The Adams-Stokes Syndrome
Robert Adams, MD, and William Stokes, MD, were both major figures in the influential Irish school of medicine in the 19th century. Twenty years apart, they independently described the classic description of heart block that bears their names.

Viewpoint: Thrombolysis or Angioplasty in the Real World: a UK Perspective

Nick Curzen, PhD, FRCP, FESC, writes about the issues surrounding the design of treatment for acute myocardial infarction in a modern health service.

Never has the challenge of disentangling a real-world policy for delivery of care from the mass of published data been better illustrated than in the context of ST elevation myocardial infarction (STEMI).

In the face of an enormous collection of heterogeneous — and often apparently discrepant — evidence we are attempting to produce pathways of optimal care for STEMI patients within our immediate catchment population and from surrounding areas within our cardiac network.

This challenging task is shared by colleagues across the United Kingdom. It is undertaken in the context of a Department of Health national initiative to train ambulance personnel to deliver prehospital thrombolysis (PHT). This initiative represents an important financial and time-consuming investment, and can be tampered with only after careful consideration.

The task also takes place in the context of widespread clinical overperformance relative to the level of economic support provided. In this climate, the degree of scrutiny about the potential financial implications of any “new” treatment (if primary percutaneous coronary intervention [PCI] can really be described as new) is intense.

So, for a centre like the Wessex Cardiac Unit, which serves its own immediate catchment population but also acts as a regional referral centre, what is the best way to treat patients presenting with STEMI? Between July and December 2005, there were 94 acute STEMI admissions generated from the immediate catchment population. Of these admitted patients, 26 (28%) had primary PCI (PPCI) (often as part of the ongoing Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events (FINESSE) trial (investigators Ellis SG, Armstrong P, Betriu A, Brodie B, Herrmann H, Montalescot G, Neumann FJ, Smith JJ, Topol E) and 53 (56%) had thrombolysis, of whom 77% also had subsequent PCI during this index admission.

Perhaps, then, it is clear-cut: all these patients should surely be transferred to a catheter lab as quickly as possible for primary angioplasty, particularly since most end up having PCI during the admission anyway. If this is the case, should we then ask our paramedics to forget their newly acquired PHT skills? Can we be confident, however, that our call-to-balloon time performance will justify ignoring the benefit to be derived from the reduction in call-to-needle time achieved by a successful PHT programme? How likely is it anyway that there will be a single answer suitable for all patients, given the variability of distances they will have to travel to reach care?

The literature is substantial in terms of volume and variety. However, interpreting this large body of evidence is complex, challenging, and pregnant with the risk of personal bias. That is to say, to an interventionist, primary angioplasty must be better. Furthermore, some classic pitfalls of data interpretation can be expected. Four examples are (a) applying data from randomised studies that have excluded many more STEMI patients than they have included, to a real life population; (b) significant relative reductions in combined endpoints that turn out to be driven by only one endpoint difference, such as reinfarction in the thrombolyis versus “transfer for PCI” trials; (c) the importance of crossover between study groups, particularly when thrombolytic patients subsequently undergo PCI anyway; and (d) interpreting older evidence in the context of new trial data, such as REACT or ASSENT-4.

Given such pitfalls, upon what can this important strategic judgement about STEMI treatment be based? First, it is fundamentally clear that the prime objective in STEMI is to re-establish complete perfusion after thrombolysis in myocardial infarction (TIMI 3 flow) as soon as possible because this correlates with the greatest mortality reduction. Second, even the best thrombolytic therapy achieves TIMI 3 flow in only about 60% of patients, and this represents an important limitation for a therapy that cannot address the underlying inflamed plaque. In addition, the rate of early (13%) and 30-day (30%) reocclusion of the infarct-related artery following thrombolysis is substantial.
Third, meta-analysis of PPCI versus thrombolysis trials demonstrates mortality advantage, as well as significant reductions in other important endpoints, such as stroke, for PPCI.7

Fourth, a series of randomised trials have demonstrated a significant advantage of PPCI, even in STEMI patients who have to be transported some distance to the revascularisation facility, compared to local thrombolysis.5,8,9

Fifth, a substantial proportion of patients treated with thrombolysis require either urgent PCI or in-hospital PCI or has subsequent outpatient angiography and revascularisation. For example, 35% of the PHT group in the CAPTIM study15 required rescue angioplasty, and in total 68% were revascularised within a year.

