conceivable that the same result could be more easily obtained by conventional dialysis, where the dialysate solutions are engineered to target a given strong ion difference. Either way, the manipulation of strong ion difference to achieve specific therapeutic effects is slowly gaining traction, and similar approaches have recently been shown to enhance respiratory support (15, 16). Whatever the future holds for these therapies, it behooves us to start teaching the physicochemical approach to our medical students and junior colleagues sooner rather than later. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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Mounting Clarity on Enteral Feeding in Critically Ill Patients

Like many questions in the ICU, best practices for provision of nutrition remain unclear. Several factors contribute to the relative lack of robust ICU nutrition research. Critical care clinical research is immensely difficult for a variety of reasons, not the least of which are extraordinary clinical heterogeneity and multiple overlapping interventions. Furthermore, our understanding of specific nutritional needs during severe physiologic and metabolic stress is poor. Finally, the field is historically fraught with strong opinions on all sides and heavy influence from industry. Despite important questions that remain unanswered, we are fortunate that several large investigator- or network-initiated randomized controlled trials (RCTs) studying enteral calorie delivery in critically ill patients have been published over the past 8 years. In this issue of the *Journal* (pp. 814–822), Deane and colleagues (1) report the 6-month outcomes of nearly 4,000 participants in the TARGET RCT (The Augmented versus Routine Approach to Giving Energy Trial) that investigated delivery of 70% versus 100% caloric requirements in mechanically ventilated critically ill adults.

How Does 100% versus 70% Caloric Intake Affect Critically Ill Patients 6 Months after Study Enrollment?

In the large, initial TARGET trial, the full- and reduced-calorie groups received 103% and 67% of calculated caloric needs, respectively (2). Average age and body mass index (BMI) were 57 years and 29 kg/m^2, respectively. The amount of protein delivered to both groups was similar. Neither 90-day mortality (the primary outcome) nor additional secondary outcomes were significantly different between the two arms. However, recovery does not stop at 90 days, and in their current work, Deane and colleagues (1) undertook telephone contact of over 2,700 survivors 180 days after randomization. The

Originally Published in Press as DOI: 10.1164/rccm.202001-0126ED on February 3, 2020

major 6-month outcome was quality of life, and additional functional outcomes (workforce participation, disability, and participation in activities), together with mortality, were also assessed. No discernible differences in 6-month functional status or mortality between the two groups were identified.

What Do These Data Mean in the Context of Prior Literature?

Including the TARGET trial, there have now been three large, multicenter RCTs investigating caloric dose in critical illness. The first of these (the EDEN [Early versus Delayed Enteral Feeding to Treat People with Acute Lung Injury or Acute Respiratory Distress Syndrome] trial) was conducted by the NIH Acute Respiratory Distress Syndrome Network and randomized 1,000 patients with acute respiratory distress syndrome to early "trophic" versus full enteral feeding for the first 6 days, with all participants then progressing to full feedings (3). Participants' mean age was 52 years, and their mean BMI was 30 kg/m^2. Participants received roughly 25% and 80% of calculated caloric needs in the trophic and full groups, respectively. Those in the full feeding group received more protein. There were no differences in ventilator-free, ICU-free, and organ failure–free days; 60-day mortality; or infectious complications. Needham and colleagues then assessed 1-year outcomes, both in person and via telephone calls, in patients participating in this RCT, and they found no differences in physical or cognitive function, psychological symptoms, or quality of life (4, 5).

The second RCT (the PermiT [Permissive Underfeeding versus Target Enteral Feeding in Adult Critically Ill Patients] trial), published in 2015 by Arabi and colleagues, randomized 894 critically ill patients (both medical and surgical) to early restricted versus standard enteral feeding for up to 14 days. Participants' mean age was 50 years, and their mean BMI was slightly less than 30 kg/m^2 (6). Although the restricted group received 46% of calculated caloric needs compared with 71% in the standard group, both groups received similar amounts of protein. There were no differences in 90-day mortality or in secondary outcomes, including hospital and ICU lengths of stay and infectious complications.

Taken collectively, data from these three trials and their subsequent analyses, including the paper by Deane and colleagues (1), provide strong evidence that the amount of nonprotein calories delivered during the first 1–2 weeks in the ICU to a general population of critically ill patients who are relatively young and well nourished does not significantly affect short- or longer-term outcomes. Feeding trophically or delivering full calculated calories, or any amount in between, is reasonable in most patients.

