation; UGFS = ultrasound-guided foam sclerotherapy; VCSS = Venous Clinical Severity Scores.

Please cite this article in press as: Siribumrungwong B, et al., Quality of life after great saphenous vein ablation in Thai patients with great saphenous vein reflux, Asian Journal of Surgery (2015), http://dx.doi.org/10.1016/j.asjsur.2015.10.004

Table 2 Comparison of preintervention EQ-5D between endovenous procedures and surgery.

EQ-5D	Endovenous procedures $n = 54$	Surgery $n = 27$	p
Mobility			
No problem	27 (50)	10 (37)	0.35
Some problems	27 (50)	17 (63)	
Severe problems	0 (0)	0 (0)	
Self-care			
No problem	48 (89)	22 (81)	0.49
Some problems	6 (11)	5 (19)	
Severe problems	0 (0)	0 (0)	
Usual activities			
No problem	39 (72)	21 (78)	0.63
Some problems	14 (26)	5 (19)	
Severe problems	1 (2)	1 (4)	
Pain/discomfort			
No problem	14 (26)	7 (26)	0.94
Some problems	34 (63)	16 (59)	
Severe problems	6 (11)	4 (15)	
Anxiety/depression			
No problem	27 (50)	17 (63)	0.57
Some problems	24 (44)	9 (33)	
Severe problems	3 (6)	1 (4)	

Data are presented as *n* (%).
EQ-5D = EuroQol descriptive system.

3.1.2. Postintervention EQ-5D changes by intervention

After receiving intervention, mobility was significantly worse in the surgical group compared with the endovenous groups (i.e., 22% vs. 6%, $p = 0.038$) at 1 week after the intervention. There were no significant differences in the other four domains (Table 3). Among endovenous interventions, only pain/discomfort was significantly worse in patients who received UGFS compared those who received RFA (16% vs. 0%, $p = 0.025$) at 1 week after the intervention. The others were not significantly different at both 1 week and 1 month after the intervention (data not shown).

3.2. VCSS, utility gain, and time to return to work

Health utility scores were, respectively, 0.617 and 0.888 before and after the intervention at 1 month in all patients, yielding significant utility gain of 0.255 [95% confidence interval (CI): 0.197—0.313]. The utility gain was also significantly higher in the CEAP C3 category than in the C2 category—0.319 (95% CI: 0.254—0.386) versus 0.122 (95% CI: 0.025—0.219), respectively ($p = 0.001$). Among endovenous procedures, the health utility scores were 0.629 and 0.874 before and 1 month after the intervention, which yielded utility gain of 0.225 (95% CI: 0.154—0.296).

Changes in VCSS for individual patients were calculated by subtracting preintervention VCSS from postintervention VCSS at each time (i.e., 1 week and 1 month). The change was then averaged and compared across the three intervention groups (Table 4). Although the mean VCSS change was higher in the RFA and UGFS groups than in the open surgery group for both periods, it was not statically different. Seven (21%), three (13%), and five (19%) patients who received RFA, UGFS, and surgery, respectively, did not gain utility postoperatively at 1 month ($p = 0.73$). Median times to return to work were 2.5 day (IQR 2—4), 1 day (IQR 1—5), and 5 day (IQR 3—8.5) for RFA, UGFS, and surgery,

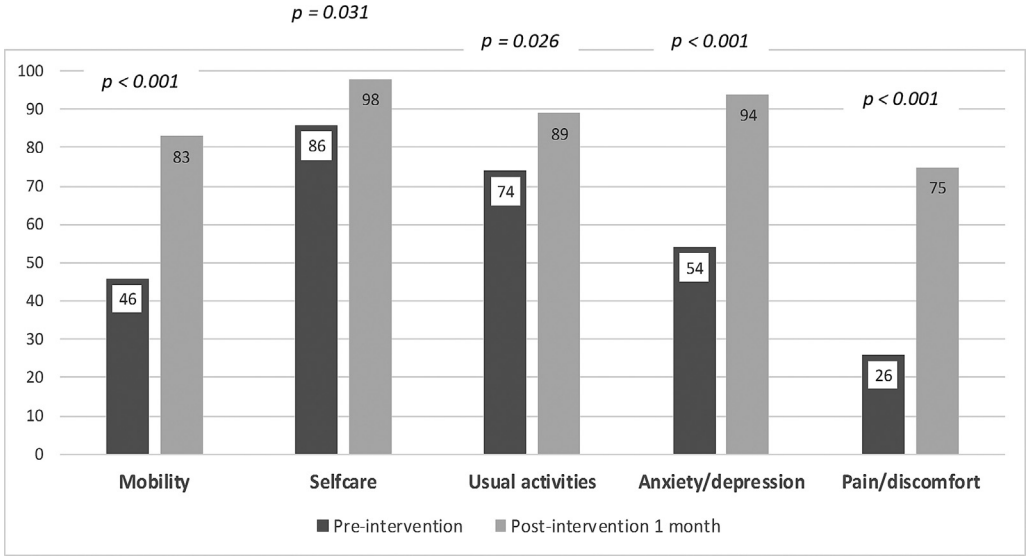

Figure 1 Comparison of patient reporting no problems in each domain of the EuroQol descriptive system (EQ-5D) questionnaires preintervention and at 1 month postintervention. The Y axis shows the proportion of patients (%); the X axis shows the EQ-5D domains. The *p* values were obtained using McNemar's chi-square test.

