nary life-support in cardiac arrest, and we congratulate Chen and colleagues for their efforts to develop an evidence base for such systems. Future studies should use subgroups of patients with cardiac arrest of cardiac origin and no response to the conventional CPR for more than 10 min who are likely to benefit from extracorporeal life-support. Moreover, if progress is satisfactory, we expect that patients getting conventional CPR will benefit from extracorporeal life-support in the near future.

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We declare that we have no conflict of interest.

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Do we need to justify epidural analgesia beyond pain relief?

Published Online August 11, 2008 DOI:10.1016/S0140-6736(08)61122-8

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Epidural anaesthesia or analgesia after major surgery has benefits that include improved analgesia,[1] attenuation of the stress response, and reduced respiratory and cardiac morbidity.[2–4] A systematic review has shown that epidural anaesthesia reduced mortality after major surgery.[5]

In today's *Lancet*, Duminda Wijeysundera and colleagues report a large population-based cohort study in which epidural anaesthesia or analgesia was associated with reduced 30-day mortality after intermediate-risk to high-risk surgery.[6] Administrative health-care databases were used and propensity score methods were applied to match 44 094 patients who received epidural anaesthesia to those who did not. These cases were drawn from an original population of 56 556 patients who had received epidural anaesthesia or analgesia and 202 481 who had not. Although the investigators report a statistically significant finding in favour of epidural anaesthesia, they, not unreasonably, point out the small treatment effect (number needed to treat 477), and conclude that to use epidural anaesthesia or analgesia for the main purpose of reducing mortality is not supported.

In their analysis, the investigators controlled for confounding factors in the cohorts; however, neither regression modelling nor propensity scores can control for unknown confounders.[7] For example, the number of patients who received a combined spinal-epidural anaesthetic is unknown. By contrast, well-designed randomised trials allow for unknown confounders, hence their results are more robust. However, randomised trials can be criticised for being too specific for the study population, whereas the results of a large population review might be more generalisable.

The main exposure in this study was epidural anaesthesia or analgesia defined by physicians billing for the insertion of an epidural catheter within 1 day of surgery. From the clinician's point of view, we would define epidural anaesthesia or analgesia as a period of anaesthetic care in which the vertebral level of catheter insertion, drugs used (local anaesthetic, opioid, adjuncts), duration of infusion, postoperative

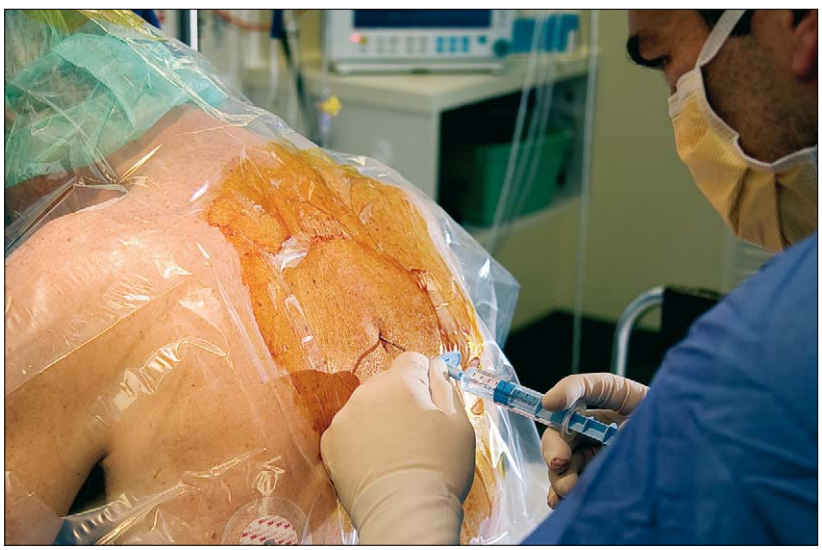
environment, and surveillance given to the patient are all important factors for a successful outcome. An acute pain team or individual provider of anaesthesia would supervise the epidural analgesia, be available to give the optimum amount of analgesia, and manage side-effects and potential complications. We do not know which of these aspects featured in the care of the patients in Wijeysundera and colleagues' study.

Large randomised trials have addressed the effect of epidural anaesthesia or analgesia on outcome, but have not had sufficient power to detect infrequent adverse events, a common limitation of randomised trials.[8,9] Wijeysundera and colleagues calculated that to show a statistically significant reduction in mortality (relative risk 0·89), 55 000 participants would be needed in a randomised trial. To implement a randomised trial of that size with epidural anaesthesia or analgesia as the intervention would be logistically overwhelming.

An alternative to randomised trials and administrative databases is databases that are specifically designed to prospectively gather information and capture events that are important to clinicians. These clinical databases can provide the clinician with data from large cohorts of patients and can be used to benchmark and detect trends in practice and rare events. The American Society of Regional Anesthesia and Pain Medicine has set up a postoperative pain database[10] and there is a similar project on non-neuraxial regional anaesthesia by the Australasian Regional Anaesthesia Collaboration.[11] We await the outcome of these projects with interest.

