Table 1. Amount of Atelectatic Lung in the Postoperative Chest Computed Tomography

Analyzed Range	Unit (% of Total Lung)	Group		*P* Value*
		PEEP 4	Titrated PEEP	
−100 to +100 HU	% lung volume	2.3 (0.5–4.1)	0.9 (0.4–1.9)	0.015
	% lung mass	8.4 (2.6–12.0)	3.4 (1.5–5.5)	0.005
−200 to +100 HU	% lung volume	3.1 (0.9–5.5)	1.9 (0.8–2.9)	0.027
	% lung mass	11.5 (4.0–16.2)	5.7 (2.8–8.4)	0.017

Values in median (interquartile range).

*Mixed model analysis considering PEEP group and type of surgery.

HU, Hounsfield unit; PEEP, positive end-expiratory pressure.

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(Accepted for publication May 9, 2019.)

Where's the Beef Indeed!

To the Editor:

The editorial by Henthorn and Olofsen in the February 2019 issue of Anesthesiology[1] provides a wonderful discussion on the importance of measuring biophase drug concentrations when conducting pharmacokinetic–pharmacodynamic studies. The editorial addressed an important study that examined the relationship between modeled, non–steady-state concentrations of remifentanil and respiratory depression in adults with moderate-to-severe obstructive sleep apnea.[2] That study, owing to practice constraints, used a modeling approach, rather than measured remifentanil concentrations. Henthorn and Olofsen term that "economized pharmacokinetic/pharmacodynamic." In their assessment of three different approaches to modeling techniques, Henthorn and Olofsen conclude that model-predicted concentrations are not as useful as measured drug concentrations. They suggest that caution is warranted in "drawing conclusions in the language of pharmacokinetic–pharmacodynamics when there are no drug concentration (pharmacokinetic) data and when there is non–steady-state effect data and either the onset of effect or offset of effect is missing."

We recently reported the effects of remifentanil in pediatric patients with moderate-to-severe obstructive sleep apnea, also using a fixed-rate infusion.[3] Venous remifentanil concentrations were measured 1, 2, 4, 6, 10, and 15 min after starting the infusion. Projected arterial remifentanil concentrations were also calculated, using Rugloop II (DeMed, Belgium) and the Minto model with dose, sex, height, age, and weight.[4] Measured and simulated remifentanil plasma concentrations over time are shown in figure 1. Measured remifentanil concentrations had considerable variance from the predicted concentrations, and substantial interindividual variability. While it is expected that arterial and venous concentrations would differ (arterial higher), particularly at non–steady-state and early

<zdoi;DOI: 10.1097/ALN.0000000000002834>

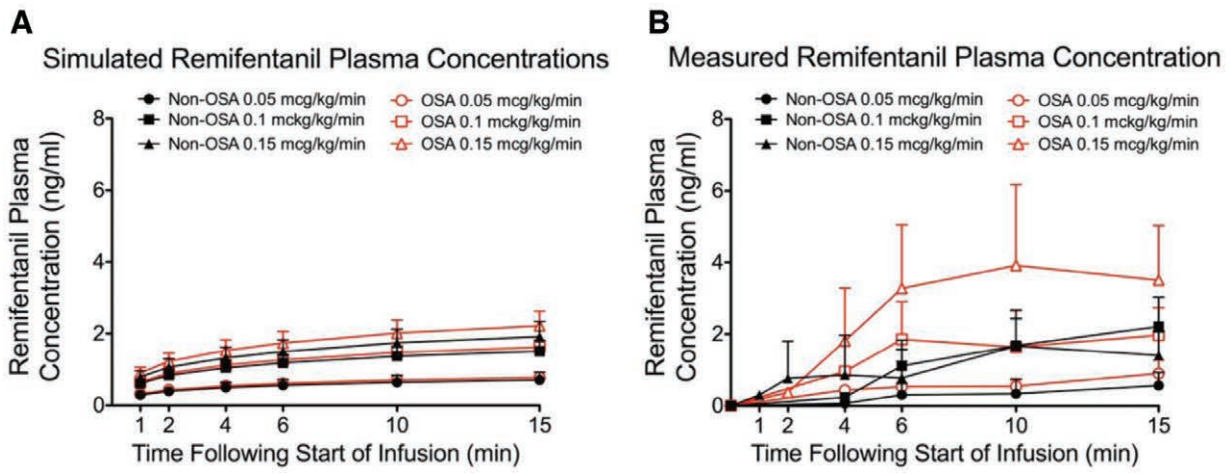

Fig. 1. Simulated arterial and measured venous plasma remifentanil concentrations.

in an infusion, venous measured concentrations were higher than arterial predicted concentrations, and much more variable.

Interindividual variability can lead to several-fold differences in predicted *versus* measured plasma drug concentrations, especially for short duration, non–steady-state infusions.[5,6] In addition, for remifentanil, the optimal model for predictions may yet be uncertain.[7] The relevant consideration is that discordance between modeled *versus* measured remifentanil (or any drug) concentrations illustrates the importance of measuring actual drug concentrations when performing pharmacokinetic–pharmacodynamic studies, lest pharmacokinetic differences be misattributed as pharmacodynamic effect.[8] I wish to thank Drs. Henthorn and Olofsen for bringing attention to these important considerations.

Research Support

Supported by a Faculty Development Award from the Pharmaceutical Research and Manufacturers of America Foundation (Washington, DC) and the Department of Anesthesiology, Washington University in St. Louis, St. Louis, Missouri.

Competing Interests

The author declares no competing interests.

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DOI: 10.1097/ALN.0000000000002836

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(Accepted for publication May 9, 2019.)