media were harvested. TGF-β secretion in response to stress was determined by ELISA.

Results: No difference was noted in the number of TGF-βRI-positive and TGF-βRII-positive cells between a-fbs and nn-fbs; however, TGF-βRII density was reduced 40% as determined by MFI in a-fbs compared with nn-fbs (151 ± 25 vs 51 ± 27, n = 6; $P = .03$). In healthy commercial nn-fbs subjected to constant mechanical stress for 24 hours, there was no change in TGF-β secretion compared with the static (control) nn-fbs. However, there was a fourfold increase in TGF-β secretion (284 ± 133 vs 1076 ± 238 pg/mL, n = 4; $P = 0.03$) in a-fbs exposed to mechanical stress compared with their control.

Conclusions: Previous studies investigating venous ulcer fibroblasts have shown alterations of TGF- β and their receptors. This study reveals that these alterations may occur as part of the normal aging process as demonstrated by baseline differences seen between nn-fbs and a-fbs. Furthermore, a-fbs should be considered for use as controls because they possess normal age-specific characteristics that may more closely reflect venous disease in the adult population.

Post-Thrombotic Vein Wall Remodeling: Preliminary Findings

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Background: Post-thrombotic syndrome (PTS) is characterized by a fibrotic vein injury after deep vein thrombosis (DVT), resulting in a less compliant vein wall. We sought to quantify the change in vein wall thickness and to determine if vein wall damage, defined as wall thickening, is worsened in patients when DVT fails to resolve by 6 months, and also whether there were differences in blood or plasma levels of proteins associated with tissue remodeling.

Methods: Patients presenting with suspected lower extremity DVT were evaluated. Ultrasound imaging of the lower extremity venous system was performed, and blood was collected. Patients with DVT received repeat evaluation with blood draw and ultrasound imaging at 6 months. DVT resolution was assessed using ultrasound examination. The thickness of the vein wall was quantified by ultrasound imaging in each segment affected by thrombus, and a contralateral, unaffected vein wall served as a control. Messenger RNA was extracted from whole blood using the PAXgene system, and serum proteins were analyzed using enzyme-linked immunosorbent assay (ELISA). Analysis of variance or *t* tests were used. $P < .05$ was significant.

Results: Thirty patients (10 with DVT resolution at 6 months, 10 with persistent thrombus, and 10 healthy controls) were compared. Resolving and nonresolving DVT were both associated with 1.5- to 1.8-fold increased vein wall thickness at 6 months (n = 10-12; $P = .008$) compared with nonaffected vein wall segments. However, the thickness of the affected segments was 1.4-fold greater in patients who had total resolution of the DVT by 6 months than in patients who had persistent chronic thrombus 6 months after presentation (n = 10-12; $P = .01$,). There was a four- to fivefold increased level of MMP-9 in all thrombosed groups compared with controls (n = 5; $P < .05$). Toll-like receptor-9 (TLR-9) expression was threefold less than in controls (n = 5; $P < .05$). There were no statistically significant differences in the levels of associated factors such as D-dimer, *P*-selectin, or inflammatory and remodeling markers such as SLC or matrix metalloproteinase (MMP)-2 by ELISA. There were no significant differences in the gene expression of C-reactive protein, MMP-2, MMP-9, or TLR-4.

Conclusions: This preliminary study suggests ongoing vein wall remodeling after DVT. At 6 months, the vein wall is markedly thickened, but this change is independent of thrombus resolution and is associated with elevated MMP-9 but not other inflammatory markers. This suggests that the vein wall damage is initiated early after thrombus formation and persists even in the presence of total resolution.

Development of a Questionnaire to Evaluate the Burden of Chronic Venous Disease in Daily Life

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Background: In a difficult economic context, the burden of chronic diseases is becoming a greater concern for public health authorities. Health care professionals and institutions need an evaluation tool to assess objectively the burden of chronic venous disorders and its consequences. This study is a very preliminary approach.

Methods: A questionnaire was developed according to a strict methodologic process to guarantee its credibility and reliability. A literature review and face-to-face interviews enabled the identification of 66 items linked to the pathology. Items were reduced to 36 after evaluation and suppression of redundant, nonspecific, and nonsensitive items.