Limitations and Remaining Unanswered Questions

Although the authors should be congratulated on a remarkable investigation, there remains work to be done. One important feature of both the PermiT and TARGET RCTs is that protein delivery was equivalent in both arms, thus allowing dissociation from calories. Emerging evidence suggests that although calories are likely not important in many patients, protein delivery may be (7). Research to understand the role of protein supplementation in the recovery of ICU patients, including RCTs of standard-dose versus high-dose protein, are needed. In addition, average BMI in all three RCTs was high; thus, participants were likely well nourished. Although a *post hoc* analysis of the PermiT trial comparing outcomes between participants at high versus low nutritional risk, as measured by the Nutrition Risk in Critically Ill ("NUTRIC") score (8, 9), did not demonstrate any differences in outcomes, trials targeting malnourished high-risk patients remain a high priority. Furthermore, recent trials started enteral feedings very early in the ICU course, as current guidelines recommend (10). Although meta-analyses of many small and mostly single-center RCTs suggest that early enteral feeding (within 48 h of ICU admission) is associated with fewer infectious complications and at least a trend toward improved mortality (11, 12), large multicenter RCTs of early enteral nutrition versus a brief delay are lacking, despite calls for this research for nearly 25 years (13). Finally, we must remember that these RCTs were designed to study superiority, not equivalence. Thus, we cannot conclude that delivery of more or fewer calories is the same, only that it is not different.

In summary, this rigorous and thoughtful investigation comparing 100% versus 70% calorie delivery in critically ill patients helps to end the era of our focus on calorie delivery in the ICU. We should now turn our attention to other ICU nutrition questions. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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Rethinking Delivery of Care for Patients Requiring Prolonged Mechanical Ventilation

Patients requiring prolonged mechanical ventilation because of persistent respiratory failure experience a transition from the acute phase of illness responsible for intensive care admission and mechanical ventilation to one of rehabilitative and, in some cases, palliative care. This transition requires adaption of their clinical management plan and the way care is delivered (1). Important domains of care include liberation from ventilation; symptom relief; nutrition; physical, cognitive, and psychological rehabilitation; and discharge planning (2, 3). In the United States, this transition is frequently accompanied by transfer from an ICU to a lower intensity care setting located in a long-term acute care hospital. These hospitals specialize in care delivery for patients requiring extended hospitalization, providing rehabilitation services to patients requiring prolonged mechanical ventilation and those with other prolonged acute conditions (4).

In this issue of the *Journal*, Rak and colleagues (pp. 823–831) report a large and rigorously conducted ethnographic study of delivery and organization of care to patients requiring prolonged mechanical ventilation in eight long-term acute care hospitals (5). Using a positive–negative deviance approach, the study objective was to identify care practices common to high-performing hospitals but infrequent or absent at low-performing hospitals. The overall aim was to develop a framework for optimal care delivery for patients requiring prolonged mechanical ventilation. Participating sites were recruited from those long-term acute care hospitals identified as within the highest or lowest performance quartiles identified using a previously validated model of risk-adjusted mortality. Data comprised 329 hours of direct observation (2–3 observers for 4 d at each site), 196 key informant interviews, and 39 hours of job shadowing.

From these data, the authors identified four important, yet interdependent, domains of effective care practices considered influential for liberation from ventilation: ventilator care; mobilization; nutrition; and management of pain, agitation, and delirium. Identification of these domains in themselves is not novel because other authors have described these care practices as having an important role in successful liberation (6, 7). Importantly, however, Rak and colleagues extend our understanding of these domains through the identification of attributes of effective care within them (i.e., finding the appropriate and individualized balance between aggressiveness and responsiveness of care). As an exemplar, the investigators define aggressiveness of care as the degree to which ventilator management emphasizes physiological progress at the expense of day-to-day patient cues (i.e., continuing a spontaneous breathing trial despite patient distress and request to discontinue). Conversely, responsiveness of care is the degree to which ventilator management emphasizes day-to-day patient cues at the expense of physiological progress (i.e., discontinuing a spontaneous breathing trial at the request of the patient despite respiratory parameters being within normal ranges).

A key finding of the study was that high-performing hospitals achieved the optimal balance between aggressiveness and responsiveness individualized to a patient's needs. This occurred through a mechanism of action that reflects the concept of relational coordination: a mutual process of communicating and relating (i.e., shared goals, shared knowledge, and mutual respect); in other words, interprofessional teamwork and collaboration (8) for the purpose of task integration (9).

The complex, interrelated, dynamic, and frequently emotionally charged care for patients requiring prolonged mechanical ventilation and, indeed, all critically ill patients necessitates effective interprofessional communication and collaboration to enable a shared team approach to care delivery (10). Unfortunately, a substantial body

Originally Published in Press as DOI: 10.1164/rccm.202002-0292ED on February 19, 2020