Chronic Lymphedema: Contemporary Concept on Diagnosis & Management

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DISCLOSURE OF CONFLICTS OF INTEREST
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I do not have any relevant financial relationships with any commercial interests.

Chronic Lymphedema

Epidemiology - WHO data
- 140 million patients throughout the world: one among twenty persons on earth?
- 30 million - primary lymphedema
- 20 million - postmastectomy lymphedema

John Casley-Smith (1993)

Chronic Lymphedema

Once neglected chronic lymphedema is now mandated for contemporary interpretation based on newly obtained knowledge through the last two decades mostly based on the lymphodynamics as well as pathophysiology of lymphatic system.

Lymphatic System

Anatomy:
- Capillary lymphatics (initial lymphatics) remains only 'open' conduit system among three circulation systems with unique structure of a single series of 'adjacent and/or overlapping' endothelial cells without a basement membrane and valves: "protein homeostasis"
- Thin filament which anchors lymphatic endothelial cells to surrounding connective tissue will extend and relax by the tissue movement.
- This movement allows constant change of the cellular junctions of the lymphatic vessel wall between open and closed condition to maintain appropriate lymphatic drainage from the tissue into the vessel lumen.
**Lymphatic System**

**Anatomy:**
- **Lymphangion** is the hallmark of the lymphatic system representing 'segmental unit' of the collecting lymphatics between well-developed intraluminal valves.
- Lymphangion behaves as the functional unit based on 'spontaneous intrinsic segmental contraction' of lymphatic trunk to precipitate lymph propulsion.
- When pressure reaches to 3-4 cm H$_2$O, the stretched wall contracts to empty the lymph fluid to next chamber/segment.

**Lymphatic System**

**Physiology - Function**
- Fine adjuster of tissue microenvironment;
  - helps maintenance of fluid, protein and osmotic equilibrium around cells.
  - aids absorption and distribution of nutrients and disposal of waste.
- “Microcirculatory Homeostasis”: Physiological equilibrium in pressure balance at microcirculatory level between tissue and vascular microcirculation.
- Colloidal-osmotic/oncotic pressure - decisive role for the microcirculatory balance as the pressure generated by the protein molecules in endovascular and interstitial sites.

**Lymphatic System**

**Physiology - Function**

Lymphatic capillary as an integral part of a single phlebolymphatic unit – Reabsorption of 10 to 20% of the total liquid and all the protein macromolecules filtered out from arterial capillary under normal physiological conditions.
- Venous capillary – 80 to 90% of ultrafiltered liquid portion only, leaving a liquid-protein fraction in the interstitial area.
- Lymph production – 2 liters in average per day in normal status with extreme compliance to 20-30 liters in maximum.

**Lymphatics**

**Physiology - Function**

Such unique hydrodynamic status of lymphatic system is solely based on the spontaneous peristalsis led by the 'lymphangions'.
- When normal lymphatic truncal contraction fails (e.g. lymphatic obstruction) resulting in persistent lymph-stasis, the fluid column within the lymphatic system becomes continuous like venous system.
- Such abnormal lymphodynamics would become identical to the venodynamics, and skeletal muscles or external compression becomes effective pumping mechanism like venous system to aid lymph transport.

**Chronic Lymphedema**

**Definition - Old concept**
A clinical condition of diffuse swelling of affected limb/region due to the lymphatic circulation disorder; the blockage of lymph-transporting/collecting system by various causes.

**Lymphatics**

**Definition - Changing concept**
- Chronic lymphedema starts as a simple condition of limb swelling following the mechanical failure of lymph-transporting/collecting system.
- But such simple 'reversible' edema in early stage soon changes to a chronic degenerative and inflammatory process, and the impact of lymphatic fluid accumulation, initially limited to the lymphatics and lymph nodes, would soon spread to entire surrounding soft tissue and skin resulting in 'irreversible' damage.
Chronic lymphedema accompanies high tendency to harbor bacterial and fungal infections frequently and this infection, either clinical or subclinical/occult, accelerates chronic inflammation through the process of ‘dermato-lipo-fibrosis’.

Then, the soft tissue with pitting swelling soon becomes rubbery firm with extensive skin/soft tissue change (e.g. elephantiasis) leading to a disabling and distressing condition in its late stage.

**Definition - Changing concept**

- Chronic lymphedema is a steadily progressive condition affecting the entire soft tissue of the body and results in a disabling and distressing condition.
- Bacterial and fungal infection
- Chronic inflammation: dermato-lipo-fibrosis
- Immunodeficiency and wasting phenomenon
- Malignancy: Kaposi sarcoma, lymphangiosarcoma

**Definition - New concept**

A steadily progressive condition affecting the entire surrounding soft tissue and results in disabling and distressing condition.

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Lymphedema can no longer be considered as a simple 'static' clinical manifestation of mechanical failure of lymphatic system to transport interstitial fluid out of tissue. But it should be considered a “chronic degenerative and inflammatory disease” of skin and soft tissue beyond the lymphatics and lymph nodes.

A complicated degenerative condition through the recurrent dermato-lymphatico-adenitis forms a vicious cycle between recurrent sepsis and steady fibrotic change resulting in various degrees of physical, psychological and financial disability.

Hence, precise diagnosis including its etiology and clinical stage for the accurate management warrants proper understanding of new concept for the contemporary strategy to aim not only to manage this condition as a systemic rather than a local disease but also to reduce, if not prevent, the risk of development at the same time.

