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

BobbieJean Sweitzer, M.D.: 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 authors of a publication that appears in the March 2017 issue of the journal. With us is Dr. Daryl J. Kor. Dr. Kor is the senior author of an article titled, “Risk Factors and Clinical Outcomes Associated with Perioperative Transfusion-Associated Circulatory Overload.” He is an Associate Professor of Anesthesiology at the Mayo Clinic in Rochester, Minnesota. He also heads up a clinical research laboratory termed METRIC, for Multidisciplinary Epidemiology and Translational Research in Intensive Care. Welcome, Dr. Kor.

Daryl J. Kor, M.D.: Thank you so much, Dr. Sweitzer. It’s a privilege to be here with you, and thank you for the opportunity to spend a bit of time talking about our work.

BobbieJean Sweitzer, M.D.: Joining Dr. Kor is Dr. Edward L. Murphy, who wrote an accompanying editorial to this publication titled, “Adjusting the Focus on Transfusion-Associated Circulatory Overload,” known as TACO. Dr. Murphy is Professor of Laboratory Medicine and Epidemiology/Biostatistics at the University of California, San Francisco. We are pleased to have you with us, Dr. Murphy.

Ed Murphy, M.D.: Great, Bobbie and Daryl. Thanks very much, and I’m happy to discuss this important article.

BobbieJean Sweitzer, M.D.: So, I’ll start with you, Dr. Kor. Can you tell us a bit about what transfusion-associated circulatory overload, or TACO, is exactly?

Daryl J. Kor, M.D.: Absolutely. Transfusion-associated circulatory overload is one of the two most common causes of transfusion-associated respiratory insufficiency. Specifically, transfusion-associated circulatory overload is believed to be the result of hydrostatic lung edema that is the result of a transfusion episode.

BobbieJean Sweitzer, M.D.: Are there specific criteria or a specific definition of TACO?

Daryl J. Kor, M.D.: Yes. For sure. And that’s probably because I think that, traditionally, clinicians just feel that TACO can be treated quickly with diuretics, and is more a complication of their administration rather than related to the blood product itself.

BobbieJean Sweitzer, M.D.: Interesting. So, Dr. Kor, can you summarize the findings of your study for us?

Daryl J. Kor, M.D.: Absolutely. So, again, the primary aim of our study was to understand the risk factors for transfusion-associated circulato-

Daryl J. Kor, M.D.: That’s really a great question, and oftentimes a very difficult differentiation to make in the clinical setting. Essentially, it comes down to the underlying pathophysiology between the two conditions. Both manifest themselves as acute hypoxemia associated with pulmonary edema. The primary difference between transfusion-associated circulatory overload and transfusion-related acute lung injury is the underlying mechanism, which is believed primarily to be hydrostatic or fluid-related, in the setting of transfusion-associated circulatory overload, versus more of an inflammatory injury to the lung parenchyma and the alveolar capillaries, which is what we see traditionally in transfusion-related acute lung injury.

BobbieJean Sweitzer, M.D.: So, can you tell our listeners what you set out to do with this research?

Daryl J. Kor, M.D.: Specifically, what we were hoping to do in the present work was to accomplish two primary aims. The first was to understand in a more thorough way specific risk factors for the syndrome of transfusion-associated circulatory overload, and specifically focusing on a surgical population. The second primary aim of this particular work was to understand what the impact of development of transfusion-associated circulatory overload was on patient-important outcomes like ICU and hospital length of stay, as well as the need for ventilatory support after surgery.

BobbieJean Sweitzer, M.D.: So, Dr. Murphy, you had me with the first sentence of your editorial. I was a bit surprised to learn that TACO is the second most common cause of deaths related to transfusion as reported to the FDA; and yet you point out that Dr. Kor’s study was the first to focus on a noncardiac perioperative population, and that TACO is historically underreported, and possibly underrecognized even, in perioperative settings. Why do you think this is?

Ed Murphy, M.D.: Well, Bobbie, I think that TACO suffers from falling into the gap between clinicians and transfusion medicine specialists. Clinicians are focused on the patient and on the patient’s volume status, and that includes both internists and anesthesiologists. Transfusion medicine specialists are focused more on immunologic transfusion reactions, and have historically underestimated the effects of TACO. What it really needs is a kind of cross-disciplinary approach to recognize this reaction and to bring both sides of the equation together to better recognize and report it.

