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

Dr. BobbieJean Sweitzer: Hello. I’m BobbieJean Sweitzer, Professor of Anesthesiology at Northwestern University and an Associate Editor for *Anesthesiology* and you are listening to an *Anesthesiology* podcast designed for physicians and scientists interested in the research that appears in our journal.

Today we are speaking with the author of a publication that appears in the July 2019 issue of the journal. With us is Dr. Domenico Luca Grieco. Dr. Grieco is the lead author of an article titled “Airway Closure During Surgical Pneumoperitoneum in Obese Patients.” He is an Attending Physician in the Intensive Care Unit and a Research Fellow in the Department of Anesthesiology and Intensive Care Medicine at the Catholic University of the Sacred Heart in Gemelli Hospital in Rome, Italy. Welcome, Dr. Grieco.

Dr. Domenico Luca Grieco: Thanks for the invitation. It’s a great privilege for us to present the results of this paper to the anesthesiology community.

Dr. BobbieJean Sweitzer: We’re delighted to have you. So, can you start by telling us what is meant by “airway closure” or, I guess, as defined as it applies to your study?

Dr. Domenico Luca Grieco: Thanks for the question. I think it is one of the most interesting points of our results. In fact, airway closure has been described in the 70s and 80s during general anesthesia, but that kind of airway closure was related to small airway closure.

In our paper recently published in *Anesthesiology*, we report the existence of complete airway closure which involves all the airways in anesthetized patients during pneumoperitoneum before Trendelenburg and after Trendelenburg position. This airway closure is airway collapse that occurs during expiration and that implies that during the following inspiration before inflating the tidal volume, a threshold of airway opening pressure has to be overcome.

Dr. BobbieJean Sweitzer: So, are we still talking about, I guess, airway closure in the alveoli only or is this, like, all the way up into major bronchi?

Dr. Domenico Luca Grieco: We still don’t have any idea of the real sites of airway closure because we have data showing – old studies showing that airway closure occurs in is more bronchioli, but what we are reporting and that implies that during the following inspiration before inflating the tidal volume, a threshold of airway opening pressure has to be overcome.

Dr. BobbieJean Sweitzer: Interesting. So, as defined the way you’ve just done it, is this airway closure a phenomenon in spontaneously breathing non-anesthetized humans and people who aren’t critically ill, CPR, those kinds of situations?

Dr. Domenico Luca Grieco: Well, we have a lot of data about expiratory flow limitation in COPD patients doing spontaneous breathing and we know that small airway closure, distal and regional airway closure contributes to flow limitation and to the originality of a PEEP high, intrinsic PEEP in these patients through spontaneous breathing.

But this specific phenomenon we are reporting, which is a closure of the airways with a single airway opening pressure—and has been described in the RDS and in cardiac arrest patients—occurs in the absence of spontaneous breathing.

We don’t know about the time course of these phenomenon once spontaneous breathing is reestablished after paralysis and mechanical validation.

Dr. BobbieJean Sweitzer: So, has airway closure of this type been reported previously in patients having general anesthesia or is the first time?

Dr. Domenico Luca Grieco: There are a couple of studies from Professor Talmor and Professor Loring from Boston. They showed something on the low-flow inflation pressure-volume curve of this artery system very similar to the airway closure we are describing.

Their interpretation of that phenomenon, which was an opening pressure, was related to the transpulmonary pressure. They find that critical pressure to overcome to inflate the lung has the pressure needed to achieve a transpulmonary pressure that is positive.

In our study we found something a bit different because we found that this critical airway opening pressure was unrelated to a positive transpulmonary pressure.

Moreover, we have data coming from a large group of investigators led by Takeshi Yoshida in a publication in the Blue Journal last year showing that the pleural pressure has vertical gradient from the nondependent to dependent part of the lung. So, the pleural pressure is not constant across the lungs, so transpulmonary pressure is not constant.

So, we left one transpulmonary pressure. Transpulmonary pressure is a variable–wide phenomenon, we are reporting an all-or-nothing phenomenon with one opening pressure that accounts for all the lungs and the airways.

