ΠΑΘΟΦΥΣΙΟΛΟΓΙΑ ΤΩΝ CTOs

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ΘΕΣΣΑΛΟΝΙΚΗ, 10 ΟΚΤΩΒΡΙΟΥ 2014
CHRONIC TOTAL OCCLUSION

Perception

- Difficult
- Inability to cross or dilate
- Expensive
- Unnecessary

High incidence of restenosis and re-occlusion

Approach

Understanding anatomy and pathophysiology:

- Explain difficulties
- Insights in developing revasc therapies
- Improve pts selection
- Improve material choice
**CHRONIC TOTAL OCCLUSION**

**Mechanisms**

I. ACUTE
- major plaque rupture with massive thrombus

*usually associated with transmural regional MI*

II. SLOWLY PROGRESSIVE
- lipids and fibro inflammatory response
- repeated (minor plaque) disruptions

*clinically silent or episodes of angina or history of MI*

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**Lysis**
Cellular decay

**Organization**
Ingrowth of SMC, small vessels connective tissue

**Organized**
Fibrotic scarring, +/- recanalization

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Late evolution of an acute occlusion

- Thrombus formation develops proximally and distally. The original thrombus turns into organized thrombus.

- Thrombus formation develops up to the side branch ostium. The originally occluded area turns into fibrotic plaque with calcified lesions.

- Aged chronic total occlusion with fibrotic plaque and calcified lesions.

*Sumitsuji S et al. JACC Intv 2011;4:941-51*
Morphologic characteristics of CTO

A: Acute TO with luminal thrombus.

B: Early CTO with inflammation, hemosiderin, smooth muscle cell infiltration and proteoglycan (green).

C: Late CTO with collagen matrix and relatively little calcification. Negative remodeling with a persistent flow deficit.

D: Late CTO with physiologic recanalization.

Finn A et al. JACC Img 2010;3:806-810
Classification of typical CTOs

**Huge variations in tissue component make-up**

**SOFT**
- Recent CTOs: soft lipids, thrombus
- Matrix composed of fibrin and proteoglycans
- Vessels

**HARD**
- With time, collagen replaces thrombus and lipids, especially at proximal/distal ends or caps
- Increasingly dense fibrous collagen and calcification occurs

Or a mixture of both!

*Hoye A.*
*Eurointervention* 2006;2:382-8
Data derived from:

- a. Post Mortem studies
- b. In vivo IVUS studies
- c. IVUS VH studies
- d. By procedural behavior
Despite angiographic appearance of a CTO, microvessels are quite common in human CTO (>75%)

1. *Vasa vasorum* derived (source of bridging collaterals)
2. *Inside the lesion* (recanalization of thrombus)
   - 100-200μm diameter, parallel course
   - loose proteoglycan rich matrix around the vessels

*Strauss et al. J Interv Cardiol 2005;18:425-436*
Bridging collaterals: Rich neovasculature network that often traverses the vessel wall, moving from *adventitial vasa vasorum* across the media and into the lesion *intima*.

- Large capillaries (100-500μm)
- Course through the CTO’s body
- Partially recanalize the distal lumen
- Guidewires may use microchannels as a passage to reach the distal vessel

*Stone G et al. Circulation 2005;112:2364-72*
CTO: What’s in the lumen?

Histopathology of 96 angiographic chronic total coronary occlusions -influence of occlusion duration- ( <1yr and >1yr)-

-49% of all angiographic CTO were only 90-99% occluded by histologic assessment

Neovascular channels: <1yr CTO: 74% >1yr CTO: 85% NS

Increasing CTO age: -Fibrocalcific component
-Cholesterol or mixed component p= 0.0003

Srivatsa et al. J Am Coll Cardiol 1997;955-963
Fibrous tissue is *particular dense* at the proximal ("entrance") and the distal ("exit") of the lesion.

*Strauss et al. J Interv Cardiol 2005;18:425-436*
CTO: What’s in the lumen?

- Tapering types
  - Loose fibrous tissue
  - Multiple and dispersed loose fibrous tissue
  - Shorter
  - Less likely to have SB at the proximal cap

- Abrupt types
  - Small vascular channel
  - No recanalization

Katsuragawa M et al, JACC 1993;21:604-11
- 96% of the lesions contained calcium (68% mild)
- In blunt stump CTOs Ca++ was concentrated around proximal cap
- In 74% of blunt stump CTOs a calcified arc was demonstrated in the wall opposite the side branch
- In a smaller proportion calcification found perpendicular to the SB origin
- A smaller number were found on the ipsilateral aspect of the SB
CTO containing VH-fibroatheroma

- 84% of the lesions
- NC > 10%

CTO not containing VH-fibroatheroma

- More fibrofatty and fibrous tissue
- Less DC and NC

Important factors that relate to feasibility of crossing the occlusion with a wire:

- **Plaque composition**
  - Gradual replacement of cholesterol and foam cells with fibrous and calcific material
  - Straightforward relationship with lesion age

- **Extent of vessel recanalization**
  - Associated with looser fibrous tissue and less resistance to wire passage
  - DOES NOT seem to have a clear relationship with age, nor lesion length

*Irving J. Curr Cardiol Rev 2014, 10:99-107*
**Definition:** Vascular connections linking parallel arteries without an interfering capillary bed

**May lead to:**
- Myocardial ischemia prevention
- Myocardial ischemia reduction
- Ventricular function preservation
- Prognosis improvement

**Formation:**
- Acutely
- Pre-exist in an underdeveloped stage
  - Thin-walled structures
  - 20-200mm
  - Variable density

*Berry C et al. EHJ 2007;28:278-91*
PATHOPHYSIOLOGY OF COLLATERAL CIRCULATION IN CTO

Arteriogenesis: a 3 stage procedure...

1st stage
- first 24h
  - passive widening
  - Blood flow velocity and endothelial shear stress mediates vessel remodeling through proteolytic enzymes secretion and SMC recruitment

2nd stage
- 1day-3weeks
  - Inflammation and cellular proliferation

3rd stage
- 3weeks-6months
  - Thickening of the vessel wall (GF, cellular proliferation)
  - Mature collaterals
    - 3-layer structure!
    - 1mm LD

Collateral flow to a CTO is influenced by:
- a. anatomical distribution of the donor artery
- b. microvascular function
- c. vessel occlusion duration
- d. left ventricular function

Berry C et al. EHJ 2007;28:278-91
PATHOPHYSIOLOGY OF COLLATERAL CIRCULATION IN CTO

Anatomical description: Epicardial
Intramyocardial: More rapid reduction in flow following successful PCI

Usefulness of collaterals: Retrograde contrast opacification
Retrograde guidewires access

After a successful CTO PCI: - Collateral flow reduces
- Regression may persist in the long term and in some pts collaterals may not be suitable any more in response to acute ischemia

Berry C et al. EHJ 2007;28:278-91
Half of all CTOs are <99% stenotic when observed by histopathology despite the angiographic appearance of total occlusion with TIMI grade 0 flow.

No relationship exists between the severity of the histopathological lumen stenosis and either plaque composition or lesion age.

There are CTO-age related changes in tissue composition from a “soft” to a “hard” tissue composition.

Significant (neo)vascularization in most (>75%) lesions
- in the artery (recanalization)
- around the artery (bridging collaterals)

Collateral circulation is an important protective response to acute and chronic ischemia as well as a commonly used track for a CTO PCI.