Introduction

Lymphatic Interventions: The Real Next Frontier

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Lymphatic System-Structure

Reverse tree

Trunk – Thoracic duct

Branches are 3 Lymphatic Systems

- Peripheral Lymphatic System
- Liver
- Intestine
Lymphatic System-Flows

Reverse tree

Trunk – Thoracic duct

Branches are 3 Lymphatic Systems

- Peripheral Lymphatic System
- Liver
- Intestine

Liver

Intestine

Lumbar, extremities, soft tissue
Lymphatic Flow Diagram
Central lymphatic flow physiology was extensively studied in up to the 1970’s.

40 years of Hiatus!

- Absence of lymphatic imaging methods
- Absence of interventional techniques
Traditional Lymph Flow Imaging Techniques

PEDAL LYMPHANGIOGRAM

PEDAL LYMPHOSCINTIGRAPHY
Lymphatic Vessels Imaging

- **Intranodal Lymphangiogram**
- **Facilitate Interventions**

**Contrast Enhanced MR Lymphangiogram**

- **Diagnosis**

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Intranodal Lymphangiogram

24-27 G spinal needle

Intranodal Lymphangiogram

Shunt to Vein

Intranodal Lymphangiogram
Upstream Access
Intranodal Lymphangiogram
Upstream Access
Contrast Enhanced MR Lymphangiogram

Intranodal injection

Combined MR and Fluoroscopy Machine

XMR

>150 cases performed

MR Lymphangiogram
MR Lymphangiogram

Idiopathic Chylothorax
Thoracic Duct Embolization

Constantine Cope first described minimally invasive lymphatic intervention.

Therapeutic Approaches to Lymphatic Flow Disorders

### Lymphatic Embolization
- Chylothorax
- Plastic Bronchitis
- Pulmonary Lymphangiomatosis
- Chylous Ascities

### Liver Lymphatic Embolization
- Ascities
- Protein Loosing Enteropathy
- Liver Lymphorea

### Thoracic Duct Externalization
- Congenital Lymphodysplasia
Thoracic Duct Embolization

Treat Chylothorax

• Minimally invasive alternative to Thoracic Duct Ligation

Rational

• Lymphangiogram
  • identification of the leak
• Minimally invasive
  • less mortality, morbidity
Intranodal Lymphangiogram
Intranodal Lymphangiogram
Thoracic Duct Access

Access duct as soon as you see contrast

Peripheral duct

Fast “stubbing” movement

Can go through “everything”

Cisterna Chyli
TD Injection
Embolization

Microcoils

- Nester 0.018

Liquid embolic agent

- Glue - n-Butyl Cyanoacrylate (n-BCA)
Coil Deployment
Glue injection
Traumatic Chylothorax

Clinical Success

The overall (intent to treat) success rate was

- 77/109 (71%)

The overall success-attempted interventions

- 77/88 (88%)

Itkin et al JTCVS 2010
Traumatic Chylothorax
Clinical Success-Intranodal Lymphangiogram

55 adult patients over the last two years
53/55 (96%) successfully treated with TDE
Overall >400 cases
   60 cases post unsuccessful TD ligation
   89% success of embolization after failed TD ligation

Nadolski et al SIR 2016
Nadolski et al CIRSE 2016
Pulmonary Lymphatic Perfusion Syndrome (PLPS)
TD Flow Components
Pulmonary Lymphatic Perfusion Syndrome (PLPS)-aka Lymphatic Reflux
Pulmonary Lymphatic Perfusion Syndrome

Congenital Lymphatic Variant

- Plastic Bronchitis
- Pulmonary Lymphangiomatosis
- Non-traumatic Chylothorax
Plastic Bronchitis

Formation of large gelatinous or rigid branching airway casts
Contrast Enhanced MR Lymphangiogram

Perfusion of the Right Hilum

Thoracic Duct Injection

Plastic Bronchitis
Bronchoscopy TD Injection  Methylene Blue  Plastic  Bronchitis
Embolization-Lipiodol

Plastic Bronchitis Embolization - Outcome

- 18 Patients with PB
- 16 demonstrated pulmonary lymphatic perfusion
- 15/16(94%) – significant improvement of their symptoms

(Dori et al. Circulation 2016)
PB Anatomic Categories

Type 1

Type 2

Type 3

Type 4

Type 5

(Dori et al. Circulation 2016)
Lymphatic Anomaly – Kaposiform Lymphangiomatosis

Presentation 2014

March 2015 on Sirolimus
Lymphatic Anomaly – Kaposiform Lymphangiomatosis
Lymphatic Anomaly – Kaposiform Lymphangiomatosis
Lymphatic Anomaly – Kaposiform Lymphangiomatosis
Follow up

07/2015

09/2015
Neonatal chylothorax

Pulmonary Lymphatic Perfusion Syndrome

Congenital Lymphatic Variant

- Plastic Bronchitis
- **Pulmonary Lymphangiomatosis**
- Non-Traumatic Chylothorax

