Host: Welcome to the Anesthesiology journal podcast, an audio interview of study authors and editorialists.

Dr. James P. Rathmell: Hello. I’m Jim Rathmell, Professor of Anesthesia at Harvard Medical School and Chair of the Department of Anesthesiology, Perioperative and Pain Medicine at Brigham and Women’s Hospital in Boston, Massachusetts. I’m one of the Executive Editors of Anesthesiology and you’re listening to an Anesthesiology podcast that we’ve designed for physicians and scientists interested in the research that appears in the journal.

Today we’re going to be talking to the lead author of an original research article that appears in the December 2018 issue. With us today is Dr. Marcelo Amato. Dr. Amato is Chief of the Experimental Pulmonary Laboratory at FMUSP, the University of São Paulo, and Professor at the University of São Paulo in São Paulo, Brazil.

Dr. Amato is the senior author on an article that appears in the December 2018 issue of the journal and it’s titled “Individual Positive End-expiratory Pressure Settings Optimize Intraoperative Mechanical Ventilation and Reduce Postoperative Atelectasis.” Dr. Amato, thank you for joining us.

Dr. Marcelo B. P. Amato: Hello, Jim. Thanks for this opportunity.

Dr. James P. Rathmell: Also with us today is Dr. Robert Kacmarek. He serves as the Director of Respiratory Care Services at Massachusetts General Hospital and has done so for the last 35 years. Dr. Kacmarek wrote an editorial view that accompanies Dr. Amato’s original research article in the December 2018 issue titled “Lung-protective Ventilation in the Operating Room: Individualized [Positive End-expiratory Pressure] PEEP is Needed?” Dr. Kacmarek, thank you for joining us today.

Dr. Robert M. Kacmarek: You’re welcome.

Dr. James P. Rathmell: Dr. Amato, congratulations on the publication of your work. I want to start by explaining what’s meant by lung-protective ventilation. If you could explain for listeners and then tell us what you hypothesized about how using this strategy in the operating room might impact patient outcomes.

Dr. Marcelo B. P. Amato: For a long time, we have been doing research in acute lung injury and when the lung is inflamed we had lots of evidence suggesting that to treat the lung gently was key to reduce inflammation, more or less like bone fracture where you need some rest of the tissue to have a good healing of the process and inflammation.

But it has been debated for a long time if the same principle applies to normal lungs. We had some evidence that this was true and also along the years we have collected data showing that despite the fact that the inflammation is moderate, we have lots of inflammation during surgery or during normal mechanical regulation even for a few hours.

So, the idea is that if there is inflammation, we need some lung protection and the principles of lung protection they include both: a certain restriction of tidal breaths, so you need lower driving pressures, but at the same time, there is always an optimum PEEP that can minimize the stress on the lung.

We know for a long time that it cannot be too much because then you caused overstretch of the tissues with loss of elasticity and then the driving pressures increase again. But on the other hand, if we apply too low PEEP or too low baseline pressure, you have some units of the lung that are excluded from ventilation and then driving pressures increase again with increased stress and inflammation.

So, we tried to apply these principles in patients during anesthesia to check. Basically this study was just analyzing some consequences of lung collapse or some signals of lung overdistention during surgery. And we tested in 40 patients during general anesthesia.

The lung collapse was measured by CT in the postoperative phase and the signals of lung overdistention were measured by EIT, electrical impedance tomography, which was also used to detect the optimum PEEP.

Dr. James P. Rathmell: So, we’re going to get into more details of the study, but I like what you said: treat the lung gently. So, you hypothesized that low fixed-positive end-expiratory pressure, or PEEP, might not be optimal for all patients, just one size fits all, but individually titrated PEEP during anesthesia might improve lung function during and after surgery.

Tell us how you went about this study. What patients—exactly what patients you used, 40 surgical patients. But what patients did you choose and how did you actually conduct the trial?

Dr. Marcelo B. P. Amato: We tried to use common patients in our hospital. I was surprised by the amount of obese patients we found and this is a reflection of the current situation of Brazil that we have some obese patients. Not that much like in United States, but the average body mass index was 28.

Maybe also there was some unavoidable patient selection because we chose abdominal surgery and many of these patients they have the phenotype of obese woman around the 40’s.

Dr. James P. Rathmell: So, they were randomized to receive PEEP of 4 cm of H2O or a variable level of PEEP guided by electrical impedance tomography. Tell us in simple terms how this electrical impedance tomography works.

Dr. Marcelo B. P. Amato: Electrical impedance tomography is the result of 15 years of research trying to find a tool to better understand the mechanics of the lung during mechanical ventilation. We knew that the lung was heterogeneous based on (sounds like: fatigue studies) and we knew also that an average output like general compliance or general mechanics that we measured with the endotracheal tube can sometimes misguide us.