BobbieJean Sweitzer, M.D.: I think that gets back to, you know, Dr. Kor’s defining the difference between TRALI and TACO. Because it seems to me like TRALI has gotten a lot more publicity and we’re more aware of it as a problem than we are of TACO.

Ed Murphy, M.D.: Yes. For sure. And that’s probably because I think that, traditionally, clinicians just feel that TACO can be treated quickly with diuretics, and is more a complication of their administration rather than related to the blood product itself.
ry overload following surgical transfusion episodes, and we looked at a variety of domains of risk factors, that being premorbid conditions, baseline medications, specific information related to the procedure being performed, as well as intraoperative care delivery factors, patient responses to those delivery factors, and information related specifically to blood components and blood product types.

And what we found, really, were that there were data elements from each of those domains that could be used to help us better understand who is at risk for this transfusion-associated respiratory complication. In terms of medical comorbidities, we identified that patients with left ventricular dysfunction manifest by preoperative transesophageal or transthoracic echocardiogram portended increased risk for developing TACO. We also identified that patients who had chronic kidney disease were at increased risk for this condition as well.

In terms of baseline medications, those that presented on beta-blockers were identified as being at higher risk for this syndrome than those who did not present on beta-blocker therapies.

And in terms of procedural details, we specifically matched patients who did develop TACO and did not develop TACO on their surgical procedure, and we did that because we had previously identified that specific surgeries do tend to be at increased risk for the syndrome of transfusion-associated circulatory overload—surgery like thoracic surgery or vascular surgery and transplant surgery. In this particular study, we also identified that patients who present for emergent surgical procedures are also at greater risk for this syndrome than those who present for elective procedures.

In terms of intraoperative care delivery factors, we identified that the administration of higher total volumes of nonsanguineous fluid therapies increased risk for transfusion-associated circulatory overload, as did specific blood product types. For example, plasma and mixed-product transfusion episodes were associated with a higher risk for transfusion-associated circulatory overload than those who received exclusively red cell products.

And then, for the second aim, trying to identify whether or not TACO was associated with adverse patient-important outcomes, we did confirm many prior studies which have suggested that indeed patients who develop TACO, controlling to the best extent we can for the types of procedures and risk factors that patients might have, if you did develop TACO, you had increased length of ICU and hospital stay, you had an increased need for postoperative mechanical ventilation, and you had significantly reduced both short-term and long-term survival.

BobbieJean Sweitzer, M.D.: So, Dr. Murphy, were you surprised by the results of Dr. Kor’s study?

Ed Murphy, M.D.: I would say, broadly, no, because I think, you know, his results are similar to findings from some of my own research. However, I think it was really important to extend those results to the specific surgical population that Daryl studied. The other thing that was, I think, a novel finding was the underrecognition of clinical cardiac disease. In other words, he found a poor correlation with echocardiographic heart failure versus previously-recognized clinical heart disease.

BobbieJean Sweitzer, M.D.: Dr. Kor, based on your findings, can you characterize for us a typical patient that would be at risk for TACO?

Daryl J. Kor, M.D.: In terms of surgical populations, as I noted, we specifically matched patients based on the surgical procedure being performed, but our prior work would suggest, as I noted a little earlier in our podcast, that specific surgical procedures do tend to be associated with a higher risk for developing TACO, and those types of procedures would include patients undergoing lung resection surgery, patients undergoing major vascular surgery, and those undergoing solid organ transplantation.

We also identified in the present study that for those coming in with emergency surgery, they’re also characteristically more likely to develop TACO. And then, classically, those, as Ed mentioned, who are at risk with significant comorbidities like congestive heart failure; and even more than the clinical diagnosis of congestive heart failure, which in our particular study we did not associate with TACO, but rather objective evidence of left ventricular function, like a reduced left ventricular ejection fraction, or elevated filling pressures on the echocardiogram, also portended risk for transfusion-associated circulatory overload. And prior work has also identified age, for example, to be a risk factor for TACO.

So, the classic patient would be an elderly patient undergoing emergent thoracic or vascular surgery with comorbidities such as chronic kidney disease, and echocardiographic evidence for left ventricular dysfunction.

BobbieJean Sweitzer, M.D.: So, in this paper you note that transfusion volume was not associated with TACO, and in fact you didn’t mention in that typical patient anything about the volume. And you discuss in the paper the possibility that other mechanisms, such as perhaps an inflammatory process, may contribute to TACO. But currently, is there evidence to actually support this?

