

Identifying a research question

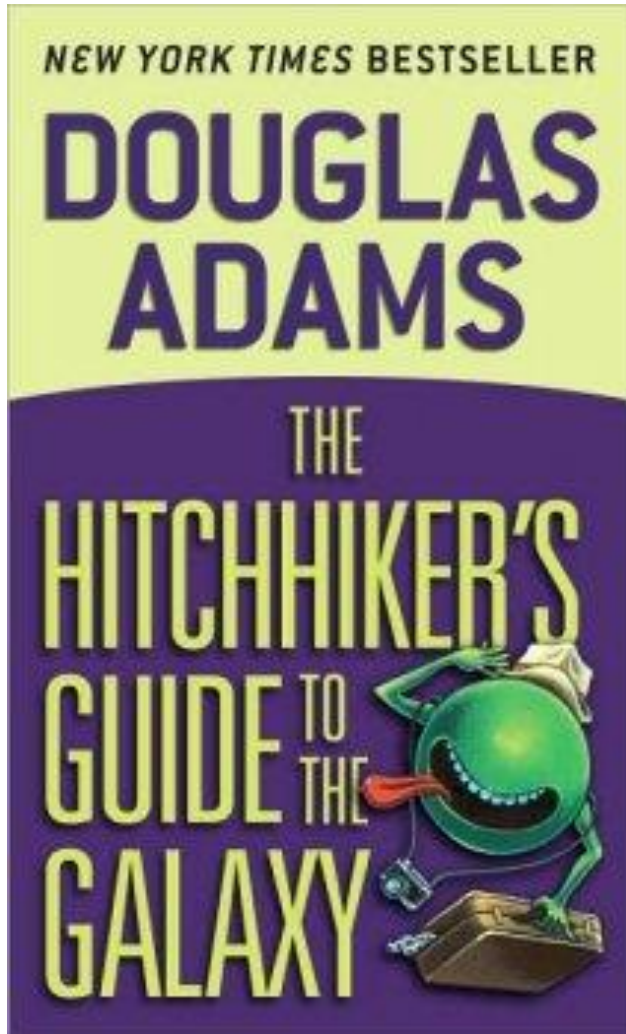


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The all important research question



The answer to life, universe
and everything is...

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The prerequisites for good research

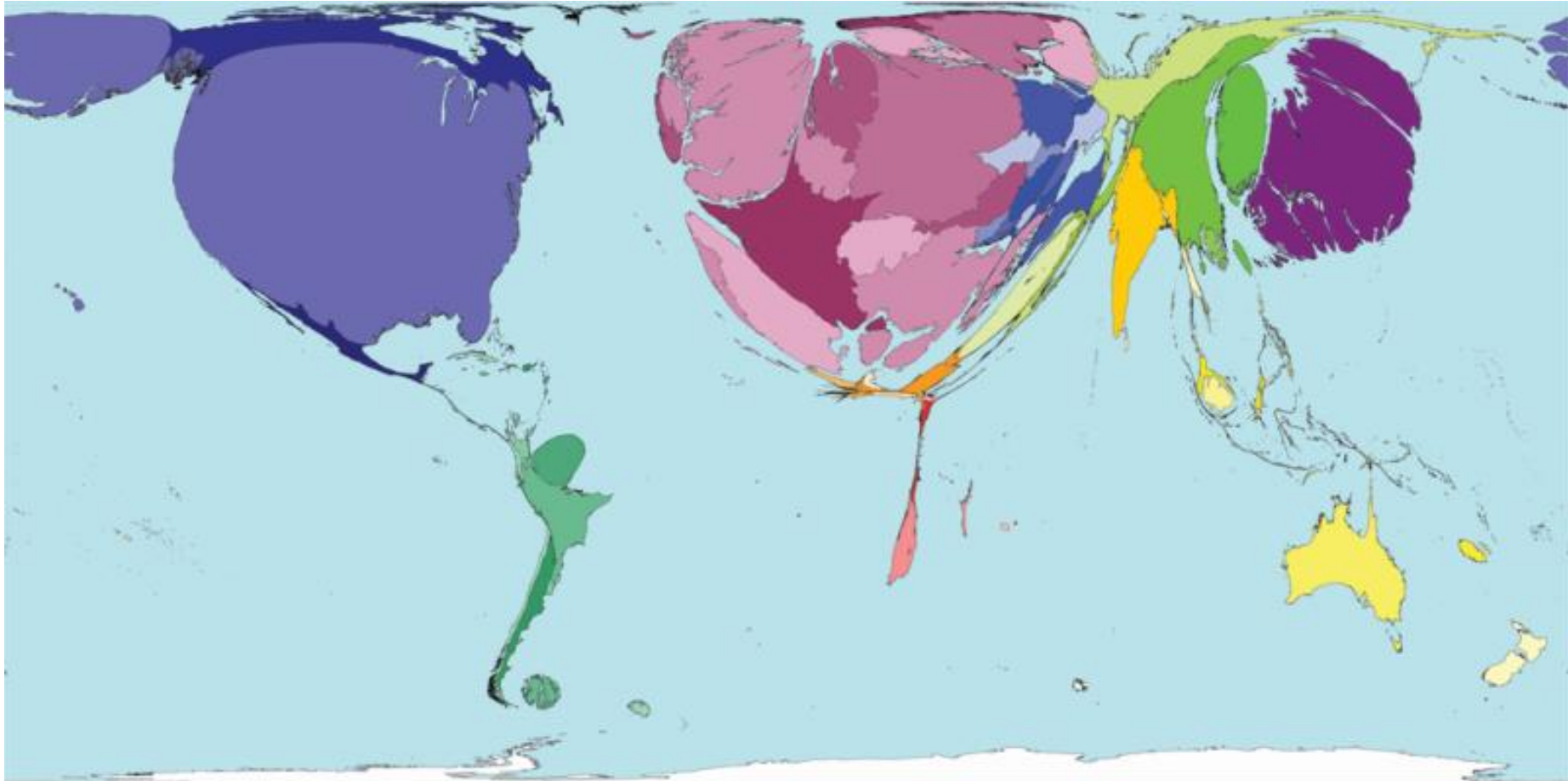
1. Ask a patient-important question
2. Answer it reliably