Results: Exploratory evaluations have shown that the concept of burden could be structured around six aspects: pain, daily life, family and personal relationships, work, psychologic effect, and treatment by a general practitioner. For a complete evaluation of the burden, evaluation of these six aspects was complemented with three visual analog scales (VAS): psychological, physical, and living with the disease. The Assessment of Burden in Chronic–Venous (ABC-V) Disorders questionnaire was administered to individuals consulting spontaneously for CVD with a phlebologist, who confirmed the CVD. Eight centers throughout France recruited 328 individuals: 82.7% were women (average age, 54.6 ± 13 years), 59% had a professional activity, and 32% were overweight or obese according to the body mass index. The correlations between the ABC-V score and the Specific Quality of Life and Outcome Response – Venous (SQOR-V and Center for Epidemiologic Studies Depression Scale (CES-D)scores (recognized and validated questionnaires) were sought. The ABC-V score is highly positively correlated to SQOR-V and CES-D scores. The three aspects with the greatest impact on the burden were the Pain, Physical, and Living with the Disease VAS. The two aspects with the lowest impact on the burden are Treatment by GP and Family Life (Table).

Conclusions: Chronic pathologies such as venous disease remain frequent and crippling diseases that are difficult to assess with only clinical elements or QOL instruments because the effect can be multidimensional. Several existing questionnaires attempt to evaluate one or another of these aspects. The ABC-V takes them all into consideration to express the global nature of the handicap and burden of chronic diseases.

BVD	Average ± Standard deviation	Proportion of the total score
« Pain » aspect	4.46 ± 3.04	19.91%
« Physical » VAS	3.75 ± 2.68	16.74%
« Living with the disease » VAS	3.69 ± 2.83	16.47%
« Psychological » VAS	**2.96 ± 2.64**	**13.21%**
« Daily life » aspect	**2.17 ± 2.65**	**9.69%**
« Psychological » aspect	**2.15 ± 2.60**	**9.60%**
« Work » aspect	**1.65 ± 2.23**	**7.37%**
« Doctor » aspect	1.07 ± 1.85	4.78%
« Family life » aspect	0.49 ± 1.67	2.19%

BVD, Burden of vascular disease; *SD,* standard deviation; *VAS,* visual analog scale.

Fig. Assessment of Burden in Chronic-Venous results

A Novel Method of Measuring Human Lymphatic Pumping in Healthy and Lymphedematous Legs Using Indocyanine Green Fiuorescence Lymphography

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Background: The lymphatic system possesses numerous active pumps to propel lymph to the central lymphatic systems. Decreased pumping activity may be associated with lymphedema. However, there are no noninvasive methods to measure lymphatic pump force in clinical practice. The aim of this study was to introduce a new method to measure lymphatic pumping and compared the activity between healthy and lymphedematous legs using indocyanine green (ICG) fluorescence lymphography.

Methods: ICG fluorescence lymphography was performed by subcutaneously injecting 0.3 mL of ICG (10% in normal saline) into the dorsum of the foot. Fluorescence images were obtained with an infrared-light camera system in a supine position. Sphygmomanometer cuffs were wrapped around the lower legs and connected to a standard mercury sphygmomanometer. The cuffs were inflated to 60 mm Hg, then, gradually deflated to lower the pressure by 10-mm Hg steps until the fluorescence dye exceeded the upper border of the cuff, when the lymphatic contraction overcame the cuff pressure. The value of the cuff pressure was taken as lymph pumping pressure (Ppump; Fig 1). In nine volunteers without swollen legs (18 legs), we compared the Ppump obtained with ICG fluorescence lymphography with that obtained from dynamic lymphoscintigraphy. With dynamic lymphoscintigraphy, Ppump was measured from the time-activity curves using the same sphygmomanometer cuff technique (Fig 2). With ICG fluorescence lymphography, we compared Ppump between 27 healthy volunteers (54 legs) and 22 lymphedema patients (26 swollen legs).

Results: A significant correlation between Ppump with ICG lymphography and dynamic lymphoscintigraphy was identified ($r^2 = 0.58$, $P < .001$; Fig 3, *A*). In lymphedematous legs, Ppump was significantly lowered vs healthy legs (16.2 ± 4.0 vs 30.0 ± 2.5 mm Hg, respectively; $P < .01$; Fig 3, *B*).

Conclusions: Ppump measurement with ICG fluorescence lymphography is easily applied at the bedside. This novel method enables real-time measurement of lymphatic pumping in the extremities. In lymphedematous legs, an impaired lymphatic pump may be involved in the pathogenesis of lymphedema.

Fig.1

Fig 1. Setup to measure lymph pumping pressure.

