

GLOSSARY**EUROSCORE**

European System for
Cardiac Operative Risk
Evaluation

The learning curve in cardiac surgery

In coronary artery surgery, mortality has been associated with the number of operations that surgeons have performed. This observation prompted Ben Bridgewater and colleagues to examine the 'learning curve' effect, by comparing mortality in patients operated on by newly appointed and established surgeons.

Data were collected on 18,913 patients in northwest England undergoing isolated coronary artery surgery for the first time. In 5,678 cases, the surgery was carried out by surgeons who had been appointed as consultants within the previous 4 years. The remainder of the operations were performed by more experienced colleagues. Observed mortality and predicted (EUROSCORE) mortality were recorded.

There was no significant difference in observed mortality for patients treated by newly appointed or experienced surgeons (1.9% and 2.0% mortality, respectively; $P=0.71$). Mortality in patients treated during the first year of a surgeon's appointment, however, was significantly higher than in the fourth year (2.2% and 1.2%, respectively; $P=0.049$). Adjusting for time and case mix, mortality decreased from 2.3% to 1.0% from the first to the fourth year ($P=0.019$).

While a learning curve effect has been clearly demonstrated, the overall mortality in patients treated by newly appointed or experienced surgeons was similar. The authors stress the importance of managing the learning curve effect by supporting, monitoring and further training newly appointed surgeons, and offering experienced clinical support in non-technical areas such as case selection and perioperative management.

Original article Bridgewater B *et al.* (2004) Improving mortality of coronary surgery over first four years of independent practice: retrospective examination of prospectively collected data from 15 surgeons. *BMJ* 329: 421–425

REPLACE-2: long-term efficacy results

The Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events (REPLACE)-2 trial showed that the direct thrombin inhibitor bivalirudin, with provisional

glycoprotein (Gp) IIb/IIIa inhibition, was non-inferior to heparin plus planned Gp IIb/IIIa inhibition in preventing acute ischemic endpoints at 30 days. Major in-hospital bleeding rates were significantly reduced using the bivalirudin strategy, although concerns were raised about a small excess of periprocedural non-Q-wave myocardial infarctions (MI) in this group. Long-term (6 months and 1 year) results from this 6,010-patient trial have now been reported.

A trend towards a lower death rate was shown in the bivalirudin group at 6 months and at 1 year, although MI and revascularization rates tended to be lower in the heparin group at the 6-month stage. None of these trends was statistically significant. Subgroup analysis showed that the trend towards better survival with bivalirudin was greatest in 'high-risk' patients.

The authors conclude that bivalirudin with provisional Gp IIb/IIIa blockade and heparin plus planned Gp IIb/IIIa blockade offer comparable long-term clinical outcomes. They note that the statistically significant reduction in bleeding observed in patients receiving bivalirudin may offset the nonsignificant increase in early MI rate in these patients. Furthermore, bivalirudin offers advantages in terms of cost savings and ease of administration.

Original article Lincoff AM *et al.* (2004) Long-term efficacy of bivalirudin and provisional glycoprotein IIb/IIIa blockade vs heparin and planned glycoprotein IIb/IIIa blockade during percutaneous coronary revascularization. *JAMA* 292: 696–703

Benefits of drug-eluting stents: a meta-analysis

EBM Drug-eluting stents (DES) are designed to reduce the extent of in-stent restenosis following percutaneous coronary intervention (PCI), via the controlled elution of an antimetabolic drug such as sirolimus or paclitaxel. Clinical trials investigating the benefits of DES over bare-metal stents (BMS), however, have been insufficiently powered to generate useful data on rates of mortality, myocardial infarction (MI) or other complications. Babapulle and colleagues have performed a meta-analysis of randomized trials in order to provide this information.

The authors identified 11 appropriate trials involving 5,103 patients, comparing the benefits

and safety of DES (with sirolimus or paclitaxel) and BMS. All trials provided 6–12 months' clinical follow-up after index PCI. Using a hierarchical Bayesian random-effects model, the team pooled the results, stratifying by the type of drug and presence of carrier polymer.