What is a good research question?

1. It should address a common, or locally relevant disease condition
2. Should be clear about what you wish to know about the disease
3. Ideally, what you find should impact clinical practice

Clinical practice research

Why study locally relevant diseases?



Genesis of the question

- Clinical experience
- Gaps identified in literature
- Discussion with other researchers at professional meetings/conferences
- Discussion with mentor
- Brainstorming/Journal clubs
- Imagination: idea-based research

The purpose of the question should be clear

Research question	Objective
What proportion of the population are living with the disease? (any outcome of a disease)	Prevalence (burden)
What proportion of patients experience the outcome	Incidence/Prognosis
What could be the cause of this problem ?	Etiology
What are the risk factors associated with the outcome	Risk factor analysis Prognostic factors
How good is the test in detecting the disease?	Diagnostic tests
Is this treatment/treatment strategy effective?	Therapy

The purpose of the question should be clear

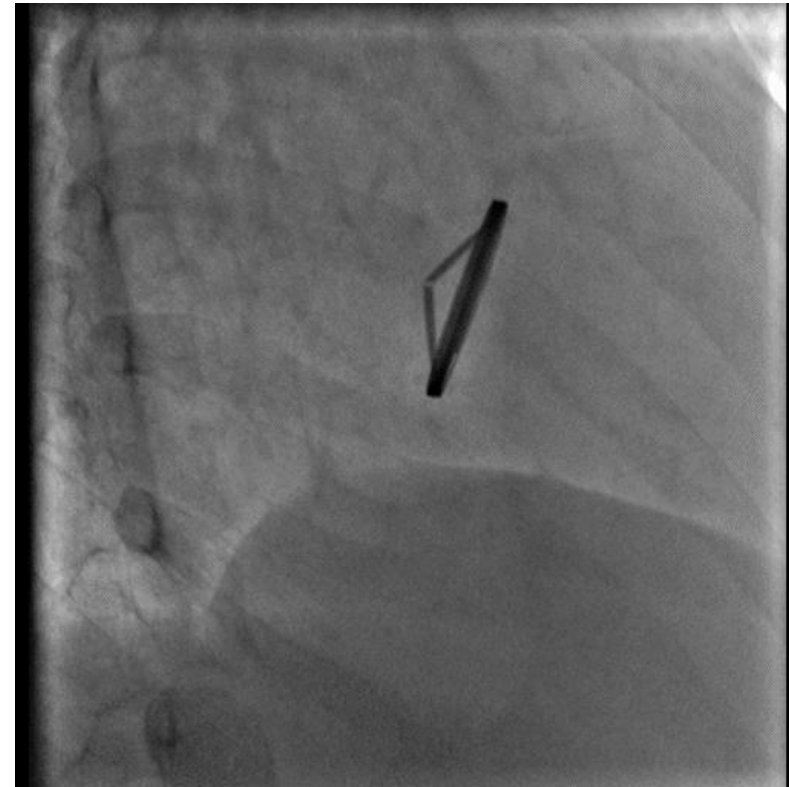
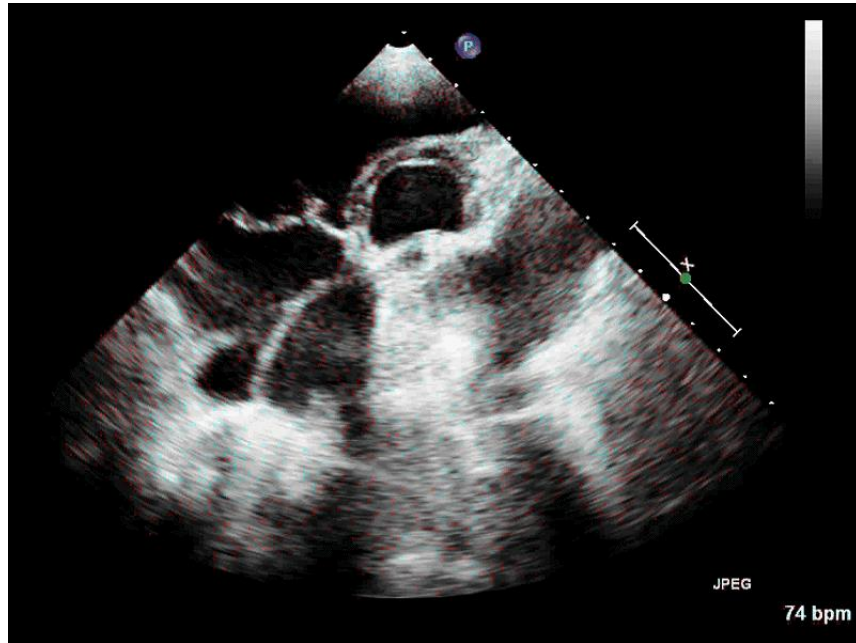
Research question	Objective	Study design
What proportion of the population are living with the disease?	Prevalence (burden)	Cross-sectional study
What proportion of patients experience the outcome	Incidence/Prognosis	Prospective cohort
What could be the cause of this problem?	Etiology	Cohort
What are the risk factors associated with the outcome	Risk factor analysis Prognostic factors	Cross sectional, case control, Cohort (prognostic)
How good is the test in detecting the disease?	Diagnostic tests	Cross-sectional
Is this treatment/treatment strategy effective?	Therapy/preventive strategy	Quasi experimental/ Randomized trials

Feasibility over idealism

- Do you have the time?
- Do you have the support of colleagues, students and superiors?
- Who will give you the money?

