Thrombolytics in 2013: Never Say Never

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Clinical Case
Evolution of STEMI Therapy

“The importance of absolute rest in bed for several days is clear”

James B Herrick
1861 – 1954

The New England Journal of Medicine

Angiography on 322 patients within 24 hours of myocardial infarction

• < 4 hrs: 87% had occlusion
• > 12 hrs: 65% had occlusion

DeWood et al. 1980; NEJM 303:897-902.
Evolution of STEMI Therapy

Intra-coronary streptokinase
Coronary thrombolysis
Myocardial Salvage

Markis et al. NEJM 1981 305: 777-82
Rentrop et al., Circulation 1981 63: 307-317

Evolution of STEMI Therapy

Lilly et al. 2011
Evolution of STEMI Therapy

Reductions in AMI-associated 30-d Mortality

US and Europe

Yeh et al. 2010; NEJM

Boersma et al. 2003; Lancet

Evolution of STEMI Therapy

Markis et al. NEJM 1981 305: 777-82
Rentrop et al., Circulation 1981 63: 307-317
Evolution of STEMI Therapy

- Establish Vessel Patency
- Limit Infarct Size
- Reduce Mortality

Thrombolysis: Clinical Efficacy

- **ISIS-2** (n = 17,187)
  - 1985-87
  - Streptokinase

- **GISSI-1** (n = 11,806)
  - 1984-85
  - Streptokinase

- **ASSET** (n = 5,011)
  - 1986-88
  - Alteplase (tPA)

- ~26% reduction in 30d mortality

Thrombolysis: Clinical Efficacy

- 22 randomized trials 1983 – 1993, n = 50,246
- Thrombolysis vs placebo in STEMI
- Mortality benefit if < 2 hours from symptoms
Thrombolysis: Clinical Efficacy

- 9 randomized trials, over 1000 patients each

**Risk**

- Complete thrombosis, low risk of bleeding

*Complete thrombosis, low risk of bleeding*

**Benefit**

*Complete thrombosis, low risk of bleeding*

**Lancet 1994; 343: 311-22.**

Thrombolysis: Clinical Efficacy

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**Thrombolysis: Clinical Efficacy**

**GUSTO-I:** 41,021 with AMI, 4 thrombolytic strategies

30 – day stroke rate up to 1.5%; primarily hemorrhagic

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**GORE et al. 1995; Circ 92:2811-18**
Thrombolysis: Clinical Efficacy

Absolute Contraindications
- Prior intracerebral hemorrhage
- Known cerebrovascular lesions or neoplasm
- Ischemic stroke within 3 months
- Suspected aortic dissection
- Active bleeding or bleeding diathesis (excluding menses)
- Significant closed-head or facial trauma within 3 mo
- Intracranial or intraspinal surgery within 2 mo
- Severe uncontrolled hypertension (unresponsive to emergency therapy)
- For streptokinase, prior treatment within the previous 6 mo

Relative Contraindications
- Poorly controlled hypertension
- History of prior ischemic stroke
- Dementia
- Traumatic or prolonged (>10 min) CPR
- Major surgery (<3 wk)
- Recent (within 2 to 4 wk) internal bleeding
- Noncompressible vascular punctures
- Pregnancy
- Active peptic ulcer
- Oral anticoagulant therapy
- > 85 years old

Thrombolysis: Why Now?

New PCI Centers, 1997 - 2008

Horowitz et al. Lancet 2013; 128:803-810
Thrombolysis: Why Now?

Clinical Trials vs Real Life
Weather
Off-Hours presentation
Transfer Times


Thrombolysis: What Now?

- Choose Thrombolytic
- Ancillary Medical Therapy
- Transfer
Thrombolysis: What Now?

- Alteplase (tPA): Better outcomes than streptokinase (mortality and vessel patency); costly, short T1/2.
- Retepase (rPA): Similar to alteplase, easier to administer
- Tenecteplase (TNK-tPA): Equivalent to Alteplase, less bleeding, longer T1/2 and easier to administer, long T1/2
- Streptokinase: Less costly yet less efficacious, neutralizing antibodies develop, and risk of hypersensitivity upon re-exposure.

Choose Thrombolytic

Ancillary Medical Therapy

Transfer
Thrombolysis: What Now?

Adjunctive Therapies

- Micro-embolization
- Fibrin-specific
- Increased free thrombin

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Thrombolysis: What Now?

- Choose Thrombolytic
- Ancillary Medical Therapy
- Transfer
Thrombolysis: What Now?

Thrombolysis in STEMI: Conclusions

“In the absence of contraindications, fibrinolytic therapy should be given to patients with STEMI and onset of ischemic symptoms within the previous 12 hours when it is anticipated that primary PCI cannot be performed within 120 minutes of first medical contact.”

“...even when interhospital transport times are short, there may be advantages to the immediate delivery of fibrinolytic therapy versus any delay to primary PCI for patients with STEMI and low bleeding risk who present within the first 1 to 2 hours of symptom onset.”
Thrombolysis in STEMI: Conclusions

- Provide Adjunctive Medical Therapies
- Be realistic about transfer times
- Know contraindications to thrombolysis
- Transfer after thrombolysis

Questions?

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