Possible Effects 5-10% of Population

- CHF
- Chronic Bronchitis
- Interstitial Lung Disease
- Bronchopulmonary Dysplasia
Liver Lymphatic System

Ernst Starling (1894)

• First described liver lymphangiogram flow

Normal liver lymph contributes 30-40% of the flow to the TD

Estimate 500-800 ml/day

40% of total body proteins returned to blood circulation through TD
Liver Congestion

Congested liver (cirrhosis, CHF)

- Flow increases 10 folds
- 10 - 20 liters a day in adult

Original theory of liver ascities

- Leakage of the lymph in the peritoneal cavity


Liver Lymphangiogram

First described in 1962 Moreno et al

Few publications

- Curiosity (Clain 1968, Ocuda 1976)
- Investigation of portal hypertension (Moreno 1963)
- Hepatic Lymphorea (Matsumoto 2000)
- Lymph nodes metastasis (Teramoto 2002)
Penn/CHOP Experience

Liver Lymphoedema

Ascities

Protein Loosing Enteropathy (PLE)
Hepatic Lymphorea

56-year-old male
History of hepatitis
Whipple procedure
Postoperatively large volume ascites
Denver Shunt failed

Liver Lymphangiogram
Embolization with Onyx
Outcome

• One paracentesis day after the procedure-cured from ascities
• US showed periportal thickening

Ascities in Right Side CHF

• 60 YO

• Tricuspid valve insufficiency (repaired)

• Developed severe ascites few months after surgery

• Not clear chylous
Liver Lymphangiogram
Liver Lymphangiogram

Liver Lymphangiogram CHF Ascites
Outcome

Significant improvement of the ascites

• Prior to procedure twice a week
• After 14 days one parenthesis (3 liters)
• Five months later recurrence of the symptoms
• Repeat lymphangiogram
Liver Lymphangiogram
Liver Lymphatic Embolization

Contrast Injection

Glue Injection
Outcome

No paracenthesis since the procedure 5 months
Protein Loosing Enteropathy

Severe loss of serum proteins into the intestine
PLE Pathophysiology Concept

Physiology:

- Liver generates albumin and delivers it into blood stream through lymphatic system
- Liver lymph high concentration of proteins
- The lymphatic flow in liver increases significantly in patients with CHF

Hypothesis:

- The loss of the albumin in PLE happens from the liver lymph leaking into the intestine
PLE Treatment Concept

Perform liver lymphangiogram

If leak attempt to embolize
Liver Lymphangiogram PLE

Contrast in duodenum
Intraprocedure Endoscopy

Injection of the methylene blue into liver lymphatic ducts
PLE
Initial Experience

Four patients with congenital cardiac disease-severe PLE

• First 2 lipiodol embolization, Last 2 n-BCA glue embolization

• Outcome
  
  • Three patients temporary improvement of the albumin and significant improvement of symptoms
  
  • First two patients duodenal bleeding after lipiodol injection
    • Lipiodol crossing mucosa, can potentially cause irritation of the mucosa and bleeding
  
  • Last two patients no lipidol injection into lymphatic ducts-no complications
Outcome

Patient 1 (lipiodol)

Patient 3 (1:6 diluted glue)
Liver Lymphangiogram PLE
Outcome

Patient 4 (1:2 diluted glue)
Follow up/Bone Scan for PLE

- Three weeks latter, albumin dropped to 1.5
- Most of the symptoms recur
Second Procedure
Bone Scan for PLE
Follow Up Of Second Procedure

- 7 days
- Albumin 1.3-2.5
- All symptoms (ascites, edema, diarrhea) disappeared
PLE Treatment Future

• Loss of the albumin happen due to leakage of liver lymph into intestine

• Need to achieve more sustainable response
  • More extensive embolization
  • Magnetic navigation technology
  • Ablation of duodenal mucosa “leakage points” using laser ablation technology
Where we are today…

1. Treatment of Chylothorax
   - 100% success rate in treatment of traumatic chylothorax
   - 95-100% success rate in treatment of non traumatic chylothorax

2. Discovered etiology and developed treatment for Plastic Bronchitis
   - 94% success

3. Discovered etiology and developed treatment for Neonatal Chylothorax

4. Discovered etiology and developed treatment for Protein Loosing Enteropathy

5. Discovered etiology and conceptualized treatment Pulmonary Lymphangiomatosis

6. Successful treatment of Chylous Ascites
Future

MRL and Lymphatic Embolization

- Chronic Bronchitis
- Interstitial Lung Disease
- Bronchopulmonary Dysplasia

Liver Lymphatic Embolization

- Cardiac Ascities
- Liver Cirrhosis Ascities

Thoracic Duct Externalization

- Congenital Lymphodysplasia
- HIV
- Immunotherapy (car T cell)
- T cell depletion therapy
Future

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Future...

- Development of the new lymphatic imaging agents
- Liver lymphatic Imaging
- Intestinal Lymphatic Imaging
- Development of the new treatment of the CHF
- Pulmonary Perfusion Syndrome
- Development of the Lymphatic Pump
Team

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