Please cite this article in press as: Siribumrungwong B, et al., Quality of life after great saphenous vein ablation in Thai patients with great saphenous vein reflux, Asian Journal of Surgery (2015), http://dx.doi.org/10.1016/j.asjsur.2015.10.004

Table 3 Comparison of EQ-5D at 1 week and 1 month postinterventions between endovenous procedures and surgery.

EQ-5D	1 wk Postintervention			1-mo Postintervention		
	Endovenous procedures $n = 49$	Surgery $n = 27$	p	Endovenous procedures $n = 40$	Surgery $n = 24$	p
Mobility						
Better or equal	46 (94)	21 (78)	0.038	39 (98)	24 (100)	>0.99
Worse	3 (6)	6 (22)		1 (2)	0 (0)	
Self-care						
Better or equal	40 (82)	17 (63)	0.072	40 (100)	24 (100)	—
Worse	9 (18)	10 (37)		0 (0)	0 (0)	
Usual activities						
Better or equal	42 (86)	19 (70)	0.108	38 (95)	23 (96)	>0.99
Worse	7 (14)	8 (30)		2 (5)	1 (4)	
Pain/discomfort						
Better or equal	46 (94)	24 (89)	0.440	36 (90)	23 (96)	0.64
Worse	3 (6)	3 (11)		4 (10)	1 (4)	
Anxiety/depression						
Better or equal	43 (88)	26 (96)	0.410	39 (98)	24 (100)	>0.99
Worse	6 (12)	1 (4)		1 (2)	0 (0)	

Data are presented as n (%).

respectively, with significantly shorter time after UGFS compared with surgery ($p = 0.02$).

4. Discussion

Our results demonstrate significant improvement in QoL in all five domains of the EQ-5D questionnaires after treatment in Thai patients with GSV reflux. Significant improvement was seen in the "pain/discomfort" domain followed by improvement in the mobility, anxiety/depression, usual activities, and self-care domains in descending order. Utility gain was significantly better after intervention in the CEAP category C3 than C2. Patients in the endovenous groups had better QoL in the mobility domain than those who received surgery at 1 week after the respective procedures.

Our results were similar to those reported by Nesbitt et al[9] who also used the EQ-5D questionnaire and also with studies that measured QoL using other type of questionnaires (i.e., Short Form-36), which found improvements in bodily pain, physical function,[8] and mental health after GSV ablation.[16] These data affirm the negative effect of GSV reflux on both physical and mental QoL.

In our study, surgery had a significantly worse QoL score in the mobility domain and showed a trend toward worsening self-care compared with endovenous procedures at 1 week after the intervention. This probably explains why patients in the endovenous groups can return to normal activities and work faster than those who received surgery.[12,17] However, we could not identify any difference in the pain/discomfort domain between types of intervention at 1 week after the intervention, which is in contrast to results from a randomized control trial from Denmark,[17] which found that bodily pain, physical function, and role were significantly better in patients who received RFA and UGFS than surgery at 3 days postoperatively. However, this apparent advantage was not present at 1 month, suggesting that RFA and UGFS only had a limited impact on patients.

The utility scores in our study demonstrated significant improvement at 1 month after treatment and this was more marked in patients with more severe disease (i.e., CEAP C3). Utility gain in our study was significantly higher when

Table 4 Comparison of changes in Venous Clinical Severity Scores and utility gain between types of intervention.[a]

Time measured postintervention	Overall $n = 83$	RFA $n = 33$	UGFS $n = 23$	Surgery $n = 27$	p*
At 1 wk					
VCSS	3 (2—4)	3 (3—4)	2 (2—4)	2 (2—4)	0.19
Utility gain	0.12 (−0.46—0.31)	0.18 (0—0.31)	0.05 (−0.12—0.16)	0.08 (−0.12—0.31)	0.16
At 1 mo					
VCSS	4 (2.5—5)	4 (3—5)	4 (2—5)	3 (2—5)	0.43
Utility gain	0.27 (0.05—0.39)	0.23 (0—0.37)	0.19 (0.05—0.39)	0.30 (0.09—0.41)	0.08

Data are presented as median (interquartile range).
RFA = radiofrequency ablation; UGFS = ultrasound-guided foam sclerotherapy; VCSS = Venous Clinical Severity Scores.
* Comparison between three types of intervention.
[a] Changes of VCSS = VCSS at preintervention − VCSS at postintervention.

Please cite this article in press as: Siribumrungwong B, et al., Quality of life after great saphenous vein ablation in Thai patients with great saphenous vein reflux, Asian Journal of Surgery (2015), http://dx.doi.org/10.1016/j.asjsur.2015.10.004

compared with that reported by Nesbitt et al[9] [0.255 (95% CI: 0.197–0.313) versus 0.094 (95% CI: 0.087–0.102); $p < 0.001$]. This might be due to increased proportions of severe spectrum of disease in our studied population (68% CEAP C3) or treating asymptomatic patients. Unfortunately, Nesbitt et al[9] did not report severity of disease. Nevertheless, caution should be exercised when comparing health utility gain between different countries because of different socioeconomic and cultural backgrounds.

