COMMENT

Fluid resuscitation is the first line of treatment for most hemodynamically unstable patients. After an initial bolus of crystalloids, ongoing administration of such fluids may both be ineffective in further maintaining intravascular volume and lead to edema formation. Therefore, it has been postulated for many years that further fluid resuscitation with colloids should be considered. Over the years, different colloids have been used. Although albumin appears to be the colloid of choice, being the natural colloid component of the plasma, its use is restricted owing to high cost and lack of proof that it is better than synthetic colloids. Of the synthetic colloids, HESs are the most commonly administered. The smaller and newer of these molecules (130 kDa/0.4 substitution), 6% HES is supposed to produce less adverse effects than the older and larger molecule-based starch solutions. However, previous data from randomized trials failed to show superiority of HES solutions over other resuscitation fluids. To resolve the role of modern HES in fluid resuscitation, a large multicenter study is being conducted at present in Australia and New Zealand (CHEST; Crystalloidal versus Hydroxyethyl Starch Trial). During the study, it was discovered that a substantial amount of the research proving the safety and efficacy of HES was falsified. After the retraction of the publications by Joachim Boldt, the CHEST investigators conducted this current meta-analysis to assess the safety and efficacy of HES and to proceed safely with their own study.

The current publication is a report of a meta-analysis of articles that compared fluid resuscitation with 6% HES (130/0.4) to other resuscitation fluids excluding the retracted studies. The authors included 25 studies that met their inclusion criteria. These studies included a total of 1608 patients. Six of the studies were multicenter, and the largest included 200 patients. The overall quality of the studies was not very high, with none having low risk of bias and more than 50% carrying a high risk of bias. Overall, the studies do not show a notable effect on mortality. Confidence intervals on mortality were very wide, allowing for a potential effect on mortality by up to 40% either way. The authors conclude, and rightly so, that large multicenter studies are needed to address the question of whether HES solutions are safe and carry any efficacy in the process of volume resuscitation of hemodynamically unstable patients.

Exercise Testing in Survivors of Intensive Care—Is There a Role for Cardiopulmonary Exercise Testing?

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Little information has been published on the optimal physical rehabilitation strategy for survivors of critical illness after hospital discharge. The contribution of cardiac, respiratory, and musculoskeletal impairment to exercise limitation has not been thoroughly characterized. Cardiopulmonary exercise testing (CPET) offers an objective, noninvasive assessment of the physiologic response to exercise that may identify cardiac, respiratory, or musculoskeletal contributions to any exercise limitation. The anaerobic threshold (AT) is an objective measure of functional or aerobic capacity that occurs at 50% to 60% of peak exercise capacity. This study was designed to determine the feasibility and safety of CPET as a tool for objective assessment of exercise capacity in adult survivors of intensive care unit (ICU) stays and to help characterize the pathophysiology of any exercise limitation present in the patients.

Fifty patients who had been ventilated for 5 or more days underwent CPET within 6 weeks of hospital discharge. The exercise involved a standard ramped protocol with a maximal, symptom-limited incremental CPET using a cycle ergometer. The patients sat on a bicycle ergometer with a 12-lead electrocardiogram and gas exchange monitoring. Peripheral oxygen saturations and noninvasive blood pressures were monitored during the entire test period. Patients rested for 1 to 3 minutes to allow the respiratory exchange ratio to plateau; they then completed 3 minutes of unloaded cycling at 60 revolutions per minute. Load was applied to the pedal in a ramp-like manner, increasing by 10 to 15 W/min until maximum exercise capacity was attained. The test was terminated immediately if the patient had chest pain, altered sensorium, ST depression greater than 2 mm on the electrocardiogram, or emotional distress. Anaerobic threshold was determined using a combination of the V-slope and ventilatory equivalents methods. Data were collected for AT, peak VO2, ventilatory equivalents for CO2, oxygen pulse (V02/heart rate), HR reserve, breathing reserve (BR) at peak exercise, and static spirometry. Health-related quality of life was measured by the Medical Outcome Study Short Form 36 version 2.0 questionnaire performed immediately before the CPET. Physical component summary (PCS) and mental component summary (MCS) scores were obtained to determine patients' self-reported physical and mental well-being.