It’s like observing the mean income of Brazil and not observing that medians were starving because we have many rich people at the same time. So, we were trying to find a way of having some regional information about the lung and the EIT is now a bedside tool in which you can have some representation of small parts of the lung.

In terms of the diameter of the anterior-posterior axis of the thorax, imagine a cross section of the thorax like in a CT. The EIT has a resolution of one-tenth of the diameter. So, you can distinguish at least 8-to-10 layers of the lung and then you can understand what is happening in each layer.

Dr. James P. Rathmell: So, what did you learn? How did you use electrical impedance tomography-guided PEEP? And how did that affect subsequent outcomes that you measured?

Dr. Marcelo B. P. Amato: To use the EIT properly, you have to do some PEEP trial while you are monitoring with EIT. So, it’s like when we are also monitoring mechanics during a decremental PEEP trial.

It’s important that the trial must be decremental because there is a good sequence of events that allow us to calculate the amount of tissue that is excluded from ventilation at lower PEEP levels and at the same time it’s possible to calculate the amount of tissue that is overdistended when PEEP is above the optimum point.

So, basically, when we try to titrate PEEP according to electrical impedance tomography, we try to get a balanced equilibrium between units that are excluded from ventilation and units that are overdistended and mainly in the anterior region of the thorax.

So, we can identify this crossing point of the two phenomenon; we feel we have a very good procedure with EIT.

Dr. James P. Rathmell: And what outcomes did you measure and what did you conclude from the study?

Dr. Marcelo B. P. Amato: We measure atelectasis after the surgery by performing CT analysis in all patients after one hour of extubation. So, they—very interesting finding is that many patients had lots of atelectasis, something like 20% of the lung was collapsed after one hour of extubation after some physiotherapy sessions, so this means that some patients they have persisting atelectasis for three or four days after surgery.

Dr. James P. Rathmell: What did you conclude from the study in the titrated PEEP versus the standardized PEEP?

Dr. Marcelo B. P. Amato: The titrated PEEP was enough to prevent atelectasis. It was reduced by many folds in the titrated PEEP. It was not 0 because our intention was not to apply open-lung PEEP. We just wanted to apply enough PEEP to prevent massive atelectasis and the study showed that we were successful.

And at the same time, we realized that the amount of overdistension that we had to cause in the nondependent lung was not substantial; in fact, it was
the same or sometimes even less than what we observed in the conventional PEEP of 4 cm of H2O. So, I believe that we could achieve a good balance between overdistention and collapse.

The physiology during surgery also told us—and especially the physiology measured before extubations, we measured shunt levels, PO2 and compliance of the patient, they all indicated that the patients, when they finished the surgery, they had better lung mechanics which was already reflecting a lower amount of collapse.

And then this was translated; after extubation, we saw less atelectasis as measured by CT.

Dr. James P. Rathmell: Well, versus the standardized PEEP of 4 cm of H2O, what was the average PEEP? So, a BMI of 28 was your average. And what was the average level of titrated PEEP?

Dr. Marcelo B. P. Amato: This was a surprise. The average number was 12 which was much higher than I was expecting. I was expecting something around 8 or 7 considering the obesity of these patients. So, I was surprised to see that we needed such an amount of PEEP.

But one important fact in this study is that these optimum PEEP varied from 6 to 16 and although there was some correlation with body mass index, which was significant, the range of PEEP for the same body mass index was very large; something like 8-to-10 cm of H2O. So, by just looking at the phenotype of the patient, you cannot predict how much PEEP you need; you just have an idea that he needs a little bit more, but you need some individualized titration.

Dr. James P. Rathmell: So, what do you think the take-home message is for practicing anesthesiologists? Is it practical to use electrical impedance tomography in the operating room every day?

Dr. Marcelo B. P. Amato: As far as you can stand, five minutes of evaluation before the surgery is what we need. We need the anesthesiologist to look at the patient for five minutes and doing these maneuvers with the help of electrical impedance tomography.

It was interesting because in our hospital, especially in the early morning, the surgeons are in a hurry and then we had to convince them that we could do the procedure very fast.

Dr. James P. Rathmell: Some things are the same the world over. Dr. Kacmarek, I want to turn to you now and your editorial view. You wrote this together with Dr. Jesús Villar from Madrid, Spain and it’s titled “Lung-protective Ventilation in the Operating Room: Individualized PEEP [Positive End-expiratory Pressure] is needed!”

Obviously you’re a fan of individualized PEEP, but you can start by telling us about ventilatory parameters. These are now well acceptable for providing protective lung ventilation regardless of the location where that mechanical ventilation is being carried out.

So, could you review those for us? You do a nice job in your paper.

