admission to the recovery room, was related to the stimulation of an endotracheal tube at the time of extubation.

The peak effect of the neostigmine occurs 5 to 10 min after administration. This typically corresponds to the time of tracheal extubation. It would not be possible to conduct a comprehensive examination of patients for signs and symptoms of muscle weakness immediately before or after the removal of the endotracheal tube. This assessment was performed 15 min after postanesthesia care unit (PACU) admission, at a time when patients were sufficiently awake to cooperate with the research team. Given the duration of effect of neostigmine (typically 40 min or longer), \(^2\) we would likely have observed neostigmine-induced muscle weakness, if it were present, in the PACU. In contrast, patients who were administered neostigmine exhibited fewer symptoms of impaired neuromuscular recovery, compared to the control group. Furthermore, patients were carefully examined for any evidence of airway obstruction or hypoxic events from the time of tracheal extubation until 30 min after PACU arrival. No clinical evidence of an adverse effect of neostigmine on airway function was observed. In fact, the incidence of hypoxic events in the PACU was twice as high in the control-saline group.

Acceleromyography may recover slightly earlier than electromyography or mechanomyography. However, stand-alone electromyography and mechanomyography are no longer commercially manufactured, and acceleromyography is now considered the “gold standard” for clinical trials. As Drs. Phillips and Stewart note, some patients may have received neostigmine before full neuromuscular recovery had occurred, as documented with acceleromyography. However, many likely recovered hours before neostigmine was administered, since a small dose of rocuronium was given for induction and none thereafter; no clinical evidence of neostigmine-induced muscle weakness was observed in any of these subjects. In addition, as the authors note, two acceleromyography measurements made in the PACU may be discordant in awake patients; however, most of our acceleromyography assessments were performed in patients before emergence, and those measured in the PACU that differed by more than 10% were not recorded.

In our clinical investigation, with a careful examination of patients for adverse respiratory events and a thorough assessment for signs and symptoms of incomplete neuromuscular recovery, we were unable to detect any evidence of neostigmine-induced muscle weakness. Given the relatively high incidence of residual neuromuscular blockade observed in our study (21%), despite the low doses of rocuronium administered (25 mg) and long duration of cases (163 min), we believe our findings support the routine use of reversal agents, unless quantitative monitoring is used.

**Competing Interests**

Dr. Murphy has received speaking fees and has served on the advisory board for Merck (Kenilworth, New Jersey). The remaining authors declare no competing interests.

**References**

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**Colloids in Major Abdominal Surgery: Are They Really Better?**

*To the Editor:*

With great interest we have read the article by Joosten et al.\(^1\) recently published in ANESTHESIOLOGY. In their study they investigated the use of colloids versus crystalloids in relation to postoperative complications in major abdominal surgery. They conclude that a colloid-based, goal-directed fluid therapy is associated with fewer postoperative complications than a crystalloid-based approach, possibly as a result of a lower intraoperative fluid balance when colloids are used.

In the last decades many studies have focused on hemodynamic optimization in high-risk surgery with fluids, inotropes, and advanced hemodynamic monitoring.\(^2\) As protocol adherence remains an issue in most studies, the use of an automated closed-loop system for fluid administration in the study of Joosten et al.\(^*\) is exceptionally elegant. After reading the article we have one major concern: are the groups really comparable? As the authors point out, despite the randomized setup, the baseline characteristics show that surgery duration and anesthesia duration (and hence duration of mechanical ventilation) are both more than an hour longer in the crystalloid group than in the colloid group.

No results of statistical tests are provided to verify that the difference is indeed statistically significant, but it is highly likely. Despite the comparable amount of blood loss, the incidence of high-risk surgery, and the Physiological and Operative Severity Score for Enumeration of Mortality and...
Morbidity (POSSUM) between the groups, the only right conclusion about the longer surgery time must be that surgery in the crystalloid group was more difficult. It is likely that difficult surgery is associated with more tissue damage and therefore more inflammation. Accordingly, longer surgery is associated with increased markers of inflammation. Moreover, the longer duration may still indicate a difference between the groups, an underlying (inflammatory) condition. Thus, an increased state of systemic inflammation in the crystalloid group could have contributed to increased microvascular permeability, resulting in a higher need for fluid administration. Longer duration of surgery is also an independent risk factor for anastomotic leakage, which is significantly more present within the crystalloid group. Both could explain the results showing an observed better outcome in the colloid group. So unfortunately, in this study it may not be the intervention that makes the difference, it might be the control group.

Competing Interests
The authors declare no competing interests.

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In Reply:
We would like to thank Drs. Slagt and van Eijk for their interesting comments regarding our recent publication. These authors suggested that the complexity of surgery, resulting in a longer procedure (1 h longer in the crystalloid group), and not the type of fluid was responsible for the higher incidence of postoperative complications in the crystalloid group, due to a higher inflammatory response. We have no data to support more complex surgeries in the crystalloid group beyond the surgical time because surgical procedures and incidences of high-risk surgery were comparable in the two groups. Additionally, blood loss was also not different between the two groups, further supporting similar surgical complexity among the two groups. If the inflammatory response related to the surgical procedure was responsible for the higher fluid balance in the crystalloid group, we might also have expected a significantly higher fluid balance on postoperative day 1 in this group, which was not demonstrated. In order to take into account the difference in surgical duration, we originally presented our results in ml·kg⁻¹·h⁻¹ and observed a significantly higher fluid administration in the crystalloid group. It is true that we did not directly measure any parameter, which may have indicated a more severe inflammatory response in the crystalloid group than in the colloid group. As a result, we could not completely rule out the hypothesis of Drs. Slagt and van Eijk. To further investigate their hypothesis, we did go back to the data of the 102 patients who underwent a gastrointestinal anastomosis to compare the surgical duration between those who either did or did not have an anastomotic leakage postoperatively. We observed that surgical duration was not different between these two groups (anastomotic leakage, 240 min [204 to 387] vs. no anastomotic leakage, 268 min [185 to 336]; P = 0.850). Interestingly, fluid balance was significantly higher (6.0 ml·kg⁻¹·h⁻¹ [5.1 to 8.4] vs. 3.1 ml·kg⁻¹·h⁻¹ [1.7 to 5.0]; P = 0.021) among patients developing an anastomotic leakage. These data confirm that surgeries with postoperative complications had higher intraoperative fluid requirements, unrelated to length of surgery. It should also be noted that there have been experimental studies demonstrating that goal-directed colloid therapy significantly increases microcirculatory blood flow and tissue oxygen tension in perianastomotic colon tissue compared to a goal-directed crystalloid fluid therapy. Finally, the surgical duration could still be a result of the groups and not a confounding factor. As a result, although we cannot formally exclude that a prolonged surgical duration might have contributed to our results, we remain confident that our results are mainly related to the type of fluid used to optimize hemodynamic management as part of a closed-loop-assisted goal-directed fluid therapy.

Competing Interests
Dr. Joosten is a consultant for Edwards Lifesciences (Irvine, California). Dr. Rinehart has ownership interest in Sironis (Newport Beach, California), a company developing closed-loop systems; and does consulting for Edwards Lifesciences. Dr. Van der Linden has received, within the past 5 yr, fees for lectures and consultancies from Fresenius Kabi GmbH (Bad Homburg, Germany) and Janssen-Cilag SA (Olen, Belgium). Dr. Delaporte declares no competing interests.