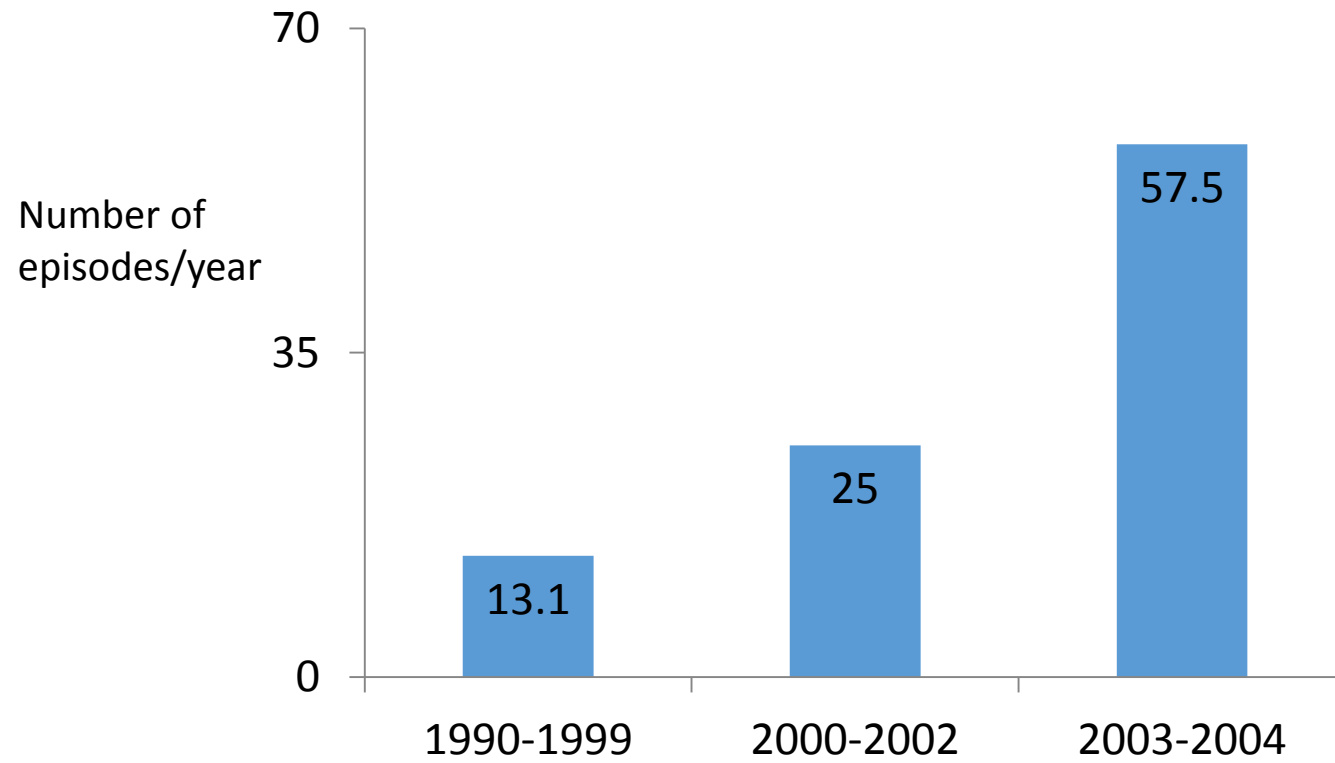
- Short-term vs. long-term studies: Get some quick runs on the board!
- Doing systematic reviews is also research