Dr. Robert M. Kacmarek: As Marcelo indicated, clearly the concern about tidal stretch should exist in every patient we mechanically ventilate. Our normal tidal volumes as we sit here discussing this are approximately 6 ml per kg.

So, the ARDSnet Trial clearly established what that range should be in critically ill patients, but increasing data shows that patients who are mechanically ventilated patients is the driving pressure because it gives you that reflection of what tidal volume is doing in association with stretch of the lung.

So, keeping the driving pressure below 15 cm of H2O, again, is an ideal approach to the way we should ventilate all patients from a lung-protective perspective.

And finally, there’s increasing data, as you’re aware, about hyperoxia and its association with poor outcome in patients in critical care. So, it seems to be appropriate that we get away from using high FiO2s on all patients and titrate that FiO2 to give us a relatively normal oxygenation status instead of a hyperoxegenation status.

So, those would be the four variables that I would say now we have good data to support the fact that any patient mechanically ventilated should be ventilated, if at all possible, within those guidelines.

Dr. James P. Rathmell: So, I want to expand on what you just said. So, tidal volume, plateau pressure, expired oxygen concentration are all kind of second nature to the anesthesiologist. No matter where they work. But driving pressure. How do we get at driving pressure in everyday life, everyday practice?

Dr. Robert M. Kacmarek: So, driving pressure is a pretty easy variable to quantify. It’s simply taking the end-inspiratory plateau pressure and subtracting the total PEEP from that end-inspiratory plateau pressure; basically, the amount of pressure necessary to overcome the elastic recoil of the lung and thorax. A surrogate, if you will, for actually measuring compliance.

So, as long as we keep that low, we know we don’t exert a significant amount of dynamic stress during the application of that tidal volume regardless of what the actual tidal volume is.

Dr. James P. Rathmell: Perfect. Now, those optimal parameters don’t include any guidance on optimal levels of PEEP. Why not?

Dr. Robert M. Kacmarek: Well, the literature isn’t as definitive when we look at the application of PEEP. And of course, PEEP is a little trickier to apply because the level that’s necessary—as you and Marcelo just discussed—is really based on the individual pathology of the patient that you’re treating and some patients require very low levels of PEEP.

And if we look at the obese population that we have here in the United States, I mean, we’ve applied upwards to 26, 28 cm of H2O PEEP in that population of patients.

So, it’s difficult to come up with any specific guideline that can be used universally without doing the individual experiment on the patient; as Marcelo indicated, doing a recruitment maneuver and doing a decremental PEEP trial. The data, though, the way that studies have been done have been inconsistent and we just do not have the consistent outcome data that I feel comfortable saying, “Absolutely, this is how we apply this” as I have said with the other variables.

Dr. James P. Rathmell: So, you’re calling for individualized PEEP. In your editorial you really nicely describe the findings of this study and how electrical impedance tomography works and I’m going to encourage listeners to go and read that editorial to get more information.

But you also talk about some other methods for titrating the level of PEEP. What other methods are used?

Dr. Robert M. Kacmarek: Yes, I think the three approaches now that give us the best indication of the PEEP level that results in the least over-distention and the least collapse are to use, first of all, electrical impedance tomography because it gives you precise percentages of each of those. But the next would be to use the decremental PEEP trial focusing on the best compliance PEEP. At least in our data, and I know Marcelo has similar data, that they correlate very well, that if we determine what is the best compliance PEEP after recruitment maneuver, achieving that in a decremental manner, it coincides plus or minus 1 or 2 cm of H2O with the PEEP level you would set if you use electrical impedance tomography.

And the third approach is the one that Danny Talmor has popularized and that’s looking at esophageal pressure. That’s probably technically the most difficult to do because it does require some skill in inserting the balloon
and positioning it, inflating it and, of course, interpreting the overall data. And the only negative part of that is it gives you the level of transpulmonary pressure at one location in the lung.

So, depending upon the pathology, you might overestimate or underestimate the amount of PEEP that should be applied, but it does give you a reasonably good estimate of what PEEP level results in establishing a lung volume that sustains the end-expiratory transpulmonary pressure positive.

So, those would be the three in that order.

Now, you were discussing earlier, what do you in the OR? Well, as you know, electrical impedance tomography today is not readily available in the United States. I expect in the future that circumstance will change dramatically, but today my recommendation to the average anesthesiologist is to do the recruitment maneuver and then do a decremental PEEP trial looking for the best compliance PEEP and use that PEEP as the setting in your patients.

Dr. James P. Rathmell: Perfect. You also go on and compare and contrast a previously published study by Ferrando that reached different conclusions than what Dr. Amato’s trial reached. Can you briefly summarize the main differences and what you concluded in comparing them?