For example, secondary lymphedema is ‘incurable’ in general but often preventable (e.g. post-infectious lymphedema), if not, controllable (e.g. post-surgical/radiation lymphedema) by proper understanding of the nature of the disease.

**Etiology – classification**

- **Primary lymphedema**
  - Congenital lymphedema
  - Lymphedema praecox
  - Lymphedema tarda
- **Secondary lymphedema**
  - Iatrogenic; post-surgical and/or post-radiation
  - Infections; filariasis
  - Tumor, trauma, etc.

**Secondary lymphedema**

- Post-surgical lymphedema; most important form in developed countries.
  (e.g. postmastectomy lymphedema)
- Post-infectious lymphedema; most important form in third world countries.
  (e.g. filariasis-induced lymphedema)
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- The surgery involving lymph nodes dissection (e.g. breast/uterine cancer surgery) or radiation therapy to lymph nodes is the most common cause of the “secondary” lymphedema in developed countries.
- Risk of lymphedema development should be anticipated as the “iatrogenic” consequence of surgical and/or radiation injury to the lymphatic system, and prepared for the aggressive control of these inevitable (?) but iatrogenic consequences even before it becomes clinically detectable.

"Because, PREVENTION is easier than treatment!"

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"Because, PREVENTION is easier than treatment!"

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Definition - Moral/Ethical concept

- A ‘neglected’ condition surgeons/radiation oncologists contributed despite fully anticipated and possibly manageable outcome:

**POSTSURGICAL/POSTRADIATION LYMPHEDEMA**

An ‘anticipated’ condition after the surgery involving lymph nodes dissection (e.g. breast/uterine cancer surgery) or radiation therapy to lymph nodes: the most common cause of the “secondary” lymphedema in developed countries.

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Lymphatic system:
- Radionuclide Lymphoscintigraphy
- MRI for the differential diagnosis
- CT scan and/or Duplex ultrasonography to exclude underlying malignancy
- Volume
- Standard (ascending) lymphangiography, limited only to the surgical candidate if indicated
- Ultrasonographic & MR lymphangiography: optional for the surgical candidate

Venous system
- Venous duplex sonography
- Airplethysmography

Diagnosis – Laboratory Tests

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Lymphoscintigraphy – Lower Extremity

Male (56 yrs)

Asymmetry Index Ratio (reduction rate): 25.8→13.9 (46.0%↓)

Radionuclide Lymphoscintigraphy

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Male (56 yrs)

1 hr
2 hr

1 hr

1 hr
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Treatment – ultimate goal

**Improvement of Quality of Life (Q.O.L.)**
- Social adaptation – socially useful life
- Functional adaptation – physically normal activity
- Psychological adaptation – psychologically accept physical deformity

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Treatment - General Plan

- Physical therapy - essential and basic care
- Medical therapy - optional if indicated
- Surgical therapy - supplemental therapy to the non- to poor-response group to physical therapy
- Reconstructive surgery
- Physiologic reductive surgery; excisional or liposuctional

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Treatment – Physical Therapy

- Decongestive lymphatic therapy (DLT)
  1. Manual Lymphatic Drainage (MLD)
  2. Compression bandage combined with therapeutic exercise regimen
  3. Compression garment (50-60 mmHg)
  4. Special skin care for prevention of infection
  5. General supportive measurement, including nutritional counseling for weight control
- Sequential pneumatic compression therapy (SPC)

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Treatment – Surgical Therapy

- Surgical treatment modalities, either for curative/reconstructive or palliative/excisional purposes, remain either as an independent treatment option or as a supplemental role to DLT based management.
- Reconstructive surgery in particular is able to provide unique opportunity of a “cure”, but its clinical application as an independent therapy remains controversial with mixed outcome of its long term results.
- Various modalities of surgical treatment can deliver the most effective outcome of controlling chronic lymphedema when combined with DLT through multidisciplinary approach.

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MRI
(standard)

MR Lymphangiography
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Treatment - principle
- Basic therapy: MLD-based DLT with or without combination of SPC-based compression therapy.
- Supplemetal therapy: Surgical therapy to the non- to poor- response group of DLT and/or compression therapy.
- Lympho-venous anastomotic surgery: clinical stage I & II
- Free lymph nodes transplant surgery: clinical stage II & III
- Ablative (excisional) surgery: clinical stage III & IV
- DLT should be fully integrated with the 'reconstructive' surgery while compression therapy was further added to the 'palliative' surgery as supplement - "mandatory-obligatory postoperative management"

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Issues – postsurgical lymphedema
- Vigilant surveillance to detect the ‘latent/subclinical’ lymphedema is essential for an early effective management with a minimum morbidity.
- Once lymphedema should set in, an active control with decongestive lymphatic therapy (DLT) therapy is warranted in earliest possible time.
- Aggressive control, if not prevention, of the infection should remain the first and most important strategy throughout the life.

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Issues - Infection
- ‘Infection’ is most neglected condition which is critical for the progress of the lymphedema because the lymphedema has an extraordinary susceptibility to secondary bacterial infection.
- Erysipelas secondary to beta-hemolytic streptococcal infection causes recurring lymphangitis and recurrent cellulitis will result in such devastating sequela of peripheral lymphedema.

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Conclusion
- Enemy number two – INFECTION
  - lymph stasis and lymph vessel damage increase the chance of sepsis and bacteremia
  - "each infection paves the way to the next"
  - W. Olszewski (1997)

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References
Thank you for your attention!