With an aging population in Thailand, we can expect to see more patients with GSV reflux and this will have an increasing impact on the health care system and health budget. Therefore, an economic assessment of interventions will be important to determine which interventions are the most cost effective for Thais.[18]

Our study had some limitations. The total number of patients was small with some attrition bias (23% at 1 month), causing less power to detect significant difference of QoL between interventions. In addition, representativeness of studied patients might be not good. Patients had selected interventions by themselves based on information provided by their surgeons. Thus, selection bias could not be avoided. The QoL analyzed in each domain separately might inflate the effect of differences with consequent risk of Type I error. We used only EQ-5D questionnaire, which is a generic QoL questionnaire that might not capture specific aspects of venous disease. The reason we chose this questionnaire is because there is no other validated disease-specific QoL questionnaire in Thai language. Thus, there is a need to validate more disease-specific measurement tools in Thai language.

5. Conclusion

GSV ablation for GSV reflux in Thai patients with CEAP C2 and C3 categories significantly improves both physical and mental QoL; patients who received endovenous procedures were found to have better early physical QoL.

Acknowledgments

We would like to thank Dr Bob Taylor for editing our manuscript.

References

1. Callam MJ. Epidemiology of varicose veins. *Br J Surg*. 1994;81:167–173.
2. Clark A, Harvey I, Fowkes FG. Epidemiology and risk factors for varicose veins among older people: cross-sectional population study in the UK. *Phlebology*. 2010;25:236–240.
3. Ruckley CV. Socioeconomic impact of chronic venous insufficiency and leg ulcers. *Angiology*. 1997;48:67–69.
4. Gloviczki P, Comerota AJ, Dalsing MC, et al. The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. *J Vasc Surg*. 2011;53:2S–48S.
5. Sakthong P. Measurement of clinical-effect: utility. *J Med Assoc Thai*. 2008;91:S43–S52.
6. Rawlins MD, Culyer AJ. National Institute for Clinical Excellence and its value judgments. *BMJ*. 2004;329:224–227.
7. Mohara A, Youngkong S, Velasco RP, et al. Using health technology assessment for informing coverage decisions in Thailand. *J Comp Eff Res*. 2012;1:137–146.
8. Durkin MT, Turton EP, Wijesinghe LD, Scott DJ, Berridge DC. Long saphenous vein stripping and quality of life—a randomised trial. *Eur J Vasc Endovasc Surg*. 2001;21:545–549.
9. Nesbitt C, Wilson WR, Lees TA, Stansby G. Interpretation of patient-reported outcome measures for varicose vein surgery. *Phlebology*. 2012;27:173–178.
10. Darvall KA, Sam RC, Bate GR, Silverman SH, Adam DJ, Bradbury AW. Changes in health-related quality of life after ultrasound-guided foam sclerotherapy for great and small saphenous varicose veins. *J Vasc Surg*. 2010;51:913–920.
11. MacKenzie RK, Paisley A, Allan PL, Lee AJ, Ruckley CV, Bradbury AW. The effect of long saphenous vein stripping on quality of life. *J Vasc Surg*. 2002;35:1197–1203.
12. Siribumrungwong B, Noorit P, Wilasrusmee C, Attia J, Thakkinstian A. A systematic review and meta-analysis of randomised controlled trials comparing endovenous ablation and surgical intervention in patients with varicose vein. *Eur J Vasc Endovasc Surg*. 2012;44:214–223.
13. Siribumrungwong B, Noorit P, Wilasrusmee C, Leelahavarong P, Thakkinstian A, Teerawattananon Y. Cost-utility analysis of great saphenous vein ablation with radiofrequency, foam and surgery in the emerging health-care setting of Thailand. *Phlebology*. September 4, 2015. http://dx.doi.org/10.1177/0268355515604258.
14. González-Consuegra RV, Verdú J. Quality of life in people with venous leg ulcers: an integrative review. *J Adv Nurs*. 2011;67:926–944.
15. Tongsiri S, Cairns J. Estimating population-based values for EQ-5D health states in Thailand. *Value Health*. 2011;14:1142–1145.
16. Smith JJ, Garratt AM, Guest M, Greenhalgh RM, Davies AH. Evaluating and improving health-related quality of life in patients with varicose veins. *J Vasc Surg*. 1999;30:710–719.
17. Rasmussen LH, Lawaetz M, Bjoern L, Vennits B, Blemings A, Eklof B. Randomized clinical trial comparing endovenous laser ablation, radiofrequency ablation, foam sclerotherapy and surgical stripping for great saphenous varicose veins. *Br J Surg*. 2011;98:1079–1087.
18. Marsden G, Wonderling D. Cost-effectiveness analysis: role and implications. *Phlebology*. 2013;28:135–140.