Daryl J. Kor, M.D.: Indeed, there is some evidence, although it really is more hypothesis-generating information at this point than anything definitive. A couple of examples might include some work from Neil Blumberg, who has evaluated their red cell washing practices. And what they’ve identified is, in over 30,000 patients who have received washed blood components, specifically red cells, they were unable to identify a single case of transfusion-associated circulatory overload. What this might suggest is that there’s something in the red cell supernatant of a stored red cell product that may portend increased risk for syndromes like transfusion-associated circulatory overload. Other investigators have also identified that patients who develop TACO oftentimes have a bit of a febrile response that precedes their TACO episode.

And then a third line of somewhat indirect evidence, but also suggesting potential alternative etiologies for transfusion-associated circulatory overload, is that there’s quite commonly a very characteristic hypertensive response in patients who receive a blood component and then develop transfusion-associated circulatory overload. And when we’ve evaluated that blood pressure response in the setting of TACO compared to other patients who develop, for example, congestive heart failure associated with nonsanguineous IV fluid therapies, that blood pressure response seems to be substantially higher in the TACO environment than it is in those who develop CHF in the setting of IV fluid therapies that are not blood component-related.

So, again, multiple lines of evidence suggestive of a potential alternate synergistic mechanism for TACO; but the exact mechanisms that might be playing a role are still very much under investigation.

BobbieJean Sweitzer, M.D.: Given all of that, what do you think is the best way to reduce the risk of TACO?

Daryl J. Kor, M.D.: Well, I think with the current evidence that we have, notwithstanding some of the more intriguing investigative work that I had mentioned is ongoing, we do know very clearly that those who have specific conditions like left ventricular dysfunction or chronic kidney disease are at increased risk. In those populations, the first and most important question to ask ourselves is, does the patient really need the transfusion therapy? And clearly, there are still many cases of liberal transfusion where we can probably avoid the transfusion episode altogether.

For those in which circumstances would mandate that indeed they do require a transfusion episode, for patients who are at particular risk
based on the factors that we've identified in this study, it would be prudent to transfuse the lowest-volume product possible; and for that volume, to transfuse it at the slowest rate possible. In the particular study that we're talking about today, we unfortunately were not able to evaluate transfusion rate as a risk factor for TACO, but multiple prior investigations have indeed associated, the faster you transfuse a blood product, the greater the risk for developing transfusion-associated circulatory overload.

And then a final potential mechanism that certainly may – has biologic plausibility to it, although it's still somewhat unclear in terms of definitive data, would be the administration of volume-reducing agents like diuretics to patients who would be at particular risk for a syndrome like transfusion-associated circulatory overload. In fact, it seems to be quite common practice that, for those who are at risk for heart failure, often-times providers are administering a dose of diuretic before administering a blood component. And while, again, we don't have robust data to suggest that indeed this does prevent TACO, certainly from a biologic plausibility perspective, this may be a meaningful preventative intervention.

BobbieJean Sweitzer, M.D.: So, Dr. Murphy, other than not transfusing a patient or giving fewer blood products, which are not always options, what are other possible approaches to lessen the risk of TACO?

Ed Murphy, M.D.: Well, I think Daryl has really covered this pretty well. I think, just to reiterate, the importance of trying to identify patients at risk ahead of time. And another elaboration on what he said, particularly in terms of reducing the volume of transfusion—the use of specific coagulation factors instead of using fresh frozen plasma, for example.

BobbieJean Sweitzer, M.D.: Dr. Kor, I know you've addressed this to some degree, but I just want to circle back and, you know, have you clarify for us how TACO differs from simple volume overload, as one would typically see if a patient had received too much crystalloid or colloid, for example.

Daryl J. Kor, M.D.: And this, again, comes very much back to what we had discussed in one of our prior questions, in terms of alternate mechanisms for transfusion-associated circulatory overload. And as I noted, really there's a lot of associative data and hypothesis-generating data; but nothing definitive that describes, what is the difference between hydrostatic lung edema that develops after a transfusion episode, versus hydrostatic lung edema that occurs simply after the administration of too much colloid or crystalloid?