Given these 5 strands of evidence, the case for PPCI appears straightforward. However, when we take into account the financial and logistical boundaries of the system within which we work, this is not necessarily true. To recommend switching to PCI would be to ignore data that are particularly relevant to the real-life setting dominated by time.

First, the delivery of PHT has unequivocally been shown to improve outcome compared with hospital thrombolysis. This finding reflects the substantial time saving that it incurs, whether in randomised trials or in real-life registry, and the sensitivity of the relationship between reperfusion and outcome. For example, a meta-analysis of 6 studies comparing PHT with hospital thrombolysis demonstrated an overall time-saving difference of 58 minutes between the 2 strategies.12

Second, it appears difficult to do better clinically than adequate reperfusion by thrombolysis within an hour of symptom onset, as demonstrated, for example, by the Myocardial Infarction Triage and Intervention (MITI) trial.13 Realistically, this target is most likely to be achieved by a paramedic’s needle.

Third, accumulated data from a variety of studies suggest that we underestimate real-life door-to-balloon time, and that interventionalists certainly do (conveniently) underestimate the relationship between delay in door-to-balloon time and outcome.14

Fourth, it is now proven that patients who fail to reperfuse with thrombolysis after 90 minutes have a significantly better outcome if they then undergo rescue PCI compared with rethrombolysis or conservative treatment.15

Scrutiny of the data from the real world, such as a registry of 1922 patients, is particularly persuasive of the outcome advantages of PHT.16 In this paper, in-hospital mortality was 3.3% for PHT, 8% for in-hospital thrombolysis, 6.7% for PPCI and 12.2% for no reperfusion therapy. The figures were 94%, 89%, 89%, and 79% for 1-year survival, respectively.

Furthermore, a multivariate analysis of risk factors related to 1-year survival showed that PHT was associated with a relative risk of death of 0.49. Significantly, in those patients who had PHT and were admitted within 3.5 hours, the in-hospital death rate was 0% and the 1-year survival was 99%. Coupled with older data that indicate good outcome from a strategy combining thrombolysis with PCI as required,17,18,19 there is a persuasive argument that we should take the pragmatic approach of recommending PHT followed by PCI as necessary.

This is certainly an attractive management approach for patients who cannot get to a catheter laboratory rapidly, and is supported by data from trials including SIAM-III20 and GRA-CIA-1.21 These trials are the foundation for international guidelines by the European Society of Cardiology recommending that all patients who receive thrombolysis, regardless of whether it is “successful,” should undergo angiography and, where appropriate, PCI within the first 24 hours.22 Such an approach has the seductive advantage of offering equitable treatment across the board to all STEMI patients.

Finally, achieving PPCI with call-to-balloon times that are included in trials is only possible for some of our patients. Data from the United States illustrate this problem clearly.23 We run the risk, if we switch to PPCI for all patients, of delivering a “superior” therapy so late that it has become inferior!

The answer to the dilemma here in Southampton is that for now we allow pragmatism to dominate, and recommend treatment that varies according to the individual patient’s circumstances. For patients with very early access to a trained paramedic crew, PHT followed by either rescue PCI at 90 minutes or “elective” PCI the following day is a good strategy. By contrast, for the patient who arrives in the accident and emergency (A&E) department at a revascularisation centre with a several-hour history, urgent PCI is the preferred strategy (see Figure).

For the patient who has a history going back several hours, we propose to let the paramedic crew make the decision about PHT or “scoop and run” for PPCI based upon their estimated delivery time to the hospital.

Finally, for the patient attending A&E in a non-revascularisation centre, we propose thrombolysis with either emergency transfer for rescue PCI for failed reperfusion at 90 minutes or elective transfer over the next 24 hours for PCI where appropriate.

We stand upon shifting sands. We anticipate with excitement the outcome of studies such as FINESSE. We plan to address important questions with other studies, such as REACT-2, that will compare primary PCI with PHT and mandated rescue PCI or routine in-patient PCI. For now, though, the best
STEMI treatment appears to depend on where the patients are and how long it takes them to call.

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References


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History of Cardiology: Robert Adams, MD, and William Stokes, MD

The Adams-Stokes syndrome is familiar to us all, but as Diana Berry explains, the physicians published their descriptions of heart block some 20 years apart.

