



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 112742

Title: Muscle mass correlates with rocuronium distribution volume and guides dose optimization in obese CRC patients

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08396845

Position: Peer Reviewer

Academic degree and professional title: PhD

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2025-08-15

Reviewer chosen by: AI Editor

Reviewer accepted review: 2025-08-15 09:22

Reviewer performed review: 2025-09-03 09:38

Review time: 19 Days

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? Yes Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes
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Is the content of the Materials and Methods complete?

Yes

Is the content of the Introduction adequate? **Yes**

Is the description of the experiments clear and complete? **Yes**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Yes**

Are the experimental data of the Results true and reliable? **Yes**

Are the quality and resolution of the images up to standard? **Not Applicable**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **No**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **No**

Are all references related to the topic of the manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Will the manuscript's content be of interest to readers?
Yes

Is the manuscript's text correct, concise, and clear? **Yes**

Are additional experiments needed for the study? **No**

Does the research scope comply with ethics? **Yes**



Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade C (Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade C (Good)
Language quality	Grade C (Good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Minor revision
Re-review	No
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

The authors have successfully developed a population pharmacokinetic model and proposed an individualized dosing strategy in obese colorectal cancer (CRC) patients based on muscle mass, which demonstrated the significant improvements in both target exposure achievement and reduction of postoperative residual neuromuscular blockade. The manuscript is well-structured, the methodology is robust, and the statistical analyses are appropriate. The use of the InBody260 analyzer to measure SMI of obese CRC patients provides a practical, non-invasive, and reproducible method for assessing



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muscle mass, which is a notable improvement over traditional imaging techniques like CT or MRI that are less accessible in routine preoperative settings. The demonstrated strong correlation between SMI and rocuronium's volume of distribution ($r=0.718$) underscores the physiological plausibility of muscle mass as a key determinant of drug distribution for hydrophilic agents like rocuronium. Furthermore, the application of nonlinear mixed-effects modeling (NONMEM) followed by Monte Carlo simulations represents a sophisticated approach to dose individualization. The model validation through bootstrap and prediction-corrected visual predictive checks (pcVPC) confirms its reliability and predictive performance. The significant improvement in target attainment (from 82.0% to 93.5%) and the reduction in residual paralysis (from 13.0% to 3.5%) are clinically meaningful outcomes that highlight the potential impact of this dosing strategy on obese CRC patient safety. The Bootstrap validation showed a 92.3% success rate, which is acceptable, but the relatively small sample size may limit the stability of parameter estimates. External validation in an independent cohort would further reinforce the model's generalizability. The proposed dosing regimen, 0.52 mg/kg SMM for induction and 0.22 mg/kg SMM for maintenance in sarcopenic patients, versus 0.64 mg/kg SMM and 0.16 mg/kg SMM in non-sarcopenic patients, is pragmatic and clinically applicable. The use of SMM for dosing simplifies calculations compared to ideal or adjusted body weight methods. The significant reduction in postoperative residual curarization (from 13% to 3.5%) is particularly noteworthy, as residual blockade is associated with adverse respiratory events, prolonged hospital stay, and increased healthcare costs. However, the study did not report on other clinical outcomes such as postoperative pulmonary complications, patient satisfaction, or economic impacts. Future studies should evaluate whether the improved pharmacokinetic profile translates into enhanced recovery and reduced morbidity.



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Academic degree and professional title: Associate Chief Physician, Chief Physician

Reviewer's Country/Territory: Germany

Author's Country/Territory: China

Manuscript submission date: 2025-08-15

Reviewer chosen by: AI Editor

Reviewer accepted review: 2025-08-16 17:43

Reviewer performed review: 2025-09-05 08:02

Review time: 19 Days and 14 Hours

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Does the research scope comply with ethics? **Yes**

Scientific quality	Grade C (Good)
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Conclusion	Minor revision
Re-review	No
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

The manuscript described a retrospective cohort study involving 100 obese patients (BMI ≥ 30 kg/m²) undergoing elective radical colorectal cancer surgery at a institution between June 2023 and January 2025. The authors provide compelling evidence that skeletal muscle index (SMI), measured via bioelectrical impedance analysis (BIA), strongly correlates with rocuronium distribution volume and clearance in obese patients undergoing colorectal cancer surgery. By leveraging population pharmacokinetic modeling and simulation, they develop an individualized dosing framework that



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significantly enhances target exposure attainment and reduces the incidence of postoperative residual neuromuscular blockade. Rocuronium is a hydrophilic compound with limited lipid solubility, meaning its distribution is largely confined to the extracellular fluid compartment, of which skeletal muscle is a major component. The demonstrated positive correlation between SMI and V_{ss} ($r=0.718$) aligns perfectly with this principle. Interestingly, the study also found a moderate negative correlation between SMI and clearance ($r=-0.502$), suggesting that CRC patients with higher muscle mass may have enhanced metabolic capacity or better organ perfusion. While the findings are compelling, their generalizability beyond obese colorectal cancer patients is uncertain. Cancer cachexia can alter body composition and drug metabolism independently of obesity. The proposed SMI-based dosing strategy outperforms traditional weight-based methods and offers a practical approach to optimizing neuromuscular blockade in obese patients. With minor revisions and additional validation, this work has the potential to change clinical practice and improve patient safety. The study also opens avenues for research into other drugs whose pharmacokinetics are influenced by body composition. Many antibiotics, sedatives, and analgesics have distribution volumes that correlate with lean tissue mass. The BIA-based approach could be extended to optimize dosing for these medications, particularly in critically ill or elderly patients with altered body composition. Based on this model, the authors developed a novel, individualized dosing regimen using Monte Carlo simulation. Instead of traditional total body weight (TBW), the new strategy bases induction and maintenance doses on the patient's skeletal muscle mass (SMM) and sarcopenia status. This optimized protocol significantly improved performance compared to the standard TBW-based approach.