I increasingly believe that there is likely synergistic mechanisms. It's likely that those components may reside within the supernatant of the red cell product. Examples of those types of modifiers might be things like red cell microparticles, free hemoglobin, and a whole variety of cytokines that are quite active in a stored red cell product. In terms of the free hemoglobin and the red cell microparticles, those have been shown in multiple studies to bind nitric oxide, and in doing so increase vascular tone. And for specific populations who are at increased risk for lung edema because of altered heart function or chronic kidney disease, you can certainly imagine that that increase in vascular resistance and workload on the left heart may well increase their risk for a syndrome such as transfusion-associated circulatory overload.

BobbieJean Sweitzer, M.D.: You used a case-control study design. Can you help me understand what this is exactly, and why it was the best way to address what you wanted to find out?

Daryl J. Kor, M.D.: So, case-control designs are very nice designs, particularly for questions where the outcomes are relatively uncommon events. And I hesitate to say that just a bit, because one of the frequently discussed issues with TACO is that it's a rare event. But in fact, I think increasingly, we're appreciating that it's maybe not so rare at all, but perhaps we just don't do a very good job of recognizing it. And some work, both by myself as well as Ed and others in this space, have suggested that in fact the frequency for transfusion-associated circulatory overload likely resides somewhere between 1 and 4% of those who receive blood component therapies.

But again, recognizing that it is a somewhat uncommon outcome, a case-control design is a nice design in that you identify all of the cases that you can find amongst your population of patients, and for those cases you can then identify similar controls to create a comparison group. And those controls can be matched in a whole variety of ways. In the particular study that we're discussing today, we attempted to match up to and including five controls for every case that we were able to identify.

BobbieJean Sweitzer, M.D.: Can you explain what multivariable analysis modeling is? I think you used this in your paper as well. And why was this step necessary?

Daryl J. Kor, M.D.: Any time we're performing an observational study, there's the persistent risks associated with observational studies of confounding and bias, and one of the best ways to try to control for confounding and bias in an observational study is the use of matching and multivariable adjustments. And we did match on a variety of factors that we knew were associated with the development of transfusion-associated circulatory overload. But in an attempt to better understand other factors that we maybe don't have as quite a clear understanding of how they play a role in the development of transfusion-associated circulatory overload, we can attempt to understand the effect that they have on that syndrome in the context of other variables that may be potentially playing a role in the development of TACO as well.

So, as an example, if we understood that patients who have chronic kidney disease are at increased risk for developing transfusion-associated circulatory overload, and recognizing that chronic kidney disease is probably associated with an increased risk of having left ventricular dysfunction, in order to try to really understand what the relationship is between left ventricular function and our outcome of interest, that being TACO, we need to adjust for the presence or absence of a condition like chronic kidney disease. So, multivariable analysis simply tries to adjust for all of the variables that are in the model and help us to better understand the impact of a specific variable of interest in the context of those other variables included in the model.

And maybe, with that, Ed, I don't know if you have anything to add from an epidemiologist's perspective, but I'll certainly allow you some opportunity to do so.

Ed Murphy, M.D.: That was a great explanation, and in fact multivariable analysis is just really there to try to remove confounding factors—in other words, variables that appear to be related to the outcome but are not in fact related, and to leave one with the so-called independent risk factors, which are the ones that really matter.

BobbieJean Sweitzer, M.D.: Thank you. Dr. Murphy, in your editorial you write about using electronic health records and decision support tools, and even risk scores, to assist clinicians to identify at-risk patients. Can you elaborate on this, and is this actually being used in real time in places?

Daryl J. Kor, M.D.: Well, it's, to my knowledge, not being used yet for TACO. But there is a good example—we work closely with colleagues at the Kaiser Permanente Division of Research in Oakland, California, and particularly Dr. Gabriel Escobar has developed a predictive dashboard,
as he calls it, for predicting decompensation of patients on the hospital ward, and thereby predicting transfer to the ICU. And what his dashboard does is, by mining the electronic health record, it comes up with a predictive score or algorithm which flags a patient as being high-risk for decompensation and ICU transfer, thereby allowing the clinician to institute changes in therapy and to try to prevent this decompensation.

So, that kind of approach is what I think we had in mind when we wrote the editorial—that, if we can really settle—and I think Daryl’s article and some work that we’ll talk about in a moment, basically identifying—you know, honing in on the actual risk factors for TACO, we could similarly look at the EHR, create predictive algorithms, and warn clinicians ahead of time of the likelihood of TACO, so that at the time they order the blood product they could institute some of the preventive measures that Daryl mentioned earlier.

