KING'S HEALTH PARTNERS

Defining Malperfusion, Pain & Rapid Growth in Acute Type B Dissections

M.R. Tyrrell

Why?

- To identify those that are going to do badly

  and therefore…

- In whom the risk of early TEVAR may be appropriate

Oxford Thesaurus of English

definition

noun

1 *there is no agreed definition of 'intelligence'*

Oxford Dictionary of English

definition | dɛfɪˈnɪʃ(ə)n |

noun

- an exact statement or description of the nature, scope, or meaning of something

KING'S HEALTH PARTNERS

Fattori R *et al.*

J Am Coll Cardiol, 2013
(Consensus Document)

- "…no uniform criteria exist to differentiate complicated versus uncomplicated type B acute dissection…"

- Definition of *complicated* type B acute dissection
  - Malperfusion indicated by impending organ failure
  - Treatment resistant hypertension
  - Increasing peri-aortic hematoma / hemorrhagic pleural effusion in two subsequent CT examinations

KING'S HEALTH PARTNERS

Why Define?

- Agreed “industry standard” / Reporting Standards
  - What is
    - “Intractable pain”?
      - ?
    - “Rapid growth”?
      - Cardiac cycle/BP
      - In mm/time?
    - “Malperfusion”?
      - At least 2 mechanical sub-varieties
      - Limbs are not organs or CNS!
      - It doesn't always matter & can’t always be fixed
    - “Resistant hypertension”?

- Identification of threatening deterioration in an individual?
  - i.e.: Defining change, not absolutes
    - Is the late, untreated (unobserved) presenter with a 38mm max aortic diameter really worse than one whose diameter is observed to dilate from 33 to 38mm while Rx is being established?

Why Define?

- To identify those that are going to do badly

  and therefore…

- In whom the risk of early TEVAR is appropriate

- i.e.: Select those that
  - *Have* complicated (19% mortality)
  - *Are likely to* complicate (?% mortality)

➢ & in whom a 2 week delay to TEVAR is disadvantageous

KING'S HEALTH PARTNERS

Why Define Reporting Standards?

- 30 day Mortality Improvement by *"Incremental Gains"*
  - Historical management (1960's) – 40% mortality
  - Current – 10-14%
    - Within the whole group:
      - 19% if "complicated" (despite intervention)
        - *Room for safer/more timely interventions?*
      - 1.2-8% if "uncomplicated" (OMT only)
        - *Room to identify & intervene for impending complications*

Wheat & Palmer J Thorac Cardiovasc Surg 1965
Estrera *et al*. Circulation 2006
Durham *et al*. JVS 2015

- So… Medical Mx has already made the "big step"

KING'S HEALTH PARTNERS

Do We Have Good Predictors of Disaster?

- Good tools for identifying **actual** complications
  - No debate – immediate TEVAR
    - BUT
    - Is this true? - Not all ”complications” are equal or lethal!
    - This is the group that suffers complications and dies despite/because of intervention
    - 15-20% of all presenters, (perhaps 47%)

- Tools for predicting conversion from “uncomplicated” to “complicated”?
  - Thin evidence
  - Vacillating opinion…

ADSORB Trialists

- *“Rather than a randomised trial that attempts to tell us whether TEVAR or BMT is best for all uncomplicated acute type B dissections, we need a study that tells us which dissections will become complicated and, thus, need TEVAR.”*

TEVAR risk vs. Time

- Intervention Risks:
  - Eggebrecht H *et al*. Circulation 2009

4750 TEVAR
Total =rAAD cases (**incidence = 1.33%)**
BUT: Mixed Acute/Chronic cohort
Outcome was fatal in 20 of 48 (42%)

  - ND Desai *et al.*

Severe Postoperative Complications

	Acute-Early intervention(70)	Acute-Delayed intervention(44)	Sub-acute Intervention(18)	P-value (All Acute vs Subacute
Paralysis *	7.04%	2.27%	5.56% ?!	1
Stroke *	5.63%	4.55%	0	1
New Renal Failure	8.45%	6.82%	0	0.61
Retrograde Type-A Dissection	8.45%	6.82%	5.56%	1
30day Mortality	12.7%	9.09%	0%	0.21
OVERALL	39.4%	29.5%	11.1%	0.05

- *Are those that rAD the same that rupture?*

KING'S HEALTH PARTNERS

“At Risk”

- *Uncomplicated but likely to complicate*
  - In whom a 2 week delay is disadvantageous
  - The (current) assumptions/opinion:
    - Delayed (2 weeks – 3 months) TEVAR carries a lower risk of retrograde dissection than immediate TEVAR, but remains effective in re-modelling the aorta
    - Early TEVAR reduces the risk of aorta-related death over the long term
    - (Early TEVAR reduces the need for complex surgery over the long-term)

KING'S HEALTH PARTNERS

Opinion

- If you were goir
  patient with an
  acute type b dis
  timescale would
  thoracic endova
  aneurysm repai

March 2016 Updates 27

IRAD data suggest that expanding use of TEVAR reduces long-term aorta-related complications for type B dissection

With 2016 being the 20th anniversary of the International Registry of Acute Aortic Dissections (IRAD), Kim Eagle, Walter Hewlett Professor of Internal Medicine and director of the Frankel Cardiovascular Center at the University of Michigan Health System, Ann Arbor, USA, and senior investigator of IRAD talks to *Vascular News* about the key findings from the registry.