The most feared complications of epidural anaesthesia are epidural haematoma and abscess. In Wijeysundera and colleagues' study, spinal decompression laminectomy was infrequent in both groups (0·02%); therefore, major neuraxial complications seemed to be rare. In a previous study, when patients were closely followed up prospectively, the incidence of laminectomy for neuraxial complications was similar at about one in 8000 (0·013%).[12] As long as selection of patients and postoperative management are appropriate, epidural anaesthesia or analgesia is a low-risk procedure.

Epidural anaesthesia or analgesia is one of many interventions that a patient undergoes in the perioperative period that might affect outcome. The recent decline in the use of postoperative epidural analgesia has been contributed to by investigations with neutral results related to outcome[8,9] combined with



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understandably heightened concerns about morbidity.[12] We could argue that reducing two deaths per 1000 cases offsets the potential risk of laminectomy.

More pragmatically, Wijeysundera and colleagues point out that our focus should be on the proven benefits of epidural analgesia. The most durable and clearly defined benefit from epidural analgesia is improved analgesia.[1] Provision of effective analgesia is our core business: it has substantial physiological and psychological benefits, and is regarded as a fundamental human right.[13] Pain after major surgery can be severe, and we think that in many cases pain relief alone is an unambiguous clinical indication for postoperative epidural analgesia.

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We declare that we have no conflict of interest.

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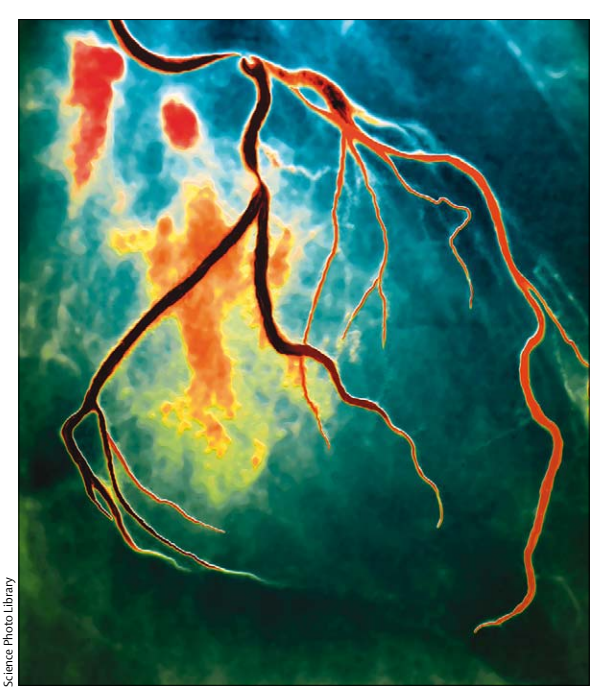
Lipid lowering: what and when to monitor

Drug treatment for dyslipidaemia is a mainstay of clinical practice in developed countries. Monitoring of lipid-lowering treatment contributes additionally to the already substantial cost.[1] In the randomised LIPID trial (pravastatin 40 mg per day) in just over 4500 patients,[1] the investigators evaluated both the short-term variation in total cholesterol (which they called noise) and the long-term variation (signal). They showed that after initiation of treatment, the signal did not exceed the noise until after 4 years—ie, when the number of true-positive increases in cholesterol exceeded false-positive elevations due to short-term fluctuations. The investigators felt that the results showed that measurement intervals could be increased, that guidelines which recommend annual or more frequent monitoring should be reconsidered, and, most specifically, that testing of adherent patients with well-controlled cholesterol every 3–5 years should be considered. How can we use these careful analyses?



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The US National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) recommends frequent monitoring.[2] The patient's response should be evaluated about 6 weeks after starting drug therapy, again at 12 weeks, and thereafter every 4–6 months or more often, if considered necessary.[2] Although many patients are unlikely to receive such careful monitoring, that is not the question. The question is, what is the best evidence-based monitoring strategy?

The provider might set a standard lipid goal, such as for LDL cholesterol or non-HDL cholesterol, or a more aggressive goal for very high-risk patients.[3] Either way, the first question to be addressed before treatment is started is what is the patient's cholesterol concentration, or the level of a more relevant lipid value? In view of the rather high short-term variation (noise), in the LIPID study (cholesterol, 95% CI –0·80 to 0·80 mmol/L) at least two baseline measures would be needed, and perhaps a third if the first two differed greatly. A lipid-lowering agent and dose would then be selected with an evidence-based probability of achieving the goal—most often a statin or including a statin. The demonstration of improved efficacy for combination therapy[4] will probably lead to increased use of such treatment. The second question is about lipid response, and the individual response to a fixed agent and dose varies greatly.[1]

Even the cautious practitioner could wait 12 weeks, at which time assay of liver enzymes is recommended (6–8 weeks if nicotinic acid has been given),[2] and lipids could be measured concomitantly. But in view of the variability, lipids should ideally be measured again