Dr. BobbieJean Sweitzer: So, under anesthesia, what would be the typical situations or inciting factors where you would anticipate airway closure to occur?

Dr. Domenico Luca Grieco: Airway closure currently is very difficult to diagnose because most of anesthesia machines do not allow to perform the low-flow pressure-volume curve which is a pressure-volume curve built during low-flow inflation.

Low-flow inflation is 5 liters per minute of inspiratory flow during volume control ventilation. Using this strategy, you’d rule out the effect of the resistive properties of the respiratory system. So, you see for each moment the alveolar pressure corresponding to the inflated volume.

Unfortunately, anesthesia machines do not have tools to perform low-flow pressure-volume curve and in our study we compared the patients affected by airway closure with a control group with similar baseline characteristics and similar preoperative respiratory function and we could not identify a factor that could predict the occurrence of these phenomena.

There is one nice recently published study by Rémi Coudroy and the group of Toronto showing that it is very likely that airway closure is closed by or at least stabilized by some alterations in the gas-liquid interfacing of the bronchioli.

And it possible that the individual characteristic of the patient about the gas-liquid interfacing in the bronchioli and the lung volume loss goes by general anesthesia. The alveolar derecruitment caused by anesthesia yields airway closure.

But regarding your specific question, it’s very hard to predict the patient that could be affected. We know that this phenomenon of choosing of these patients from our study, we don’t have any data about the possible existence of these phenomenon in none of these patients, but still a single risk factor for airway closure during general anesthesia up to date is the presence of a BMI exceeding 35.

Dr. BobbieJean Sweitzer: So, let’s talk a little bit more specifically about your study. What type of patients did you study and what surgeries were they having?

Dr. Domenico Luca Grieco: Our patients were on an analysis conducted on patients enrolled in a randomized controlled trial. We have finished it now in Rome; it is a mono-center randomized trial comparing two ventilatory strategies doing laparoscopic surgery for a gynecological surgery.

These female patients, they are randomized with these two tidal volumes and two levels of PEEP during surgery and we perform a series of respiratory mechanics measures, such as low-flow pressure-volume curves and expiratory lung volume measurement and esophageal and transpulmonary pressure assessments because of data gatherings for the randomized controlled trial.

During this study, we noticed that some patients exhibited a particular profile of being low-flow pressure-volume curve suggesting airway closure. Essentially there is a very flat part at the beginning of the pressure-volume curve and if you calculate the compliance of that part of the curve, that compliance is very close to the compliance of the occluded respiratory circuit suggesting that in that initial flat part of the curve, no volume is being inflated in the lungs, but is compressed in the respiratory circuit because of an obstacle which is distal to respiratory circuit itself but proximal to alveoli.
Dr. BobbieJean Sweitzer: So, you just happened to observe this phenomenon that you weren’t actually looking for and then you decided to expand these assessments of respiratory mechanics? Or were you already performing these sophisticated measurements in the original study and just collected the data?

Dr. Domenico Luca Grieco: We’ve got — collected the data and we were performing those measurements during the randomized trial because of its design, because it’s 60 patients randomized to two groups and each patient undergoes respiratory mechanics assessment, lung volume assessment and esophageal and transpulmonary pressure measurements during the main study.

Then we (sounds like: radioed) the signals and curves and we noticed that there was something very similar to what has been reported as airway closure in the acute respiratory distress syndrome.

From that we started the analysis and we tried to compare with our control group just what could be the difference between the affected and unaffected patients.

Dr. BobbieJean Sweitzer: So, other than being obese, which you’ve mentioned, did these study patients have significant other comorbidities, especially like any related pulmonary diseases?

Dr. Domenico Luca Grieco: We performed pulmonary function testing the day before surgery and two days after and we couldn’t find anything different between the patients that developed the airway closure during surgery and those who were not affected.

So, unfortunately at least we could not identify any pulmonary function testing that could predict the occurrence of the phenomenon.

Dr. BobbieJean Sweitzer: So, what was the mode of ventilation and ventilator settings that these patients were receiving?

