

Common comorbid conditions included cardiovascular, metabolic, and pulmonary conditions. Overall, the median length of hospital stay was 20.2 days and mean weight loss was 2.97 kg. Nutritional risk was identified as an independent predictor of postoperative complications.

	Reilly's Nutrition Risk Score	Nutritional Risk Screening 2002
Patients at nutritional risk, %	31.7	39.3
Mortality rate, % At risk vs. not	8.0 vs. 1.6*	7.0 vs. 1.8
Postoperative complication, % At risk vs. not	58 vs. 44.1	62 vs. 39.8†

* $P = 0.033$. † $P = 0.004$.

Interpretation

Nutritional risk predicts outcome after colorectal surgery; however, risk outcome may differ based on the test used to classify nutritional risk. Further studies may determine whether nutrition is a causative factor in the development of certain postoperative complications (*e.g.*, wound infection or dehiscence). It is also not known whether improvement in nutritional status with supplements will reduce complications.

A sensitive cardiac troponin T assay in stable coronary artery disease. *N Engl J Med* 2009; 361:2538–47

There is a strong association between elevated troponin levels and recurrent coronary ischemic events in patients with suspected coronary syndromes, with even small elevations resulting in increased risk of adverse outcomes. In most patients with stable coronary artery disease, plasma cardiac troponin T levels are below the limit of detection for the conventional assay that may limit risk identification.

A newly developed high-sensitivity assay was designed to determine the concentration (10× lesser than conventional measurements) of cardiac troponin T in plasma samples. In this subgroup analysis of 3,679 patients with stable coronary artery disease and preserved left ventricular function enrolled in a large randomized prospective trial (Prevention of Events with Angiotensin Converting Enzyme Inhibition trial), cardiac troponin T levels were measured using this new assay. Results were analyzed in relation to the incidence of cardiovascular events during a median follow-up period of 5.2 yr.

Concentrations of cardiac troponin T were at or above the limit of detection (0.001 $\mu\text{g/L}$) in 3,593 patients (97.7%) and at or above the 99th percentile for apparently healthy subjects (0.0133 $\mu\text{g/L}$ in 407 patients, 11.1%). After adjust-

ment for other independent prognostic indicators, there was an increase in the cumulative incidence of cardiovascular death and heart failure in the group with elevated cardiac troponin T levels. There was no association between troponin T levels and the incidence of myocardial infarction.

Interpretation

Cardiac troponin T levels are usually below the limit of detection in patients with stable coronary artery disease. A more sensitive assay revealed that patients with elevated cardiac troponin T levels (compared with normal controls) were more likely to have cardiovascular death and heart failure, but not myocardial infarction. Further research will be needed to determine whether these subtle changes in troponin T portend an increased perioperative risk for cardiovascular complications and death.

Critical Care Medicine

Jean Mantz, M.D., Ph.D., Editor

Early exercise in critically ill patients enhances short-term functional recovery. *Crit Care Med* 2009; 37:2499–505

Clinical peripheral muscle weakness has been reported in 25–33% of patients mechanically ventilated for 4 to 7 days. This may lead to prolonged intensive care unit (ICU) stays and impaired functional status and quality of life up to 1 yr after discharge. Recent evidence suggests that early activity is possible for critically ill patients; however, there is limited evidence for its effectiveness in patients in ICUs while under sedation.

A randomized controlled trial was conducted to investigate whether a daily exercise session is a safe and an effective intervention in preventing or attenuating these detrimental effects. Critically ill patients ($N = 90$) were included when their cardiorespiratory condition allowed (beginning day 5) and if a prolonged ICU stay (at least 7 more days) was expected. Patients received respiratory physiotherapy and a daily standardized passive or active motion session of upper and lower limbs and the treatment group performed a passive or active bedside cycling session for 20 min/day.

Most patients (79%) were recruited in the surgical ICU and of these most had undergone cardiac surgery (39%), transplant surgery (25%), or thoracic surgery (16%). Eighty percent of patients received assisted pressure-support ventilation. The median number of cycling sessions was 7 and the median cycling frequency was 4 sessions/week. No severe adverse events were identified during and immediately after the exercise training.

At hospital discharge, all outcomes (*e.g.*, 6-min walking distance, isometric quadriceps force, and the subjective feeling of functional well-being) were significantly higher in the treatment group ($P < 0.05$).