A unique and serious problem

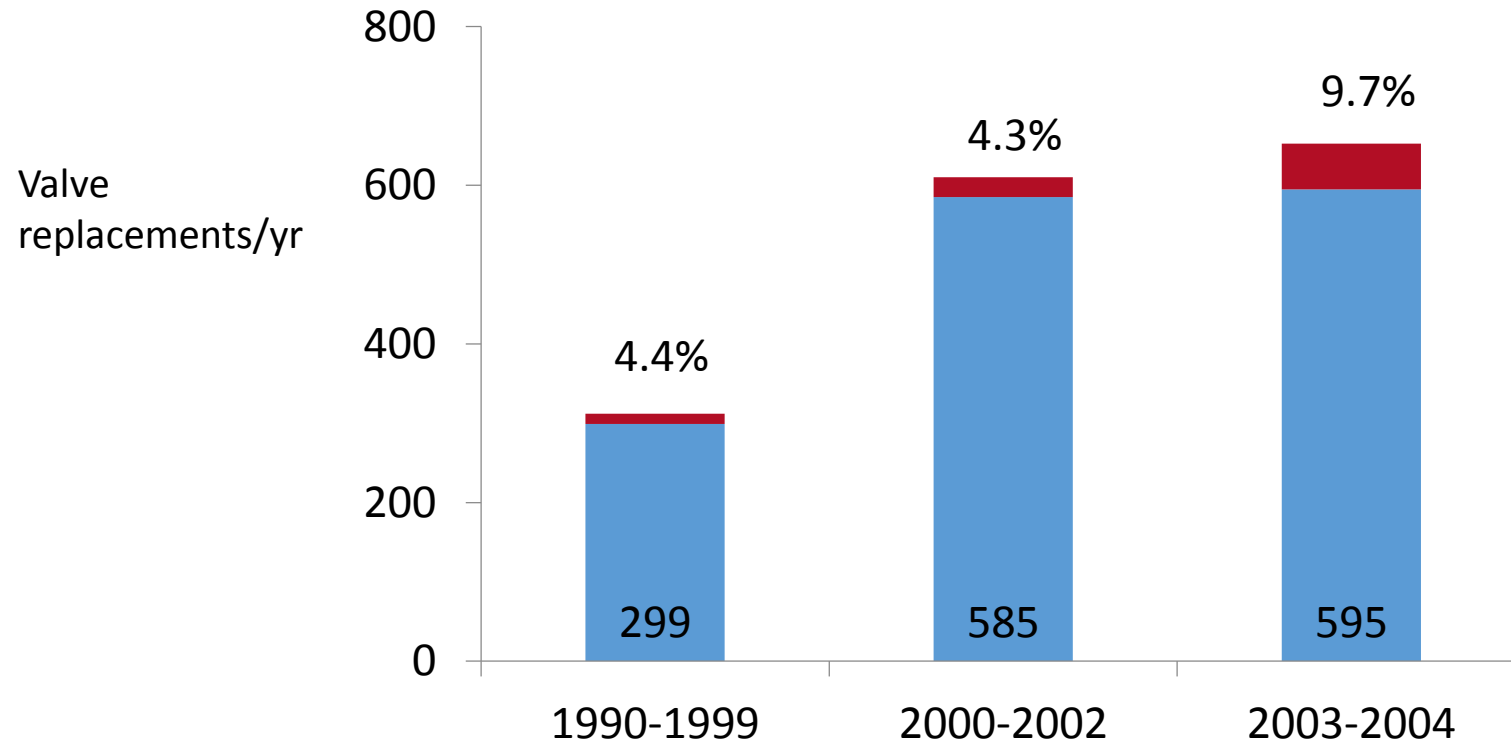


60-70% of cases due to