Catheter-directed thrombolysis for acute deep vein thrombosis
van Schouwenburg, Inge M.; Kooistra, Hilde; Veeger, Nicolaas; Meijer, Karina

Published in:
LANCET

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2012

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
Queen Mary: nobody expects the Spanish Inquisition

Three timely Offline columns by Richard Horton describe a mindless managerial rampge spreading through Queen Mary University of London, UK. Barts and The London, Queen Mary’s School of Medicine and Dentistry, has declared distinguished medical researchers to be at risk of redundancy. Queen Mary’s School of Biological and Chemical Sciences now follows suit. As we write, colleagues declared to be “at risk” just 2 weeks ago are summoned individually to closed audiences with the Head of School, attended by members of the ironically named “Human Resources” (HR) department. If targeted individuals fail to appease the inquisitor, they will be sacked. Other staff members are earmarked for demotion, with replacement “Teaching and Scholarship” contracts that will oblige them to desist from independent research.

But, one might ask, is it not high time to weed out slackers? It might help if one had any way of knowing who they are. Sadly, the “restructuring” hits exactly the wrong targets in many cases, and leaves unproductive academics unscathed. The reason is simple—the Head of School and HR have neither interest in, nor understanding of, individuals’ research, still less their research potential. This slaughter of the talented relies entirely on a carefully designed set of retrospective counts of the uncountable. These are labelled research “metrics”.

Are we here engaged in special pleading? Actually, no. Our school has a reputation, envied worldwide, for research by individuals now for the chop. Their retrospective crimes, committed between 2008 and 2011, include too few publications as a “significant” author in high-impact journals, and below-average external funding. Where the baseline of research income derived from the Higher Education Funding Council for England has disappeared, no-one seems to know. So, we are looking at the end of the road for unique and internationally leading-edge Queen Mary research. Among many outstanding projects we stand to lose are: sociogenomics of mole rats, the only eusocial mammals, and a model, incidentally, for the endocrinology of bullying; genetics of circadian rhythms and iron homeostasis from experiments on fruit-flies; imaging of neural activity in zebrafish—a paradigm for vertebrate development; and heterogeneous catalytic oxidation and carbon–carbon coupling in inorganic chemical synthesis. The list is long. Alas, there are no boxes to tick for advances in knowledge and understanding—no metrics for science itself.

Over in the Medical and Dental School, the grand inquisitor is identified as the Dean for Research, whose own research credentials are, naturally, unavailable for scrutiny. Yet, never mind, we now have the assurance from his colleague that “Each and every faculty member of the college was assessed in this process and from my own personal point of view it was done fairly...”2 What needs evidence in the face of such assurance? “Consequently, to pick him out for criticism in this disgraceful manner is quite iniquitous,”3 Yet the Dean managed to pick out others—for oblivion, not just criticism. And he got it wrong.4

The same double standard follows, now, in our School of Biological and Chemical Sciences. For example, one of the “metrics” for research output at professorial level is to have published at least two papers in journals with absolute reduction in the risk of post-thrombotic syndrome in patients on CDT to thrombolysis. Besides additional treatment, CDT is recommended in assigning the 14.4% reduction in the risk of post-thrombotic syndrome in patients on CDT to thrombolysis.

Catheter-directed thrombolysis for acute deep vein thrombosis

Tone Enden and colleagues’ randomised trial of catheter-directed thrombolysis (CDT) in patients with high proximal deep vein thrombosis (Jan 7, p 31) is well designed and the results have been eagerly awaited. However, we feel that caution is recommended in assigning the 14.4% absolute reduction in the risk of post-thrombotic syndrome in patients on CDT to thrombolysis.

Besides additional treatment, CDT patients were more compliant with wearing compression stockings than were patients who did not receive CDT. Although the difference in compliance of 11.8% is not significant, it is relevant. Daily use of compression stockings reduces the risk of post-thrombotic syndrome by 50%.2,5

On the basis of this number and
the incidence of post-thrombotic syndrome in Enden and colleagues’ study, we calculate an expected absolute risk reduction in CDT patients of 4%, owing to better compliance with compression stocking use.

Furthermore, more CDT patients than non-CDT patients had good-quality anticoagulant treatment at both follow-up points. Oral anticoagulant treatment that achieves an international normalised ratio within the therapeutic range reduces the risk of post-thrombotic syndrome by 63% compared with patients who spend more than 50% of time beneath the therapeutic range.4 Unfortunately, time in therapeutic range was not reported in Enden and colleagues’ trial and was not accounted for in examining the effect of CDT on post-thrombotic syndrome.

The CDT strategy, with its more intense treatment and hospital admission, does seem to improve outcome. However, this might not be the effect of additional thrombolysis. Instead, it could be due to more intense initial patient support, which results in more awareness of the relevance of treatment compliance. We feel that taking treatment compliance into account is important before coming to conclusions about the effect of thrombolysis on post-thrombotic syndrome and before exposing patients to costly and invasive procedures.

We declare that we have no conflicts of interest.

Inge M van Schouwenburg, Hilde A M Kooistra, Nic J G M Veeger, *Karina Meijer
k.meijer@umcg.nl
Division of Hemostasis and Thrombosis, Department of Hematology, University of Groningen, University Medical Center Groningen, 9713 EZ Groningen, Netherlands (IMvS, HAMK, NJGMV, KM); and Trial Coordination Center, Department of Epidemiology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands (NJGMV)


Tone Enden and colleagues, in their CaVenT trial,4 explore the interesting hypothesis of catheter-directed thrombolysis (CDT) in the prevention of post-thrombotic syndrome. We have several comments.

In the Introduction section, reference to the updated Cochrane review1 as suggesting a benefit of systemic thrombolysis in prevention of post-thrombotic syndrome comes with the caveat that the only study with a Jadad score of greater than 3 showed no benefit.3

The CaVenT trial was done in four specialised centres, and hence the outcomes might be very different elsewhere. Additionally there might have been a learning curve for optimum results with CDT; hence it would be interesting to have a comparison of those who entered the trial earlier versus those who entered later.

Enden and colleagues do not present the bleeding rates (if any) for the control group, and hence a number needed to harm is not available. Also, the rate of stent placement and its association with outcomes would have been interesting, especially in view of scant evidence available on the topic.4

The limitations of the open-label design might have manifested with an obvious greater adherence to oral anticoagulation in the CDT group at 6 months. Finally, Enden and colleagues imply a cost effectiveness with CDT, citing the cost associated with post-thrombotic syndrome; however, it would be interesting to assess the expense associated with CDT and other indirect costs associated with the longer hospital stay necessary.

We declare that we have no conflicts of interest.

*Saurav Chatterjee, Abhishek Sharma
sauravchatterjee@gmail.com
Maimonides Medical Center, Brooklyn, NY 11220, USA


Authors’ reply
Both sets of correspondents raise an issue about whether the noted absolute reduction in post-thrombotic syndrome of 14·4% in patients treated with additional catheter-directed thrombolysis (CDT) could be attributed to the thrombolytic treatment alone, since a higher proportion of these patients reported daily wear of elastic compression stockings and had international normalised ratios within the therapeutic range.

We agree that the non-significant tendency to better compliance could be attributable to the inherent risk of bias of this open-label randomised controlled trial, and relevance to the noted effect size cannot be ruled out. However, we think the effect on post-thrombotic syndrome cannot be simplified as suggested by Inge van Schouwenburg and colleagues. First, the two landmark studies on the use of elastic compression stockings1,2 reported on patients with any level of proximal deep vein thrombosis (DVT) from the popliteal vein and up, whereas our patients had a high proximal