Chronic Venous Disease: Best Strategy to Improve Patient’s Quality of Life
Chronic Venous Disease (CVD)-Definition

“Chronic Venous Disease (CVD) is defined as an abnormally functioning venous system due to venous valvular incompetence with or without associated venous outflow obstruction, which may affect the superficial venous system, the deep venous system, or both.”
Anatomy

Superficial vein

Perforating vein

Deep vein
“Chronic venous disease covers all the clinical anomalies - symptoms and signs - resulting from disease of the veins of the lower limbs and progressing to a chronic state.”

**Symptoms**
- Heavy legs
- Pain
- Itching
- Cramp
- Restless legs

**Signs**
- Telangiectasias, reticular veins
- Varicose veins
- Edema
- Skin changes
- Active or healed ulceration

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The CEAP* classification – Identification of CVD patient profiles

- **Class C0s:** Symptoms without visible or palpable signs of venous disease
- **Class C1a,s:** Telangiectasias or reticular veins
  - a = asymptomatic
  - s = symptomatic
- **Class C2a,s:** Varicose veins
- **Class C3a,s:** Edema
- **Class C4a,s:** Skin changes ascribed to venous disease, eg, pigmentation, venous eczema, lipodermatosclerosis
- **Class C5a,s:** Skin changes with healed ulceration
- **Class C6a,s:** Skin changes with active ulceration

* CEAP: Clinical, Etiological, Anatomical, Pathophysiological.

Risk factors

- **Age:** Aging causes wear and tear. Eventually, that wear causes the valves to malfunction.

- **Sex:** Women > Men. Hormonal changes during pregnancy or menopause. Progesterone relaxes venous walls. HRT / OCP may increase the risk of varicose veins.

- **Genetics**

- **Obesity:** Increases venous HTN.

- **Standing for long periods of time.** Prolonged immobile standing impairs venous return.
Progression of chronic venous disease: venous hypertension is key

Pathogenesis of Chronic Venous Disease

- Activated leukocyte damages the valve
- Reflux flow
- Vein Edema
- Inflammation

Permanent reflux (intervalvular)
Venous hypertension is linked to venous inflammation

Genetic predisposition, obesity, pregnancy,..
Environmental factors repeated over time

Altered patterns of blood flow, Change in shear stress

Shear stress dependent leukocyte-endothelial interaction

Chronic inflammation in vein wall and valve

Remodeling in venous wall and valves

Valve failure, reflux

Chronic hypertension

Activation of C nociceptors

Pain

“Treatment to inhibit inflammation may offer the greatest opportunity to prevent disease-related complications. Drugs can attenuate various elements of the inflammatory cascade, particularly the leukocyte–endothelium interactions that are important in many aspects of the disease »
Leukocytes and changes in venous valves
Hypertension is transmitted to capillaries

Increased Capillary Permeability

Macromolecular Leakage (Monastal Blue B)

Microhemorrhage

EDEMA

SKIN CHANGES

Adapted from Schmid-Schönbein G N. The Vein Book 2007 Academic Press
Lymphatic drainage is disturbed

Pitting edema (Lymphedema)

Adapted from Perrin M, Ramelet AA. *Eur J Vasc Endovasc Surg*. 2011; 41:117-125.
Physical Examination:

- Assessing risk factor → anamnesa
- Leg examination

Supportive assessment → Duplex scan:

- Reversal of flow in the superficial venous system
  - Lasting longer than 0.5 second
    - Indicates valvular incompetence

- Abnormal deep system reflux
  - Reversal of flow exceeds 1 second
  - Reflux severity assessment
    - Longer durations of reflux (greater reflux times)
    - Higher reflux velocities and volumes
Prevalence of Chronic Venous Disease

- **CVD (C1 to C6)** affects 75% of adults in the USA\(^1\) and around 64% worldwide.\(^2\)

- **CVI (C3 to C6)** affects 16% of adults in the USA\(^1\) and 24% worldwide.\(^2\)