sub-therapeutic anticoagulation

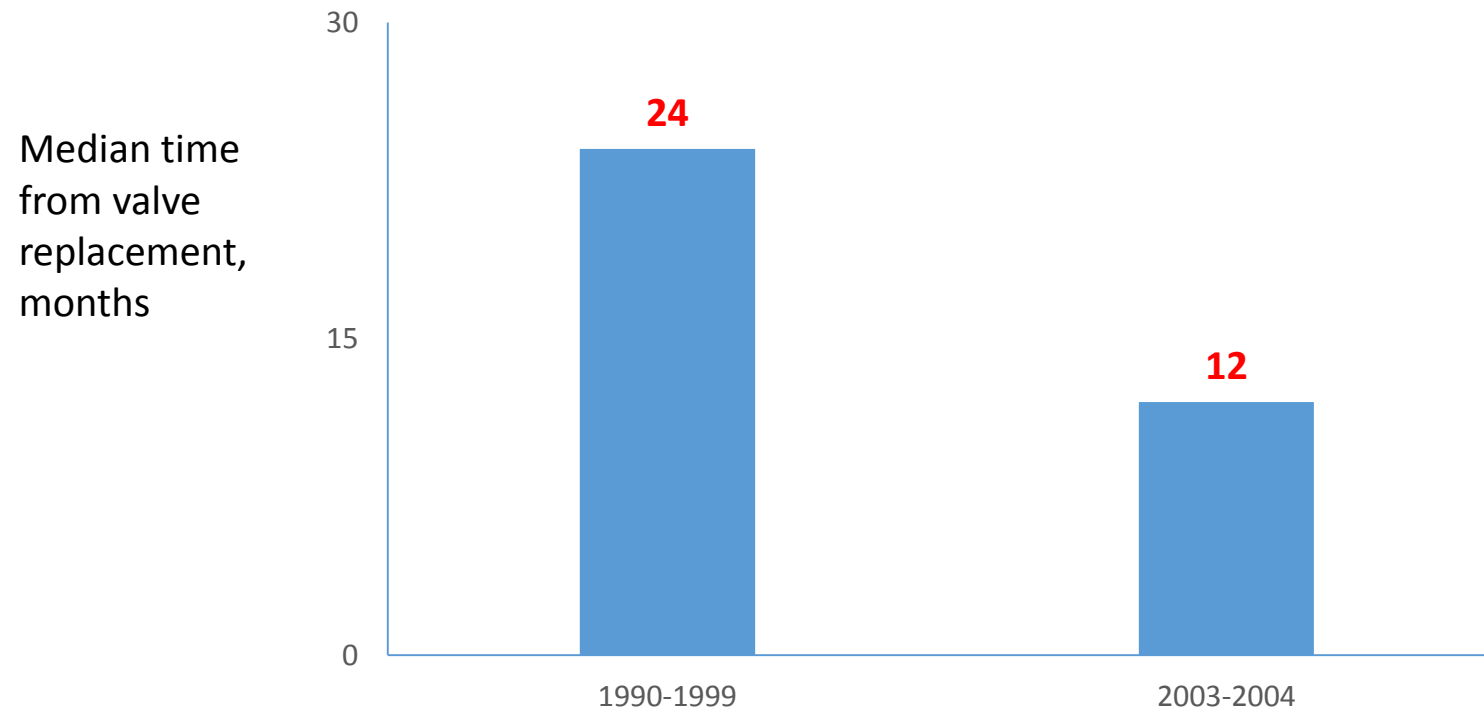
Is PVT increasing?