IRAD was established in 1996, and currently has 43 large referral centres in 13 countries participating in the registry. What do you think are the most important data to have emerged from the registry so far?

The registry has provided so much information that has illuminated the field. As a database of over 6,000 patients, it has provided the most reliable information on how acute aortic dissection presents, how it is currently managed and how patients do both in the short and long term. A new classification system according to time of onset of symptoms until the patient has been seen was published just last year. IRAD has also allowed us to see the influence of advances in treatment on outcomes. Over twenty years of study, the mortality of type A dissection has improved as surgeons around the world have been willing to operate on increasingly complex patients. Similarly, IRAD suggests that for type B dissection, the expanding use of thoracic endografts is reducing long-term aorta related complications.

What are the risk factors for acute aortic dissections?

The typical risk factors are old age, hypertension, a history of prior heart or aortic surgery, known aortic aneurysm, inherited disorders like Marfan syndrome or bicuspid aortic valve disease, repeated cocaine exposure, and possibly pregnancy in at-risk young women.

In the light of current data, are the terms "acute" and "chronic" with regard to dissection still relevant? Is there a proposal for a different temporal classification to guide management?

Our new IRAD classification system places patients into four groups based on time to presentation: "hyperacute" patients, present within the first 24 hours and have a mortality of 18% for type A dissection without surgery; "acute" patients present from day two through seven and have an additional mortality of 20% for this period if not operated; "subacute" patients present from day eight to 30 and have an additional mortality of 10%; and chronic patients present after day 30 and we see that mortality flattens out.

Management of type B acute dissection has remained challenging. In your view, what constitutes a complicated type B dissection?

Complicated type B can be defined in several domains but would include: rupture or impending rupture; malperfusion of an extremity or vital organ; unremitting pain or hypertension; and imaging evidence of progressive aortic expansion in spite of good medical treatment or dissection extension.

University of Michigan Health System

Kim Eagle

There has been some suggestion of the benefit of TEVAR when compared to optimal medical therapy alone for uncomplicated type B dissection patients. What is your view on the place of TEVAR in managing these patients?

IRAD data are consistent with a potential late benefit (after 1–2 years) in reducing aorta-related complications as a result of stent graft therapy. While I believe that we need a large randomised trial to definitively answer this question, data so far are suggesting that TEVAR promotes aortic remodelling which reduces the size and risk of rupture of the false lumen and promotes a larger and healthier true lumen.

There were new IRAD working groups launched in 2010. One of these is a dynamic imaging working group set-up to update the way in which IRAD utilises imaging results. How has the use of more modern imaging algorithms informed the evaluation of the IRAD data?

We believe that imaging has the potential to provide much more prognostic information than we have garnered in the past, and the methods which more clearly define fluid dynamics, aortic wall biology, and subtle changes in size and morphology measured over time will allow a more personalised approach to treatment and follow-up. This is the promise of new imaging techniques and protocols. IRAD seeks to capture this increased granularity of information in updated case-report forms.

Today, what are the main questions that you still have in your research into acute aortic dissections?

There are so many! As examples: Will endovascular treatment allow non-open surgery for a proportion of type A dissections? Will TEVAR become the standard of care for type B dissection? How will we develop more personalised follow-up plans for an individual? Will genetics and proteomics allow better prevention, diagnosis and treatment for dissection? How will we find "at-risk" patients in the future? What medical treatment will be optimal for the prevention of post dissection complications? With our interventional working group, we hope to delineate optimal methods of cannulation, brain and spinal cord protection, optimal endovascular stent strategies, the role for hybrid approaches, and many other critical questions.

ndicates that
a stable course
icated type B
est using a
y of 3 months
ection for

ients with
ns or
of pain
rvention
rary stent
stent grafts
open

KING'S HEALTH PARTNERS

Is This *OPINION* Evidenced?

- Intervention Gains
  - ADSORB
    - Underpowered
    - ?Value of endpoint
      - (thoracic aortic re-modelling)
  - INSTEAD
  - INSTEAD-XL
    - Entry = 14 days
    - ?Case selection/Events
      - 4/7 OMT + TEVAR deaths should not have been enrolled
    - No survival gain at original design
    - Re-modelling/Reduced intervention long-term

Remodelling & Reducing Complexity

My mother says…

- A *stent* in time saves nine!
- But it isn't true!
  - DeBakey IIIa unlikely to need complex solutions
  - Debakey IIIb visceral segment dilation unaffected by TEVAR

KING'S HEALTH PARTNERS

- “F the ab se **of**

(Guy’ -50)

KING'S HEALTH PARTNERS

Our Current Tools & Their Problems

- Malperfusion
- Pain
- Rapid Growth
- Resistant Hypertension

  – All dynamic & potentially subjective

  – Any other tools?