Fig.2

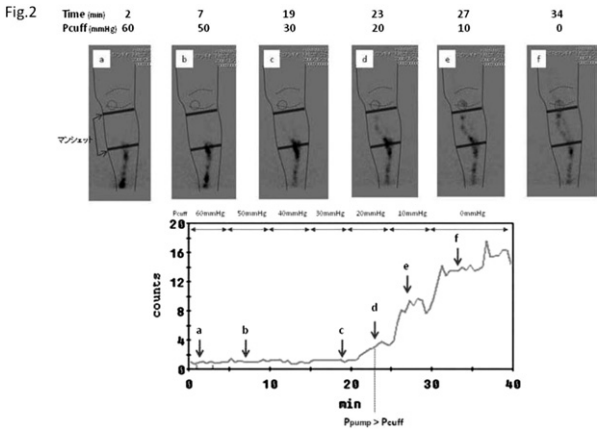

Fig 2. Lymph pumping pressure was measured from the time-activity curves using the same sphygmomanometer cuff technique.

Fig.3

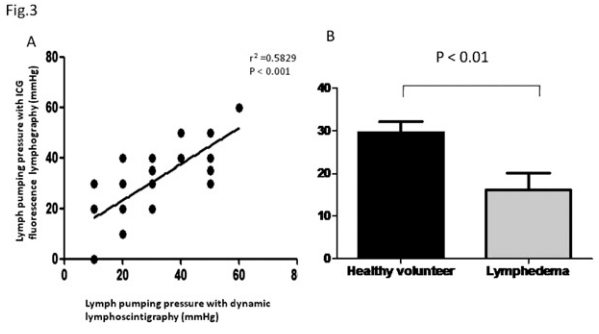

Fig 3. A, Lymph pump pressure identified with indocyanine green fluorescence lymphography was correlated with dynamic lymphoscintigraphy. **B,** Lymph pump pressure was significantly lowered in lymphedema legs vs healthy legs.

Inelastic Compression is Effective Over Time in Spite of Significant Pressure Drop

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Background: Inelastic compression has been claimed to lose effectiveness in a few days due to its fast pressure loss. We compared the improvement of venous pumping function achieved by inelastic bandages worn for 1 week with the effect of a compression stocking kit in relation to the drop of sub-bandage pressure.

Methods: In 18 patients affected by bilateral severe great saphenous vein insufficiency (CEAP C_2-C_5), ejection fraction (EF) was measured by strain gauge plethysmography before and immediately after application of compression, and 1 week later. A medical compression stocking (MCS) kit consisting of two stockings donned over each other was applied on one leg, an inelastic bandage on the other leg. The interface pressure was measured about 12 cm above the inner ankle in the supine and standing positions and during exercise.

Results: Results are summarized in the Table.

Table. Results

	Elastic stocking kit			*Inelastic bandage*		
	Baseline	*Application*	*7 days*	*Baseline*	*Application*	*7 days*
EF, %	32.9	42	40.1	33.4	77.9	64.5
IQR	23.4-41.2	39.7-44.2	35.6-46.7	18.1-39.1	69.4-100	57.9-73.8
% increase		37.2	32.3		138	90
Supine pressure		45	42		64.5	30.5
IQR		41-49	39-46.2		61-80	28-33.2
Peak pressure		49	46		103.5	61
IQR		44-51	42.7-48.5		98.2-113.5	54.7-65.7
% Pressure loss supine			5.6			54.7
% Pressure loss peak			3.9			39.6

EF, Ejection fraction; *IQR,* interquartile range.

Compared with normal values of EF of 64.6% (interquartile range, 63.3-68.5), median initial values were highly significantly reduced in both legs without compression. They increased moderately after application of MCS and strongly with inelastic bandages (both $P < .001$). Seven days later, EF was reduced in both groups: slightly with MCS, more, but still in the normal range, with bandages. At both terms, at application and 7 days later, the percentage increase of EF was significantly higher for the bandages compared with the MCS ($P < .0001$). At application, the median supine and standing interface pressure and walking amplitudes were significantly higher under the bandage than under MCS. After 7 days the percentage of pressure loss in the supine and standing position and the pressure peaks during walking were much lower under MCS than under the inelastic bandage.

Conclusions: Inelastic bandages applied with initially high resting pressure keep their beneficial hemodynamic efficacy over 1 week, despite loosing sub-bandage pressure to about one-half, probably due to the high-pressure peaks (>60 mm Hg) during exercise. The improvement of the venous pump by compression stockings is much less pronounced, both at application and 1 week later, despite of a better maintenance of both supine and peak pressure range.

A Randomized Trial of Class 2 and Class 3 Elastic Compression in the Prevention of Recurrence of Venous Ulceration

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