Is PVT increasing?



Is PVT increasing?



Why is PVT occurring early?

Admissions for left sided PVT between January 2003 through December 2004

Data obtained from review of case records and operation notes

Patients divided into those who presented

≤ 6 months and > 6 months after MVR

Univariable and multivariable analysis

Why is PVT occurring early?

	Chordal Preservation (n = 59)	No Chordal Preservation (n = 17)
Early PVT	28 (47.4%)*	2 (11.8%)*

* $p = 0.006$ for the comparison

Does recurrent PVT have a poorer response to treatment?

Extent of response	Haemodynamic			Clinical		
	First episode	Recurrent episodes	p Value	First episode	Recurrent episodes	p Value
Complete	36 (73.5)	15 (57.7)	0.16	33 (67.3)	13 (50)	0.14
Partial	7 (14.3)	5 (19.2)	0.82	10 (20.4)	7 (26.9)	0.72
Failure	6 (12.2)	6 (23.1)	0.37	6 (12.2)	6 (23.1)	0.37
Clinical failure						
Death				3 (6.1)	1 (3.8)	0.57
Stroke				3 (6.1)	6 (23.1)	0.04
Major bleed				0	1 (3.8)	–
Major complications and death				6 (12.2)	8 (30.7)	0.05
Minor bleed				2 (4.1)	1 (3.8)	0.725

What is the true success rate of fibrinolytic therapy for PVT,
and can we improve this?

Valvular Heart Disease

Accelerated Infusion of Streptokinase for the Treatment of Left-Sided Prosthetic Valve Thrombosis

A Randomized Controlled Trial

What is the true success rate of fibrinolytic therapy for PVT, and can we improve this?

Outcome	Frequency, n (%)	95% confidence interval of proportion*
Death, major bleeding, embolic stroke or non-CNS systemic embolism	20 (16.7)	12.5-20.9
Death	9 (7.5)	4.5-10.5
Embolic stroke or non-CNS systemic embolism	6 (5.0)†	2.5-7.5
Major bleeding	11 (9.2)	5.9-12.5
- Intracranial bleeding	5 (4.2)	1.9-6.5
- Other major bleeding	6 (5.0)	2.5-7.5
Minor bleeding	13 (10.8)	7.3-14.3
Fever during streptokinase infusion	56 (46.7)	41.0-52.4

* Confidence intervals were adjusted for sampling from a finite population

†One patient had coronary embolism

Analyses on the intention-to-treat population (n=120)

Rate of complete clinical response with SK was 59%

The rate of response with the standard SK protocol was only 53%!

How should we treat PVT then?

Varying guideline recommendations

Guideline	Surgery	FT	Intensification of anticoagulation
Society for Heart Valve Disease, 2005 ⁶	Only if FT contraindicated or has failed	For all patients (class I recommendation)	May be considered in patients with thrombus < 5 mm in length on TEE
European Society of Cardiology, 2012 ⁸	All critically ill patients without serious comorbidity (class I, C), large (>10 mm) non-obstructive thrombus with embolism (class IIa, C), persistent thrombus despite optimal anticoagulation	Critically ill patients with serious comorbidity, or impaired cardiac function before developing valve thrombosis, or if surgery is unavailable	Intravenous UFH ± aspirin if inadequately anticoagulated
American College of Cardiology, 2008 (Update) ⁷	For all patients in NYHA class III-IV or those with large clot burden (class IIa, C)	NYHA class I, II patients with low clot burden (class IIb, C); all others if they are at high risk for surgery or if surgery is unavailable	Intravenous UFH in patients who are class I, II with low clot burden (class IIb, C)
American College of Chest Physicians, 2012 ⁹	All patients with thrombus area $\geq 0.8 \text{ cm}^2$ on TEE (grade 2C)	All patients with thrombus area $< 0.8 \text{ cm}^2$ on TEE; all others if they are at high risk for surgery (grade 2C)	For very small non-obstructive thrombi, intravenous UFH monitored by serial echocardiography (grade 2C)

Is urgent surgery better than FT?