All 50 patients completed the CPET, and none had any adverse event during the testing. The mean time from hospital discharge to CPET was 24 ± 14 days. Leg fatigue and shortness of breath were the reasons for cessation of pedaling by 70% and 26% of patients, respectively. One patient each stopped because of back pain and anxiety. Forced expiratory volume in 1 second at baseline was 2.2 ± 0.9 L/min, and forced vital capacity was 3.0 ± 0.8 L/min; the mean forced expiratory volume in 1 second/forced vital capacity ratio was 74%. Peak VO2 was 56% ± 16% of predicted (13.8 ± 4.0 mL/kg per minute VO2), and AT was 41% ± 13% of peak predicted VO2 (10.4 ± 2.7 mL/kg per minute O2). At peak exercise, HR reserve and BR were 25% ± 14% and 47% ± 19%, respectively. Respiratory exchange ratio was 0.96 ± 0.11; the ventilatory equivalents for CO2 was 39.9. At hospital discharge, mean hemoglobin concentration was 10.3 ± 1.2 g/dL. Eighteen patients (36%) were taking rate-limiting medication at the time of the test. The mean oxygen pulse at peak exercise was 8.6 ± 2.5 mL/beat (74% of predicted). In patients ventilated for 14 or more days, AT was 9.6 ± 3.2 mL/kg per minute compared with an AT of 11.7 ± 2.2 mL/kg per minute in those ventilated for 5 to 14 days, a statistically significant difference. Patients ventilated for longer periods also had a substantially lower peak VO2 (12.9 ± 3.7 vs 15.3 ± 4.2 mL/kg per minute O2). Ventilatory limitation to exercise was considered as present if the V45 at peak exercise was greater than 80% of indirectly measured maximum voluntary ventilation (or BR <20%), or indirectly measured maximum voluntary ventilation minus V45 at peak exercise was less than 12 L/min. Based on these criteria, 5 patients had evidence of ventilatory limitation to exercise. All patients completed the Health-Related Quality of Life survey. Mean PCS and MCS
scores were 32 ± 8 and 37 ± 11, respectively. No correlation was found between exercise capacity measured by either peak VO2 or AT and either PCS or MCS.

Many factors contribute to the exercise limitation in survivors of critical illness, including premorbid pathology, anemia, V/Q mismatching, and pulmonary vascular changes and ventilatory abnormalities. Muscle deconditioning and weakness are major limiting factors affecting exercise capacity in these patients. Cardiopulmonary exercise testing provides a guide to further investigation and treatment of these patients, including a targeted physical rehabilitation program. Cardiopulmonary exercise testing can aid in exercise prescription and assessment of the response to interventions. However, appropriate clinical trials are necessary.

COMMENT

Rehabilitation after acute medical events is an integral part of the care. Orthopedic surgeons pride themselves on the detailed rehabilitation program they provide for patients after joint replacement. The same applies to the rehabilitation after cardiac events and cardiac surgery. It is completely logical that the more severe and prolonged the disease process is, the greater is the need for comprehensive rehabilitation. In that aspect, regrettably, intensive care medicine has lagged behind. Although critical care has made notable advances over the last few decades in the understanding and treatment of various clinical disorders, there has been very little work on rehabilitation of the discharged ICU patient. The UK National Institute for Health and Clinical Excellence guidelines specifically mention that data are lacking and that most ICU survivors do not receive disease-guided rehabilitation.

The current study evaluated the feasibility of postdischarge evaluation of the physical capabilities and mental function of patients about 1 month after discharge. To evaluate physical conditions, the authors conducted CPET. These tests were terminated early if any complaint or important physiological change took place to ensure patient safety. The authors found, not surprisingly, that exercise capacity was severely diminished and that most of the patients were not fully recovered mentally.

This study is important because it highlights the need for specific post-ICU follow-up and rehabilitation. It is time for the medical community to realize that the many thousands of patients who are discharged annually after more than a few days in the ICU require a specific therapeutic approach. A lot can be learned from neonatology where premature infants are in ongoing care for many years after discharge. This care integrates the care of the child with the care of the family. Just like neonatal intensive care, the burden of prolonged ICU stay is very high not only on the patient but also on the family. Long-term follow-up and management of both the physical and mental sides of the recovery process are essential to let those who recover from critical illness regain their full place in society.

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