- **Venous ulcers (C6)** affect 2.5 million patients/year in the USA.\(^3\)

- **70%** of venous ulcers recur within 5 years of healing.\(^4\)

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Prevalence of CVD in Indonesia

- Prevalence of Indonesian people with CVD: 53.5% → 1 out of 2 Indonesia suffer from CVD, starting from C0s

- Prevalence by CEAP:
  - C0s = 18%
  - C1 = 18%
  - C2 = 37%
  - C3 = 6%
  - C4 = 18%
  - C5 = 1%
  - C6 = 2%

most frequent case!!
Epidemiology of chronic venous disease

In the USA, more than 50% of adults present with telangiectases or varices (not adjusted for age, gender, or BMI)

<table>
<thead>
<tr>
<th>CEAP clinical class (% individuals)</th>
<th>USA¹</th>
<th>Germany²</th>
<th>Worldwide³</th>
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<tbody>
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<td>C0</td>
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<td>36</td>
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<tr>
<td>C1</td>
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<td>C4</td>
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<td>3</td>
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<td>C5</td>
<td>0.5</td>
<td>0.6</td>
<td>1.4</td>
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<tr>
<td>C6</td>
<td>0.2</td>
<td>0.1</td>
<td>0.6</td>
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Epidemiology of CVD

- Male VS Female Patients per Symptoms

* Figure 1. Self-reported signs by patients at VO.

*Lishov Study, 2016*
The frequency of varicose veins increases with older age

The prevalence of venous ulcer also increases with age.

Socioeconomic aspects of chronic venous disease

- Overall annual costs:
  - 900 million € in Western Europe (2% of health care budget)\(^1\)
  - Equivalent to 2.5 billion € in the USA
  - Greater than the amount spent for treatment of arterial disease

- Annual loss of work days:
  - 2 million work days lost due to venous ulcers in the USA\(^2\)
  - 4 million work days lost due chronic venous disease (C1-C6) in France
  - Ranked 14\(^{th}\) for work absenteeism in Brazil
  - Cost for loss of work days varies between 270 million € (Germany), 320 million € (France), and 3 billion USD per year in the USA\(^2\)

- CVD is progressive, increases with age, and has a propensity to recur. This further increases costs.

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Treatment

- **Non Invasive:**
  - Pharmacology: MPFF drug
  - Compression Stocking
  - Lifestyle modification

- **Invasive:**
  - Schlerotherapy
  - Endovenous Laser
  - Surgery
Compliance Issue in CVD Treatment

- **Reasons for patients not respecting time duration of VAD treatment:**
  - Forgot to take it (27%)
  - Take other pills (14%)
  - Lack of efficacy (13%)

- **Reasons for patients not respecting Compression stocking treatment:**
  - Too difficult to put on (46%)
  - Not comfortable (32%)
  - Too warm (22%)
  - Itches (18%)
  - Not Esthetic (12%)
  - Lack of efficacy (2%)

*Lishov Study, 2016*
Life Style Modification

- Move your legs as much as possible → take a small walk at least once in an hour
- Avoid high temperature place
- Avoid heavy sport
- Use comfortable shoe (less than 5 cm heel)
- Before sleeping, lift up your leg 10-15 cm above for 5-10 minutes
A review of the efficacy of MPFF on venous symptoms
What is MPFF?

Combination of several Flavanoids that works in synergy to improve microcirculation.

Leaks per cm²

- Placebo
- MPFF
- Diosmin
- Hesperidin
- Linarin
- Isorhoifolin

*P < 0.01 vs placebo

Breaking News!

In Jan 2017, MPFF is also available in 1000 mg!

How does MPFF work?