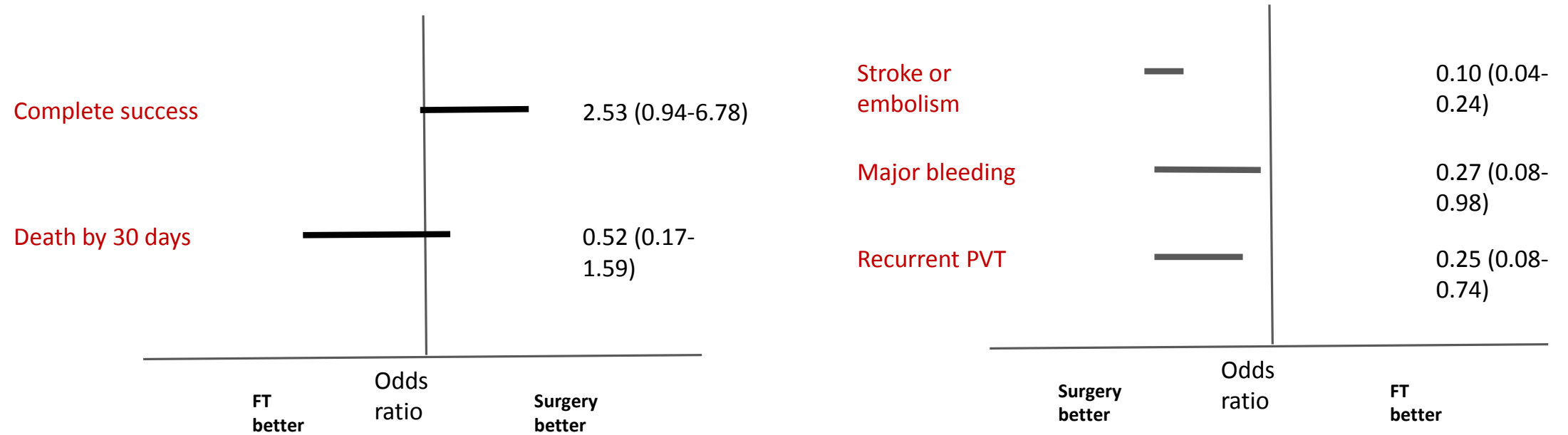


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CLINICAL RESEARCH

Urgent surgery compared with fibrinolytic therapy for the treatment of left-sided prosthetic heart valve thrombosis: a systematic review and meta-analysis of observational studies

Is urgent surgery better than FT?



Clinical impact of focused research

The 2014 ACC/AHA Guidelines on Management of Valve Disease

Class I

- 1. Emergency surgery is recommended for patients with a thrombosed left-sided prosthetic heart valve with NYHA class III to IV symptoms (610, 611, 613). (*Level of Evidence: B*)**

Prompt surgical treatment of a thrombosed prosthetic heart valve is an effective treatment to ameliorate clinical symptoms and restore normal hemodynamics, with a success rate close to 90% in patients who do not have a contraindication to surgical intervention. In contrast, a meta-analysis of 7 studies that included 690 episodes of left-sided prosthetic valve thrombosis showed a success rate for restoring normal valve function of only about 70% in 244 cases treated with fibrinolytic therapy. There was no difference in mortality between surgical and fibrinolytic therapy for left-sided prosthetic valve thrombosis, but in addition to a higher success rate for restoring normal valve function, surgery was associated with lower rates of thromboembolism (1.6% versus 16%), major bleeding (1.4% versus 5%), and recurrent prosthetic valve thrombosis (7.1% versus 25.4%). Although RCTs have not been performed, the weight of the evidence favors surgical intervention for left-sided prosthetic valve thrombosis unless the patient is asymptomatic and the thrombus burden is small.

Supporting References: (605, 613, 614)

RCT comparing urgent surgery with FT - SAFE-PVT (NCT01641549)

Summary

The key to doing fulfilling clinical practice research is to identify a “good” research question

The research question must be

- Important (locally relevant)
- Interesting
- Answerable (feasibility over a reasonable period of time)

Heart Asia

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issues*



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