In the early 19th century, the Irish school of medicine flourished, contributing important findings in clinical cardiology. Some of the most well-known names included John Cheyne, MD, who came from Edinburgh, Scotland, to settle in Dublin, Robert Adams, MD (Dublin), William Stokes, MD (Edinburgh) (pictured above), Robert Graves, MD (Dublin), and Sir Dominic Corrigan, MD (Edinburgh). Dr Adams was a surgeon with a deep interest in heart disease and was possessed of great observational skills, whilst Dr Stokes, in a sense the mainstay of the school, elaborated and confirmed the findings of his colleagues. He and Adams are best remembered for the eponymous Adams-Stokes syndrome, now recognised as heart block.

Dr Adams was born in Dublin in 1791, and in 1810 he began his somewhat intermittent university studies. In 1815, he was licenced by the Royal College of Surgeons of Ireland, and in 1818 was elected a member. He did not receive his MD until 1842. After graduation he was appointed to the staff of the Jervis Street Hospital in Dublin, and later to the Richmond Hospital in the same city.

It was in 1826 when employed at the Jervis Street Hospital that Dr Adams first encountered the condition that we now recognise as heart block. Dr Adams’ patient was “an officer in the revenue, aged 68 years, of a full habit of body” who had for some time been incapable of any exertion as a result of breathing problems and a continuous cough. When Dr Adams first saw him, his patient was recovering from an “apoplectic attack” which he had suffered 3 days previously. The patient was in a kind of stupor and very sleepy, but what particularly attracted Dr Adams’ attention was “the irregularity of his breathing and remarkable slowness of pulse, which generally ranged at the rate of 30 in a minute.”

The patient’s regular doctor described how the patient had suffered several of these “apoplectic attacks” over the years, preceded by lethargy and memory loss. Slowness of pulse and heavy breathing were also regular symptoms. Some months after Dr Adams first saw the man, his condition worsened with the added problem of oedema of the feet and ankles, until finally he experienced a further apoplectic attack “which in two hours carried him off.”

Some 20 years later in 1846, Dr William Stokes encountered a patient with similar problems, and in his paper “Observations on Some Cases of Permanently Low Pulse” he sought to redress what he considered the lack of attention to such cases given by previous writers on diseases of the heart.

Dr Stokes was born in Dublin in 1804, where his father, Whitley Stokes, MD, was a distinguished physician and Regius Professor of Medicine at Dublin University. Stokes studied clinical medicine at the Meath Hospital, Dublin, and auxiliary sciences at both Trinity College and the Royal College of Surgeons at Dublin. He completed his medical studies at Edinburgh University.

On his return to Ireland in 1825, Dr Stokes became physician to the Dublin General Dispensary, and a year later succeeded his father at the Meath Hospital where that other distinguished member of the Irish school, Robert Graves, MD, was his colleague and subsequently a lifelong friend. Jointly the two did much to improve the clinical teaching that brought worldwide fame to the school.

Dr Stokes’ patient was, like the patient Dr Adams had encountered, a man of 68 years who was experiencing fainting fits brought on “by any circumstance tending to impede or oppress the heart’s action.” He had little warning of impending attacks. They lasted about 4 or 5 minutes, leaving no unpleasant after-effects apart from occasional injuries to the tongue. The patient was suffering from a cough, had some mucous expectoration, and was in possession of all his faculties.

On examination, Dr Stokes found his chest to be “unusually resonant” with the respiratory murmur loud and with “large mucous rales.” The heartbeat was extremely slow, dull, and feeble. Dr Stokes went on to describe a “soft bruit de soufflet” that accompanied the first heart sound. The second heartbeat was “imperfect,” more so after some beats than others. The patient’s rather sluggish pulse rate ranged from 28 to 30 beats/minute. Curiously, the arteries are described as “permanently distended.”

When the patient was readmitted to the Meath Hospital some months later, Stokes encountered a new symptom: “a very remarkable pulsation in the right jugular vein” that was particularly evident when the patient was lying down. Dr Stokes went on to describe the appearance of the patient’s neck as “very singular, and the pulsation of the veins is of a kind which we have never before witnessed.”

The descriptions by Drs Robert Adams and William Stokes of the same distinctive pattern of clinical signs and symptoms led to such episodes being referred to as “Adams-Stokes attacks”, or the “Adams-Stokes syndrome”. In some teaching hospitals the names are reversed, but whichever way they are used, the names of these 19th-century pioneers live on.

Diana Berry is a medical historian and freelance writer.

References