Dr. Domenico Luca Grieco: The mode of ventilation was volume-controlled mode for all patients and the tidal volume and PEEP were chosen according to the randomization arm. So, in the control arm, the tidal volume was 10 ml per kg, in the interventional arm the tidal volume was 6 and PEEP were 5 in the control group and 10 in interventional arm.

We also looked if whether the randomization arm could have any relationship to the occurrence of airway closure, but it appears that these phenomenon occurs independently from tidal volume and set PEEP.

Dr. BobbieJean Sweitzer: So, you describe in your paper various measurements which are probably beyond the time we have to discuss in detail and you’ve mentioned a few measurements, a respiratory mechanic that you did. So, is it possible for you to maybe summarize what you did that is different than what the ventilator pressure measurements would have provided?

Dr. Domenico Luca Grieco: Yes. Dimensionally, ventilator anesthesia machines allow to measure airway pressure, inspiratory flow and inflated volume measured as the integral of the inspiratory flow. To identify airway closure or to rule out its existence, you have to remove the components related to airway resistance from the pressure.

We all know that the pressure that we’re measuring the airways during the inspiration in the volume control mode in paralyzed patients is that same of the pressure needed to overcome the resistive properties of the airways and the tubings and the elastic properties of the lung and chest wall, so the respiratory system.

To rule out the components related to the resistive properties of the airways, what is conventionally done from classical physiology is that during inflation you reduce the inspiratory flow. If you reduce the inspiratory flow, the resistive component of airway pressure becomes very low. So, for each moment of inspiration, you can record the inflated volume and the alveolar pressure if the airways are open.

What we saw in our study is that the low value which is a threshold which is the airway opening pressure, there is no lung inflation, but the only thing you do with the inspiratory flow is just to compress the gas in the respiratory circuit.

And, unfortunately, this procedure cannot be done by anesthesia ventilators. We used an ICU ventilator for these measurements because it is not possible to reduce the inspiratory flow to five to six liters per minute in those machines.

Dr. BobbieJean Sweitzer: So, what were your primary findings?

Dr. Domenico Luca Grieco: Our primary findings is that airway closure affects a very large proportion of these patients undergoing anesthesia. In our cohort, the proportion of patients affected was 22% and what is interesting is that airway closure, as said before, there is an airway opening pressure.

So, a pressure that is needed to reopen the airways that are closed and this opening pressure is increased by pneumoperitoneum, so laparoscopy in the Trendelenburg position.

And what is surprising is that this pressure can reach very high values because what we found is that the average pressure needed to reopen the airways once the patient is on Trendelenburg position during laparoscopy is about 20. And 20 of airway opening pressure corresponds to a similar pressure of end expiration in the alveoli.

That means that for these patients irrespective of the set PEEP, the alveolar pressure can be very high, up to 20, with the rare patients, with airway opening pressure exceeding 28 centimeters of water.

Dr. BobbieJean Sweitzer: So, I’d like for you to discuss your findings in regards to the specific aspects of the entire procedural course. For example, did the airway closure or airway opening pressure develop in the affected group soon after intubation while they were still supine? Or was this only after Trendelenberg positioning or insufflation of the abdomen?

Dr. Domenico Luca Grieco: The airway closure that — as soon as the patient received anesthesia and was intubated after paralysis and in all patients with this phenomenon after anesthesia, the airway opening pressure was increased by the Trendelenberg pneumoperitoneum.

While in the control group, so patients who did not have airway closure after anesthesia in the supine position, while we could not identify any patients with developing this phenomenon just as a consequence of Trendelenberg pneumoperitoneum.

Dr. BobbieJean Sweitzer: And what about other changes in respiratory mechanics from the intubations through supine positioning through Trendelenberg through the effects of the pneumoperitoneum? Was this also just changes the observed in the Trendelenberg and pneumoperitoneum settings?