Dr. Robert M. Kacmarek: Yes, this was a trial done in Spain and basically was looking at the same set of circumstances as Marcelo looked at except that they had four arms in the study and they recruited a thousand patients; two of the arms were very similar intraoperatively to what Marcelo actually did.

The big difference is what was the outcome measure of importance as Marcelo’s study looked at the amount of atelectasis immediately after the patient was extubated or within an hour after the patient was extubated. The Spanish study looked at the number of complications over the first seven postoperative days.

So, they did not evaluate the immediate postoperative period; they simply followed these patients and they had a whole litany of different complications that they were tracking, so it is difficult to correlate their lack of finding a difference globally with Marcelo’s data because they were looking at two entirely different things.

But in their secondary analysis, when they took the two arms in which the patients were managed with an open-lung approach compared to the two that used standard approach of, in this case, 5 cm of H2O PEEP, they did find that the amount of postoperative pulmonary complications again globally were lower in the group that had the open-lung approach.

What would be nice, if they went back and pulled out some of those key complications and looked at them individually instead of grouping this whole myriad of complications into one bundle; that makes it very difficult as a result to interpret their data.

Dr. James P. Rathmell: But from both trials, do you directionally conclude what you’ve told us already is that titrated PEEP is really what we need in the operating room? And you’ve told us how to do that.

Dr. Robert M. Kacmarek: There’s no question that I think that the individualized approach to applying PEEP, whether you’re in the operating room or the ICU, is correct. I mean, patients from a pathophysiology perspective are totally different.

In the OR, patients are thin, patients are obese; to assume that we can set one level and, in most of the recommendations, one level of low PEEP and expect that to avoid significant atelectasis particularly during some of the surgical procedures is just not reasonable.

And I think we should accept the fact that we should base our treatment on physiologic response and individualize it like we do most other things to the specific patients.

Dr. James P. Rathmell: Dr. Amato, I want to give you a chance to respond briefly to some of the concerns of Dr. Kacmarek.

Dr. Marcelo B. P. Amato: Thanks. I would like to say a few words about methodological errors because I have been involved in not only in research, but in education in the last 20 years. And I have seen many students and residents trying to apply some PEEP titration at the bedside and I have seen lots of mistakes and not because they are sloppy or stupid, but because it’s a stressful situation and you have to pay attention to multiple parameters at the same time.

So, I have observed that during research trials like those multicentered trials, these methodological errors, they happen all the time. And it’s like an experienced physician: he can place a central venous line easily and without too much complications. But certainly to the general young physician, it’s much better to try a central venous line with the help of an ultrasound.

So, I believe that improving the technology will help us to perform less methodological errors and I think this is one of the causes of the confusing results we have now in the literature when it comes to the human being because if you look at animal studies I think there is much more consistency in terms that we need an individualized PEEP and there is an optimum PEEP for sure.

But then when it comes to multicenter studies, it’s much more cumbersome to prove that. I really believe that methodology and some technology can help us in this case and there is another beneficial side effect of technology in this case is that we have the possibility of detecting real-time problems like accidental extubations, accidental selective intubation, secretions impairing the measurements or some overinflation of one lobe or something like this.

So, in summary, I fully agree with Bob. We have multiple ways of doing this, but this is extremely dependent on the practice of the bedside physician.

Dr. James P. Rathmell: Well, so, you’re both calling for individualized PEEP and hopefully simplification of the technology that you have detailed in your study today, maybe one of the answers ahead that will make it easier for the average practitioner.

I want to congratulate you again on the publication of your work. What’s coming next for you and your research team?

Dr. Marcelo B. P. Amato: We are going to address, again, the acute lung injury population, but using and fixing all the mistakes we did in previous trials. I think these could result in patients in the operating theater were very exciting for us because it’s a proof of concept that we have to test these approach[es], also for the general population of patients under mechanical ventilation and acute lung injury.

So, I think we are going to address this issue in the next year. And at the same time, this study was good to tell us to raise the problem that this is a very fragile population that we should address first, which is obese patients. So, these are my two conclusions after this study.

Dr. James P. Rathmell: Terrific. I hope today’s discussion will lead many of you listening to read this new article and the accompanying editorial review. They appear in the December 2018 issue of Anesthesiology. You can learn more about optimization of PEEP in the operating room.

I also want to tell you that Dr. Jon Wanderer and I created an infographic that appears in the same issue and illustrates the different methods that can be used to titrate PEEP in the operating room, including those that we talked about today.

Dr. Amato and Kacmarek, thank you for joining me today and for the terrific explanations about optimizing PEEP in the operating room and wherever mechanical ventilation is used.

Dr. Marcelo B. P. Amato: Thanks, Jim.

Dr. Robert M. Kacmarek: Thank you.

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