The PROXI trial was a double-blind randomized clinical trial conducted in 14 Danish hospitals with patients (1,400) undergoing acute or elective laparotomy to assess the benefit:risk profile of 80% oxygen use. Patients were randomly assigned to receive either 80 or 30% oxygen during and for 2 h after surgery.

No significant differences were observed in the incidence of surgical site infection or pulmonary complications between groups.

	80% Oxygen (n = 685)	30% Oxygen (n = 701)
Surgical site infection, %	19.1	20.1
After colorectal surgery	23.7	25.2
Complications, %		
Atelectasis	7.9	7.1
Pneumonia	6.0	6.3
Respiratory failure	5.5	4.4
30-day mortality, %	4.4	2.9

Interpretation

No differences were observed in surgical site infections when breathing 30 or 80% oxygen during and for 2 h after abdominal surgery. Pulmonary complications, including atelectasis, pneumonia, or respiratory failure, were also not different between groups. Whether high F_{IO_2} should be the standard for preventing surgical site infection for most operations is not clear.

On-pump *versus* off-pump coronary-artery bypass surgery. New Engl J Med 2009; 361:1827–37

The use of cardiopulmonary bypass (on-pump) coronary artery bypass grafting (CABG) has been shown to improve ischemic symptoms and prolong survival. However, postoperative complications, such as hemodynamic instability, may be reduced when CABG is performed without cardiopulmonary bypass (off-pump CABG).

A controlled, single-blind, randomized prospective study was conducted to compare morbidity and mortality in patients (N = 2,203) scheduled for urgent or elective CABG with either on-pump or off-pump procedures.

Compared with the on-pump CABG group (n = 1,099), the off-pump CABG group (n = 1,104) had a greater 1-yr composite (death, repeat revascularization procedure, or nonfatal myocardial infarction) outcome (9.9 *vs.* 7.4%). The proportion of patients with fewer grafts completed than originally planned was significantly higher (17.8 *vs.* 11.1%), and the overall rate of graft patency was lower (82.6 *vs.* 87.8%, $P < 0.01$) in the off-pump group. At the 1-yr follow-up, there were more deaths from cardiac causes in the off-pump group compared with the on-pump group (2.7 *vs.* 1.3%). There was no significant difference between off-pump and on-pump CABG in the rate of the 30-day composite (death or complications) outcome (7.0 and 5.6%, respectively; $P = 0.19$), neuropsychologic outcomes, or short-term use of major resources.

Interpretation

Patients who underwent off-pump coronary artery bypass surgery, compared with those who received on-pump surgery, had worse composite outcome (death, myocardial infarction, or revascularization procedure) and lower graft patency at 1yr. These data do not support the routine use of off-pump CABG.

Pain Medicine

Timothy J. Brennan, Ph.D., M.D., Editor

Brain gray matter decrease in chronic pain is the consequence and not the cause of pain. J Neurosci 2009; 20:13746–50

Decreases in gray matter have consistently been shown to correlate with chronic pain, although the cause of the pain and exact loci may differ between studies. However, it is not known whether these structural alterations precede or succeed the chronicity of pain.

Changes in brain structure were evaluated using magnetic resonance imaging in 32 patients with unilateral primary hip osteoarthritis and severe permanent hip pain scheduled for total hip replacement surgery and compared with healthy age- and gender-matched controls. A subgroup of patients (n = 10) were also monitored 6 weeks and 4 months after total hip replacement surgery.

Patients with primary hip osteoarthritis had reduced gray matter density preoperatively in anterior cingulated cortex, the orbitofrontal cortex, right insular cortex and operculum, right mid-orbital gyrus, left superior medial gyrus, and brainstem compared with controls. After surgery, all 10 patients were pain free, and an increase in gray matter was observed in the dorsolateral prefrontal cortex, anterior cingulated cortex, amygdala, brainstem, and right insular cortex.

Interpretation

Chronic pain causes changes in gray matter volume in the central nervous system. There is concern that chronic pain may produce long-term damage in the brain. This study demonstrates that in patients with pain caused by degenerative joint disease, pain relief produced by joint replacement partially reversed the decrease in gray matter volume.

Prevalence of and factors associated with persistent pain following breast cancer surgery. JAMA 2009; 302:1985–92

Persistent pain and sensory disturbances after surgical treatment for breast cancer are significant clinical problems with multiple pathogenic mechanisms. Patient characteristics, surgical technique, adjuvant therapy, and age may all contribute to the incidence and severity of pain after breast surgery.

A nationwide cross-sectional questionnaire study was conducted in Denmark to examine the prevalence of and factors associated with persistent pain after surgical treatment for breast

cancer. Prevalence, location, and severity of persistent pain and sensory disturbances in 12 well-defined treatment groups were assessed for an average of 26 months after surgery.