Dr. Domenico Luca Grieco: Well, we have several changes and what was expected and we found is that the chest wall elastins, which measured the rigidity of the chest wall, increases with the pneumoperitoneum in Trendelenberg position in both groups. So, both in patients with airway closure and in the patients without airway closure and this is the effect of the positioning and the increasing pleural pressure.

Both patients experienced a change in the elastic pressure of the respiratory system which is conventionally called as the driving pressure of the respiratory system. But what is interesting is that patients in airway closure group developed an increase in the tidal elastic pressure, so the driving pressure of the respiratory system, only due to increased chest wall elastins while the compliance of the lungs remained unchanged.

While in the control group increasing the respiratory system driving pressure was dependent both on increasing chest wall elastins and in reduction of lung compliance, and this is because the major effect of airway closure in affected patients was you instiute Trendelenberg pneumoperitoneum is the prevention of alveolar derecruitment.

So, if you prevent alveolar derecruitment, lung compliance remains unchanged, while if the — in the control group you cannot prevent alveolar derecruitment the alveolar pressure is the one that you set. So, the set PEEP, the pneumoperitoneum, the (sounds like: altered) reduction in the alveolar derecruitment and lung compliance.

Dr. BobbieJean Sweitzer: Was there a difference in lung volumes between the two groups of the group that had the airway closure versus the ones who did not?
Dr. Domenico Luca Grieco: There were no difference of observed anesthesiain the supine position, but after Trendelenburg position and pneumoperitoneum patients in – with airway closure at higher and exterior lung volume. And this is because the alveolar pressure was bigger than set PEEP.

So, the alveolar pressure which was increased by airway closure that prevents the lung volume to deflate during expiration prevents alveolar derecruitment and this is confirmed by the analysis on the lung volume.

Dr. BobbieJean Sweitzer: So, in a subgroup of patients you utilized pressure-controlled ventilation to provide recruitment maneuvers. Can you tell us what you found during this part of your study?

Dr. Domenico Luca Grieco: Regarding the main trial, so the randomized trial, an intervention group we provide low tidal volume, higher PEEP and scheduled recruiting maneuvers every hour. The way we perform recruiting maneuvers in this arm of study is to increase PEEP with constant inspiratory pressure during pressure-controlled ventilation.

And what we found in patients with airway closure was that pressure-controlled ventilation could not provide any lung inflation during the recruiting maneuver unless the total pressure applied—to the inspiratory pressure plus PEEP—could overcome the airway opening pressure. This is another concept of the idea that that threshold volume is not possible to inflate the lung. We think this is important because there are some studies suggesting the pressure-controlled ventilation could be using these patients to avoid excessive increases in peak pressure, peak airway pressure.

But from the perspective of our data, the use of pressure-controlled ventilation could be very dangerous because we don’t have any—I hear of all the time—the cause of the phenomenon and if the airway opening pressure changes over time, it is possible to provide apnea if the total pressure is lower than airway opening pressure or significant hypoventilation or hyperventilation if the airway opening pressure changes over time according to changes in body position, for example.

Dr. BobbieJean Sweitzer: So, I think in spite of the negative consequences of airway closure, you did find that there was maybe a potentially positive side to this. I believe you found that in these patients while they were undergoing the pneumoperitoneum, it did not cause atelectasis or I think you’ve used the term alveolar derecruitment.

Does this explain maybe previous findings that obese patients have less reduction in functional residual capacity with abdominal insufflation in the Trendelenburg position?

Dr. Domenico Luca Grieco: Yes, I think this could be an explanation for the study published, I think, in 2014 in *Anesthesiology*, if I’m not wrong, in which it was clearly shown that the laparoscopy as compared to the supine position was more likely to provide a reduction in end expiratory lung volume in known obese patients, while obese patients need to be a bit protected from the development of alveolar derecruitment.

And this could be an explanation for those results. Importantly, recently the approved (inaudible) group of the European Society of Anesthesiology published in the journal a study in which they compared these obese patients to PEEP-setting strategies and which were 4 centimeters of water or 12 centimeters of water.