Interpretation

This study confirms that exercise should be considered even in surgical patients, provided patients are evaluated for contraindications and monitored during exercise sessions. Muscle strength and functional ability are improved in the muscle territories activated by the cycling exercise. Whether early mobility and occupational therapy are feasible, safe and effective in surgical patients with wounds and multiple drains is not known. Nevertheless, exercise cycling represents a first step toward addressing muscle inactivity while patients are receiving mechanical ventilation.

Suggested by: Bernard De Jonghe, M.D.

Plasma tryptophan and tyrosine levels are independent risk factors of delirium in critically ill patients. *Intensive Care Med* 2009; 35:1886–92

Delirium may occur in as few as 20% or as many as 80% of patients in the ICU. This preventable problem may result in prolonged hospitalization, increased costs, mortality, and potential long-term problems. Although the pathophysiology of delirium remains elusive, changes in neurotransmission by serotonin, dopamine, acetylcholine, and norepinephrine using pathways may play a role. This pilot study was conducted to investigate the role of precursor large neutral amino acids such as tryptophan, phenylalanine, and tyrosine and risk of transitioning to delirium in critically ill patients.

Plasma large neutral amino acids concentrations were determined on days 1 and 3 in mechanically ventilated patients from the Maximizing Efficacy of Targeted Sedation and Reducing Neurological Dysfunction randomized controlled trial comparing dexmedetomidine and lorazepam sedation. Delirium was assessed daily using the confusion assessment method for the ICU.

At baseline, all evaluable patients ($n = 97$) had a high severity of illness (median Acute Physiology and Chronic Health Evaluation [APACHE] II, 28) and most were admitted for sepsis or acute respiratory distress syndrome (42%). After adjusting for confounders, only high or low tryptophan/large neutral amino acids ratios ($P = 0.0003$), and tyrosine/large neutral amino acids ratios ($P = 0.02$) were associated with increased risk of transitioning to delirium. Additional predictors included older age, higher APACHE II scores, and increased fentanyl exposure.

Interpretation

This study strengthens the view that alterations in the metabolism of amino acids such as tryptophan (*via* serotonin) and tyrosine (*via* dopamine or norepinephrine) contribute to the pathophysiology of delirium in patients in the ICU. This pilot study needs confirmation by future, methodologically robust, prospective trials but provides both pathophysiologic and therapeutic insights for preventing and treating delirium in patients in the ICU.

Antiplatelet drugs and outcome in mixed admissions to an intensive care unit. *Crit Care Med* 2010; 38:32–7

Activation of circulating blood platelets results in their sequestration in the microvasculature and thrombocytopenia, and these are common features of sepsis, a leading cause of death in critically ill patients. Antiplatelet agents may provide a benefit through modulation of inflammatory responses in critically ill patients; however, because of an increased risk of bleeding, the risk–benefit ratio must be examined closely.

A retrospective cohort study was conducted, which analyzed 615 consecutive patients admitted to an ICU within 24 h after hospitalization. Approximately 25% of patients received antiplatelet drugs (acetylsalicylic acid or clopidogrel).

The majority of patients were enrolled primarily to the ICU from the local emergency department (52%) or local internal medicine or surgical departments (19%). Approximately 60% of patients had active bleeding at admission or during the ICU stay. Patients who received antiplatelet drugs were markedly older and presented higher APACHE II scores on ICU admission.

Overall, no differences were observed between groups for length of ICU stay, frequency of infections, sepsis, or mechanical ventilation. Regression analysis to control for differences in APACHE II scores and age showed a significant improvement in mortality in patients with preexistent antiplatelet medication use. Benefits were higher in surgical patients.

Interpretation

Management of antiplatelet therapy is a complex issue in critically ill patients, because it requires careful evaluation of the bleeding *versus* thrombotic risk in patients with organ failure. These data are the first to suggest that, in some critically ill patients, antiplatelet drugs may decrease mortality, perhaps by preventing microvascular thrombosis and organ failure. If confirmed in future prospective, randomized trials, these findings may have an important impact for daily routine practice in ICU patients.

Association of telemedicine for remote monitoring of intensive care patients with mortality, complications, and length of stay. *JAMA* 2009; 302:2671–8

Onsite staffing by intensivists in ICUs is associated with reduced morbidity and mortality; however, this may not always be possible. Therefore, remote telemedicine technology, which enables intensivists to simultaneously monitor several ICUs from an off-site location, has become increasingly common. However, this technology is expensive, and there is little data evaluating its effectiveness.