My (current) Opinion…

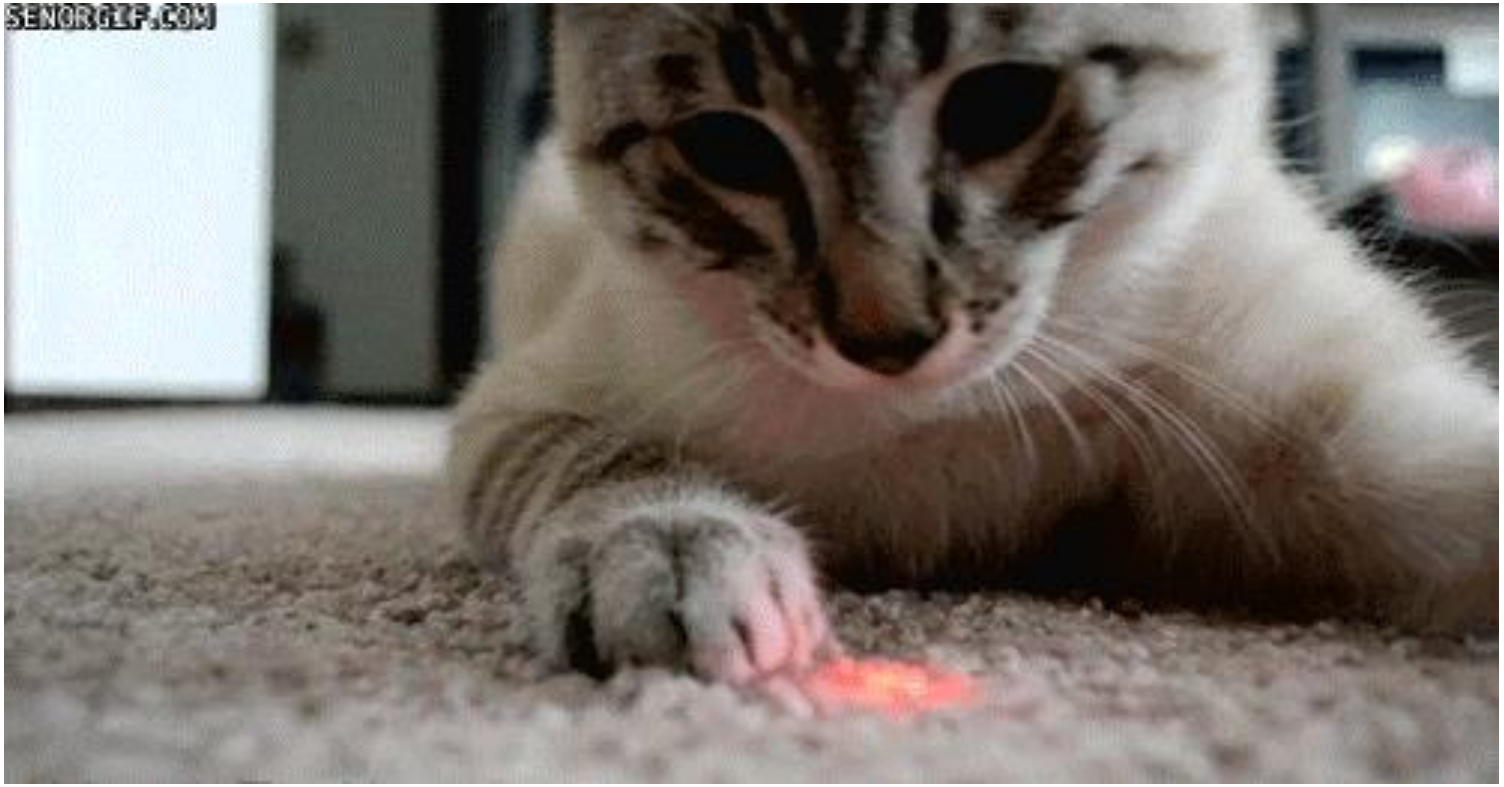
- **Intervention Gains**
  - Acutely - Minimal/Anecdotal
  - Long-term - Possibly net gain for DeBakey IIIa treated after 14 days (a small subset)
  - Others…?
- **Intervention Risks**
  - Real enough!

- In a world of incremental gains….
  - (selection is everything)

KING'S HEALTH PARTNERS

The Current Solution – MICO!

Masterly Inaction and Cat-like Observation



KING'S HEALTH PARTNERS

MICO – Where/Who By?

Monitoring:

- Specialist aortic centre
- Admitted to HDU/ICU
- Arterial line
- Urinary catheter
- Serial (gated) CTA

Initial Treatment – (to agreed goals):

- Intravenous β blocker – Labetalol
- Calcium channel antagonist
- Aim for SBP < 90mmHg(?) and pulse ≤ 60bpm
- Hypertension team involvement
- Pain relief

Definitions…

- There is no…
  - Evidence
  - Consensus
- *"You know it when you see it"*
  - *Not good enough!*

KING'S HEALTH PARTNERS

…time for a (Lille) consensus document for reporting standards?

(…there are precedents...)

KING'S HEALTH PARTNERS