- ↑ Venous tone\(^1\)
- ↑ Lymphatic drainage\(^2\)
- Protecting the microcirculation from inflammatory process
- ↓ Venostasis, ↓ Edema\(^7\)
Fast to reduce leg pain of CVD patients

Significant reduction of leg pain in 2 weeks

With 1 tablet daily

MPFF helps your patients from all CVD symptoms.
Quality-of-life improvement parallels symptom improvement

In C0s to C4s patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Change in symptoms</th>
<th>Patients with symptom improvement, N (%)</th>
<th>Increase in CIVIQ score between Day 0 and Day 180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensation of swelling</td>
<td>Improved*</td>
<td>2134 (69)</td>
<td>21.1 ± 16.8</td>
</tr>
<tr>
<td>Heaviness</td>
<td>Improved*</td>
<td>2778 (74)</td>
<td>20.1 ± 16.2</td>
</tr>
<tr>
<td>Cramps</td>
<td>Improved*</td>
<td>2189 (79)</td>
<td>21.1 ± 16.4</td>
</tr>
<tr>
<td>Pain</td>
<td>Improved§</td>
<td>1560 (80)</td>
<td>23.8 ± 16.2</td>
</tr>
<tr>
<td></td>
<td>Very much improved**</td>
<td>442 (23)</td>
<td>29.2 ± 16.9</td>
</tr>
</tbody>
</table>

* Improved: decrease of one class on 5-point scale. §Improved pain: decrease of 2.5 to 5 cm on VAS.
** Very much improved pain: decrease of ≥5 cm on VAS.

Significant improvement of the quality of life in symptomatic patients

In C0s to C4s patients

N=3948    *P = .0001

# 100 = optimal Quality of Life score

Significant reduction of leg pain associated with venous ulcer

N=459  * $P=0.0023$  **$P<0.001$

Lok C. Abstract presented at the 7th meeting of the EVF, London, UK, 29th June - 1st July, 2006
Significant reduction of leg edema which is often associated with venous pain

Allaert FA. *Int Angiol* 2012;31:310-5.
A significant decrease of venous symptoms after treatment associating sclerotherapy + MPFF

Assessment of venous symptoms on the VAS
(VAS, Visual Analogue Scale; 0 = 'No symptoms' and 100 = 'Unbearable symptoms')

RR.
- 52%
- 54%
- 54%
- 62%
- 60%
- 59%

Average

<table>
<thead>
<tr>
<th>Inclusion visit</th>
<th>Follow-up visit</th>
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<tbody>
<tr>
<td>44.4 ± 36.9</td>
<td>21.5 ± 20.4</td>
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<tr>
<td>35.4 ± 28.3</td>
<td>19.3 ± 21.0</td>
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<td>25.2 ± 17.0</td>
<td>11.8 ± 11.6</td>
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<td>20.3 ± 26.5</td>
<td>7.9 ± 15.2</td>
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<tr>
<td>15.7 ± 23.5</td>
<td>6.4 ± 13.1</td>
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<tr>
<td>10.2 ± 20.2</td>
<td>4.2 ± 11.5</td>
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</table>
MPFF (Ardium) is strongly recommended as the first and unique venoactive drug.
International Angiology 2018 Guidelines
(dipublikasikan di European Venous Forum – Juni 2018)
MPFF memberikan berbagai efek positif pada komponen vena

<table>
<thead>
<tr>
<th>Category</th>
<th>Drug</th>
<th>Venous Tone</th>
<th>Venous valve and wall</th>
<th>Capillary leakage</th>
<th>Lymphatic drainage</th>
<th>Hemorheological disorders</th>
<th>Free radical scavengers</th>
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<tbody>
<tr>
<td>Flavonoids (gamma-benzopyrones)</td>
<td>MPFF</td>
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<td>Synthetic Diosmins</td>
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<td>Benzaron/ Naphtazon</td>
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Whatever the stage

Only 1 tablet daily now!!!
CONCLUSION

- Chronic Venous Disease should be treated immediately in order to prevent disease progression.

- MPFF is clinically proven to reduce all signs and symptoms of CVD and improve patient’s quality of life.

- MPFF is now available in 1000 mg that benefits patient’s compliance of CVD treatment.
Thank You