And surprisingly, there was no difference in postoperative pulmonary complications, where I could speculate that at least a part of those results could be explained by the presence of airway closure in those patients because in patients with airway closure that alveolar pressure, if you wish, the real PEEP that is provided to the patient is independent from the set PEEP if the set PEEP is set below the airway opening pressure.

If you have 20 of airway opening pressure, for instance, and you set PEEP of 5, the patient has on himself 20 of positive end expiratory pressure in the alveoli, independently from that PEEP.

Dr. BobbieJean Sweitzer: Did you see any hemodynamic consequences in these patients who had this airway closure?

Dr. Domenico Luca Grieco: We did not have any advanced hemodynamic monitoring in those patients. I think this could be a field of great interest because as we all know, the use of ifPEEP can yield significant reduction in the venous return and cardiac output which could lead to hemodynamic instability.

We did not specifically assess these in our patients because we did not design this study with advanced hemodynamic monitoring. But for sure this is a field of great interest.

Dr. BobbieJean Sweitzer: So, let me summarize. You found a proportion of obese patients under general anesthesia had airway closure after intubation and pneumoperitoneum in Trendelenburg and this required fairly significant pressures. You’ve mentioned 20 centimeters of water pressure to open the airways.

Is there any way that— but I think it was like—I forget now what percentage of patients actually had this and there was no real difference in the preoperative or the surgical procedures or any way to tell the difference between these patients ahead of time. Is there any way that a practicing anesthesiology provider today would be aware of this even happening or able to detect this phenomenon?

Dr. Domenico Luca Grieco: Unfortunately not, at least not from our data. I think we need much more data on larger samples to try to align risk factors. The only way for now to identify this phenomenon is to perform the low-flow pressure-volume curve.

So, a very low-flow inflation, record airway pressure and if you see a marked lower inflation point, it is very likely that they sound (like: should) be affected by airway flow now.

Dr. BobbieJean Sweitzer: And likewise, because these patients—if you didn’t exceed the pressure needed to open these airways, they weren’t being actually ventilated or at least those components of the lung. So, is there any way that one would also know this is happening?

Dr. Domenico Luca Grieco: Perhaps if you use pressure control mode and you see that pressured controlled is not delivering any kind of volume at the given pressure, well, it is very likely that it is caused by airway closure. This could be an easy way to identify it with the tools that we have in the OR now.

Dr. BobbieJean Sweitzer: So, did you follow these patients postoperatively to see if there were any differences in postoperative pulmonary complications between the control group and those who had the airways closures during their procedures?

Dr. Domenico Luca Grieco: The sample is very low; our sample is 22 patients with 11 in the airway closure group and 11 in the control group. And we could not see any signal about postoperative respiratory functions. So, we measured a PF ratio one hour after surgery, one hour after extubation, 24 hours after extubation; we evaluated patients’ dispanea and we performed pulmonary functions that (inaudible) on Day 2 after surgery.

We could not identify any difference, but I would be very cautious, too, in saying that there is no difference between affected in our affected patients because the sample is very low to draw a conclusion on this point.

Dr. BobbieJean Sweitzer: So, until we know more, do you recommend that practitioners should be cautious about using pressure-controlled ventilation in a population of patients such as this, obese patients undergoing pneumoperitoneum and Trendelenburg?

Dr. Domenico Luca Grieco: This is advisable, but our most significant clinical conclusion, clinical advice is just to avoid these kinds of ventilation in these patients because it could be risky; both on the side of the risk of hypoventilation and apnea if you set the inspiratory pressure below the airway opening pressure and on the side from the perspective of hyperventilation and delivery of large tidal volumes because if the airway opening pressure group decreases because, for example, the patient’s position is changed, then you can provide a huge tidal volume to that patient.

Dr. BobbieJean Sweitzer: I hope today’s discussion will interest many of our listeners and lead you to read this important article to learn more. Thank you, Dr. Grieco, for discussing your work with us today. I wish you well as you continue your efforts to enhance the practice of anesthesiology and strive to improve the care of our patients.

Dr. Domenico Luca Grieco: Thank you for the invitation. Thank you.

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