This observational study was conducted in six ICUs at five hospitals in a large U.S. healthcare system to assess the use of tele-ICU in 2,034 patients in a preintervention period

(before tele-ICU) and 2,108 patients in the postintervention (after tele-ICU implementation) period. Local physicians delegated full treatment authority to the tele-ICU for 655 patients (31.1%) and authority to intervene only in life-threatening events for the remainder of patients.

Hospital mortality rates were 12.0 and 9.9% and ICU mortality rates were 9.2 and 7.8% in the preintervention and postintervention periods, respectively. After adjustment for severity of illness, no significant differences were associated with the telemedicine intervention for hospital mortality (relative risk, 0.85) or for ICU mortality (relative risk, 0.88). Tele-ICU intervention was significantly associated with improved survival in more sick patients but with no improvement or worse outcomes in less sick patients. Length of stay was similar in both groups.

Interpretation

It has not been determined whether telemedicine improves healthcare and reduces costs in ICU patients. Although remote monitoring of ICU patients was not associated with an overall improvement in mortality or length of stay, the complexity of ICU patients is a major issue when evaluating the contribution of telemedicine-ICU in improving outcome *versus* conventional ICU staffing.

Pain Medicine

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

Prescribing of opioid analgesics and related mortality before and after the introduction of long-acting oxycodone. *Can Med Assoc J* 2009; 181:881–2

Opioid use has increased in Canada as have reports of opioid abuse and opioid-related mortality. This retrospective study examined the potential association between increased opioid prescribing in Canada with opioid-related mortality.

Data from IMS Health Canada were collected from 1991 to 2007 for all opioid-containing analgesics and cough suppressants prescribed on an outpatient basis. Opioid-related deaths were determined by the coroner and based on high opioid concentrations or drug combination including one opioid.

Between 1991 and 2007, the prescribing of opioid analgesics increased by 29%, from 458 to 591 prescriptions per 1,000 individuals annually, and oxycodone prescriptions increased by more than 850%. The amount of drug dispensed also increased by 24%. Of 7,099 drug or alcohol-related deaths, 3,406 involved opioids. Morphine or heroin administration was the most common cause of single opioid-related deaths (36%), compared with codeine (20%), methadone (14%), and oxycodone (11%). The majority of deaths involved one nonopioid central nervous system depressant (91.6%). The addition of long-acting oxycodone to the drug formulary was associated with a fivefold increase in oxycodone-related mortality and a

41% increase in overall opioid-related mortality. The majority of deaths were deemed unintentional.

Most patients (66.4%) had visited a physician in the month before death and of the 1,095 patients for whom individual-level prescribing data were available, 56.1% had filled a prescription for an opioid in the month before death.

Interpretation

This Canadian study demonstrated an association between increases in opioid prescribing and opioid-related mortality through a 10-yr period. Most deaths were associated with the use of other central nervous depressant drugs and were not ruled intentional. Importantly, visits to physicians within the month before death indicates that there may be an opportunity for interventions to prevent mortality related to opioid use in these patients.

Spinal cord stimulation for failed back surgery syndrome: Outcomes in a workers' compensation setting. *PAIN* 2009; 148:14–25

Failed back surgery syndrome, including chronic back and leg pain that failed to improve after spine surgery, is often treated using spinal cord stimulation (SCS). Although previous trials of SCS demonstrated favorable results compared with lumbar spine reoperation and conventional medical management, they did not always include comparisons with treatments other than reoperation or patients receiving worker's compensation, which may have worse outcomes with any pain therapy.

This prospective controlled cohort study compared pain, function, medication use, and work outcomes of patients in the Washington State Workers' Compensation Program who received SCS ($n = 51$) with patients who did not receive SCS ("Pain Clinic" group; $n = 39$) and with patients who did not receive SCS or pain clinic evaluation ("Usual Care" group; $n = 68$).

The average age of patients was 44 yr and most patients were men. At baseline, the SCS group had significantly longer work time loss compensation, leg pain, and claim duration compared with the other two groups. No difference was observed between groups for the primary composite endpoint of pain, function, and opioid medication use. Few (<10%) patients in any group achieved success at any follow-up. At 6 months, the SCS group showed slightly more improvement in leg pain and function, but with higher rates of daily opioid use at 6 months compared with the other two groups. However, differences were not sustained over longer periods of time.

Interpretation

The lack of long-term effectiveness of SCS in this population does not necessarily imply ineffectiveness in other patient populations. The issues associated with workers' compensation may have significant effect on pain therapy and patient outcomes. It is possible that subgroups in this population such as those with unilateral radicular pain, higher baseline functioning, and greater mental health status may have better results.