The questionnaire was returned by 87% of patients (n = 3,253). Pain was reported in 47% of patients, including 13, 39, and 48% with severe, moderate, and mild pain, respectively. Pain complaints in areas unrelated to the surgery were associated with higher incidence of chronic pain in the surgical area (65 *vs.* 37%; $P < 0.001$). Factors associated with increased likelihood of pain included age, previous radiation therapy, and axillary lymph node dissection:

	Odds Ratio	*P* Value
Increased likelihood of pain		
Young age (18–39 yr)	3.62	< 0.001
Adjuvant radiotherapy	1.59	0.03
Axillary lymph node dissection	1.77	< 0.001
Risk of sensory disturbances		
Young age (18–39 yr)	5.00	< 0.001
Axillary lymph node dissection	4.97	< 0.001

A total of 306 patients (20%) with pain had contacted a physician within the previous 3 months for pain complaints in the surgical area.

Interpretation

Persistent pain after breast cancer surgery has generated considerable interest. Factors associated with persistent pain after breast surgery (*e.g.*, age, axillary dissection, and previous radiation therapy) provide the basis for strategies to reduce the incidence and severity of this problem.

Ketamine produces effective and long-term pain relief in patients with complex regional pain syndrome type 1. Pain 2009; 145:304–11

Many patients with complex regional pain syndrome type 1 (CRPS-1) develop chronic disease with severe pain, disability, and impaired quality of life. Although the pathophysiology of CRPS-1 is unknown, the *N*-methyl-D-aspartate receptor antagonist S(+)-ketamine has been shown to improve pain in patients with CRPS-1 with an acceptable safety profile in open-label studies.

In this double-blind, randomized, placebo-controlled parallel-group trial, patients with CRPS-1 (48 women) and severe pain received a 4.2-day intravenous infusion of low-dose ketamine (n = 30) or placebo (n = 30) using an individualized stepwise tailoring of dosage based on effect (pain relief) and side effects (nausea or vomiting or psychomimetic effects). Pain scores were measured during the 12-week study period.

The median (range) disease duration of the patients was 7.4 (0.1–31.9) years. At the end of the infusion, the ketamine dose was 22.2 ± 2.0 mg $\cdot$ h^{-1} $\cdot$ 70 kg^{-1}. Pain scores during the 12-week study period in patients receiving ketamine were significantly lower than those in patients receiving placebo ($P < 0.001$). The lowest pain score at the end of week 1 was ketamine 2.68 ± 0.51 *versus* placebo 5.45 ± 0.48, and by week 12, pain relief between groups was similar ($P = 0.07$). Treatment did not produce functional improvement. More patients receiving ketamine experienced mild to moderate psychomimetic side effects during drug infusion (76 *vs.* 18%, $P < 0.001$) compared with those receiving placebo.

Interpretation

A continuous 5-day infusion of ketamine provided pain relief for patients with CRPS-1. Long-lasting pain relief beyond the duration of the infusion occurred, but the beneficial effect subsided during the 12-week period. These results provide the basis for future studies using *N*-methyl-D-aspartate receptor antagonists to examine long-term treatment of CRPS.

Prognosis for patients with chronic low back pain: Inception cohort study. BMJ 2009; 339: b3829

Low-back pain affects 12–33% of adults at any given time, and chronic low-back pain (lasting >3 months) can be a social and economic burden. The prognosis for patients with chronic low-back pain is unclear because many trials may have underestimated prognosis because of study limitations (*e.g.*, unrepresentative survival cohorts or large losses to follow-up).

To determine the 1-yr prognosis and identify prognostic markers, an inception cohort of patients with recent-onset chronic low-back pain was studied from multiple clinics in Australia.

Of the 406 patients whose pain persisted for 3 months, 97% met follow-up criteria, and 99.9% of data on prognostic markers were available. Most patients (65%) reported mild or very mild pain at the onset of chronicity. The cumulative probability of being pain free was 35% at 9 months and 42% at 12 months, and for complete recovery, this was 35% at 9 months and 41% at 12 months. Of the 259 participants who had not recovered from pain-related disability at entry to the chronic study, 47% had recovered by 12 months. Previous sick leave because of low-back pain, high disability levels or high pain intensity at onset of chronicity, low levels of education, and greater perceived risk of persistent pain was associated with delayed recovery ($P \leq 0.05$ for all).

Interpretation

Factors associated with sustained chronic low-back pain were identified and included previous sick leave, disability and pain intensity, education, and perceived risk of pain. Identification of these risk factors may permit earlier intervention in high-risk patients to reduce the chronicity of low-back pain.

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