Daryl J. Kor, M.D.: I’ll just add on a little bit to Ed’s comments as well, because currently at our site they’re implementing exactly what Ed has talked about, and I think he’s fairly advanced in some of those strategies as well. And while we haven’t fully implemented it into our clinical environment, we have in the test space implemented specific algorithms to identify high-risk patients to understand, how can we best alert clinicians of their risks for TACO to hopefully mitigate their risk and perhaps alter the way clinicians transfuse, either by avoiding the blood product or changing things like infusion rates?

BobbieJean Sweitzer, M.D.: It sounds like a really excellent way to raise awareness, particularly in situations where there’s a lot of different things can be going on and it’s hard to keep, you know, I guess, at the top of one’s mind, the differential diagnosis, and be alerted to everything. So, it sounds like exciting stuff.

Daryl J. Kor, M.D.: Yes. And what we’ve noticed here too, Bobbie, and I think Ed would probably say the same, is that here at Mayo, which is where the work was done, we’ve had a long interest in transfusion complications like TRALI and TACO, but despite that interest we’ve identified that we really are only recognizing the outcomes of TRALI and TACO in a small minority of patients.

And I really think your point about education is an important one, and in the last 12 to 18 months here at our site we’ve had a significant effort to educate care providers about the fact that transfusion events are not risk-free interventions; that we need to keep in mind conditions like TRALI and TACO, which oftentimes simply get missed and written off as pulmonary edema, but really not related to a blood component therapy; just an unfortunate consequence of the entire episode of care. So, I think your point of educating particularly anesthesiologists and perioperative care providers, is an important one to help us improve our recognition and reporting of this important outcome following transfusion therapies.

BobbieJean Sweitzer, M.D.: So, Dr. Murphy, as someone who works in the preoperative arena and has just instituted a preoperative anemia management clinic in effort to try to decrease the amounts of blood transfusions, I was particularly interested in some of the comments you made in your editorial about preoperative practices that could help decrease the incidence of TACO. And I think you’ve specifically talked about optimizing preoperative erythropoiesis, which I think is a fancy way of saying, treat the anemia. And also, you mentioned the benefits of preoperative echocardiography. And I was hoping that you would elaborate a little bit more specifically around, you know, this whole process in the preoperative period, of trying to elucidate or impact the risk of TACO.

Ed Murphy, M.D.: Good point, Bobbie. I think you’re tapping into kind of the broader movement of patient blood management, which has been really oriented to reducing transfusion generally, has been spurred by the recognition that there is some over-transfusion out there: that patients need less blood than is sometimes given; and also, frankly, by cost considerations. A number of hospital chains and managers have looked at the blood bill and decided that, you know, ways need to be done to minimize that.

That said, the same techniques can be really brought to bear on TACO, because a patient who’s anemic preop is certainly more likely to require a transfusion. So, if the anemia could be treated beforehand, then perhaps we can minimize the risk of transfusion and thereby the risk of TACO. You mentioned, as well, the potential for recognizing, you know, as we have just been talking about, cardiac and renal disease preexisting are risk factors for TACO. So, to the extent that those conditions can be recognized and the patient’s clinical status optimized preoperatively, I think we can hope that that may reduce the risk of TACO.

BobbieJean Sweitzer, M.D.: So, Dr. Kor, I understand that you currently have another clinical trial looking at TACO, already underway. Can you tell us more about that study?

Daryl J. Kor, M.D.: Absolutely. This is a study that’s really getting back to the issue of alternate mechanisms that might be associated with transfusion-associated circulatory overload. And specifically, I had mentioned before in our podcast that there’s a concept of biologic response modifiers that may reside within the supernatant of a red cell product. What exactly those components might be include things like red cell microparticles and free hemoglobin, as well as a variety of inflammatory cytokines, like we mentioned. And so, the work of this clinical trial that we’re co-enrolling with Duke University Medical Center—the goal is really to understand what the impact of point-of-care bedside red cell washing is, in terms of mitigating risk for transfusion-associated circulatory overload as well as TRALI.