The pooled results indicated that mortality and MI occurred at similar rates for DES and BMS. Major cardiac adverse events, however, occurred at a lower rate in the DES group than in the BMS patients (7.8% vs 16.4%; odds ratio (OR) 0.42; 95% credible interval (CI) 0.32 to 0.53), as did angiographic restenosis (8.9% vs 29.3%; OR 0.18; 95% CI 0.06 to 0.40).

The authors conclude that sirolimus-eluting and polymeric-paclitaxel-eluting stents are superior to BMS in reducing the rates of angiographic restenosis and major cardiac adverse events, although no clear benefit has been shown in terms of a reduction in mortality or MI rates.

Original article Babapulle MN *et al.* (2004) A hierarchical Bayesian meta-analysis of randomised clinical trials of drug-eluting stents. *Lancet* **364**: 583–591

Spirolactone and hyperkalemia

The landmark Randomized Aldactone Evaluation Study (RALES), published in 1999, showed that spironolactone, a potassium-sparing diuretic, improves outcomes in patients with severe heart failure. The drug can sometimes cause life-threatening hyperkalemia, however, when used in combination with angiotensin-converting enzyme (ACE) inhibitors (which are also indicated for heart failure). Although this complication was rare in RALES, it is possible that physicians prescribe spironolactone more freely in practice. Juurlink *et al.* have carried out a time-series analysis to examine the effects of RALES at the population level in Ontario, Canada.

For the period 1994–2001, the investigators linked the records of all prescription drugs dispensed and all hospitalizations for over 1.3 million patients aged 66 years or older. They examined trends in spironolactone-prescribing rates, hospitalization for hyperkalemia and associated mortality.

From 1994 to 2001, there was a statistically significant increase ($P < 0.001$) in rates of spironolactone prescription, hospitalization for hyperkalemia and associated mortality. Among

patients with heart failure who were treated with ACE inhibitors, there were 560 additional hospitalizations for hyperkalemia (95% CI 285 to 754) and 73 additional inpatient deaths (95% CI 27 to 120) in 2001, compared with the expected numbers.

In conclusion, publication of RALES was associated with a sharp increase in the spironolactone prescription rate, in the rate of hospitalization for hyperkalemia and in associated mortality. The authors suggest that clinicians should take into account other risk factors for hyperkalemia when prescribing spironolactone, and that renal function and potassium levels should be closely monitored.

Original article Juurlink DN *et al.* (2004) Rates of hyperkalemia after publication of the randomized aldactone evaluation study. *N Engl J Med* **351**: 543–551

Prediction of outcome in myocardial ischemia

A report by Mueller and colleagues has provided new information about the prognostic value of the admission ECG in cases of myocardial ischemia. The study included a cohort of 1,450 consecutive patients with unstable angina/non-ST-segment elevation myocardial infarction (nonSTEMI), who were assessed by coronary angiography within 24 h of admission. Patients were divided into three groups according to the presence of new ST-segment depression ($n = 136$), T-wave inversion ($n = 419$) or no changes on the admission ECG ($n = 895$). Revascularization was carried out in the majority of patients ($n = 1,066$), most often by percutaneous coronary intervention (PCI) with stent placement. Coronary artery bypass grafting was carried out in selected patients. The primary endpoint was all-cause mortality.

Adjusting for potential confounders, the cumulative death rate at 36 months was significantly higher for patients with ST-segment depression (hazard ratio [HR] 2.2, 95% CI 1.1 to 4.6) than for patients with no ECG changes; by contrast, T-wave inversion was associated with a more favorable outcome (HR 0.44, 95% CI 0.20 to 0.96). Surprisingly, the prognostic value of these ECG changes was similar in men and women.

Mueller *et al.* conclude that ST-segment depression and T-wave inversion were important prognostic factors in patients undergoing very early revascularization for unstable angina/

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ECG

Electrocardiogram