And so, essentially, patients who are undergoing high-risk cardiac surgery, that are predicted to receive four or more units of red cells, are enrolled and randomized to either the standard-issue arm, in which case they receive transfusion therapies as they would under normal routine care, or to the red cell washing arm, in which case all red cell transfusion administered on the day of the surgical procedure undergo a bedside washing procedure to wash away all of the supernatant that the red cells are residing within; again, ultimately hoping to better understand what the impact of that washing might be on the development of the syndromes, transfusion-associated circulatory overload and TRALI.

We’re about a third of the way through enrollment with a couple of years left. And ultimately, again, we’ll hope that this will give us a bit of a better understanding, not only about TRALI and TACO, but we’ll also be secondarily looking at other organ function as well, to understand, does the removal of supernatant in stored red cells impact other organ system function as well?

BobbieJean Sweitzer, M.D.: We look forward to seeing that science. So, Dr. Murphy, in your editorial I think you mentioned a large case-control study currently being conducted on serious transfusion reactions, including pulmonary edema. Can you tell us more about that, and do you think that will also help us better understand TACO and other risks of transfusions?

Ed Murphy, M.D.: Yes. Thanks. Basically, I’m involved as the PI, and Daryl is actually on our expert panel, for a project sponsored by the NHLBI under the Recipient Epidemiology and Donor Evaluation Study, which goes by the acronym, REDS. This is a large case-control study which has enrolled medical and surgical patients at four tertiary care centers across the country, a total of 200 cases of TACO and 400 matched controls who have been transfused but do not have TACO, and are matched to the cases on the number of blood products they received.
The study basically uses an electronic algorithm to flag patients with likely TACO—in other words, those that have received a transfusion then a chest x-ray within six hours. It has a three-level triage diagnostic process, whereby the first level of screening is by a nurse researcher who reviews the medical record, followed by a pulmonologist/critical care specialist who serves as the gatekeeper, and then finally by the three-member expert panel of which Daryl is a member.

So, we feel this study, which is just finished and hopefully will soon be published, will confirm and extend upon the risk factors identified by other studies. We already feel that the study confirms the increased morbidity and mortality that occurs after TACO—so, again, sort of speaking to its seriousness as a complication. And finally, following on what we’ve been talking about as some of the biological mechanisms, the study does include the saving away of biospecimens for the measurement of NT-proBNP and other biomarkers.

BobbieJean Sweitzer, M.D.: Well, our listeners will have to watch out for that study being published, and it sounds like you’re off to a great start with a good acronym for a blood study, of REDS.

Ed Murphy, M.D.: Thanks.

BobbieJean Sweitzer, M.D.: So, I think the take-home message from this article, for me at least, is that perhaps we are not quite at the stage where we can reliably predict which patient will develop TACO. So, perhaps for now, awareness and education of this problem, as you guys have touched on, and more attention to actually recognizing the condition and instituting supportive care, may be the best approach. Do either of you want to add to that, or have some summary advice for our listeners that we haven’t already discussed?

Daryl J. Kor, M.D.: No, I think that’s a very nice summary, Bobbie. I think that if I was going to add anything, again, it’s just to reinforce the importance of our providers doing the best they can to recognize the potential for a transfusion complication like TRALI or TACO in a patient who develops respiratory distress in the setting of a recent transfusion. And if there is any thought that the condition may be associated with that transfusion episode, we would highly recommend that they contact their transfusion medicine colleagues to work through it as a potential transfusion reaction. It has important implications, not only for the recipient who development respiratory compromise, but it has the potential for very significant consequences in terms of that particular blood donor, in terms of their future donations. So, again, educating and increasing a provider’s recognition of these potential complications is really of paramount importance, in my view.

Ed Murphy, M.D.: Right. And I think I would only add that, you know, in the general sense that medicine these days is focusing much more on clinical protocols and the avoidance of unnecessary complications, again, I think as we said in the editorial, that I think it’s reasonable that TACO should be considered as a preventable iatrogenic complication, and further efforts need to be devoted towards reducing its incidence. And in a sense, one can look at the incidence of TACO as a measure of the overall quality of the hospital experience.

BobbieJean Sweitzer, M.D.: Good advice. I hope today’s discussion will interest many of our listeners and lead you to read this important article to learn more. We really appreciate Drs. Kor and Murphy being with us today and discussing their work with us. I wish you both well as you continue your efforts to enhance the practice of anesthesiology and strive to improve the care of our patients.

Daryl J. Kor, M.D.: Thank you.

Ed Murphy, M.D.: Thank you very much, Bobbie.