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Conflict of Interest Statement

The authors reported no conflicts of interest.

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Discussion Presenter: Dr Alessandro Brunelli



Dr John A. Howington (Nashville, Tenn). Your findings of worse outcomes with pneumonectomy and low BMI add to the other bodies of evidence showing poor outcomes in these groups. The findings of worse long-term outcome with open thoracotomy approach and male sex are thought pro-

voking. As an example, a 71-year-old man with good lung

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function treated with an open thoracotomy lobectomy has a score of 6 and meets group 3 criteria, with profoundly reduced long-term survival independent of pathologic T stage and independent of node negative status or pT1. We know female sex portends worse outcome in cardiac surgery procedures and many critical care trials. To what do you attribute the dichotomy of significantly worse short-term and long-term outcomes in men with lung cancer treated with surgical resection?



Dr Alessandro Brunelli (*Leeds*, *UK*). This is an important point. I would like to point out that we didn't want to recalibrate Eurolung on our population; we didn't isolate the individual factors compounding the Eurolung. So we don't really know whether these individual factors taken in isolation are

associated with long-term prognosis as they are with perioperative mortality.

The simple reason why we didn't do this is because we think we don't have the sufficient number of events and the dataset to recalibrate the score on a long-term survival. What I can say for male sex, for instance, there have been some reports associating male sex with poor prognosis and they explain this in part with cultural reasons, especially in settings where the screening programs are not implemented; perhaps male patients tend to present at a later stage with more advanced disease. Also, it is well-known that male patients have a propensity for having severe comorbidities, such as ischemic heart disease, cerebrovascular disease, and other comorbidities that may have an impact on OS.

The other explanation I can think of is that perhaps the tumor in female patients may have more favorable histologic or genetic profiles that are associated with a more favorable prognosis in this gender.

Dr Howington. My next question relates to long-term outcomes. We are well aware of the data showing worse short-term outcomes with an open thoracotomy for lung cancer resection patients. However, your data will suggest a worse long-term outcome after a thoracotomy approach, despite matched pathologic stage of disease. To what do you attribute this worsened outcome? Can you tell from your data whether fewer patients after thoracotomy completed planned adjuvant chemotherapy or other interventions?

Dr Brunelli. It is difficult to draw conclusions on individual factors of the Eurolung. However, the thoracotomy may be a surrogate variable for a more complex operation in more advanced or locally advanced disease. We have stratified the pathologic T stage, but simply by dividing the group in pT=1 or greater than 1. We may have used a thoracotomy for a tumor larger than 5, 6 cm or a tumor invading neighboring structures or for a sleeve resection.

All these operations performed for more locally advanced tumors are associated with a worse prognosis.

Regarding the adjuvant chemotherapy, obviously in a retrospective series, it is difficult to retrieve the exact indications to adjuvant chemotherapy and especially the reasons why patients didn't undergo adjuvant chemotherapy. We looked at those patients with the pathologic N1 and pathologic N2 disease, which is a more clear-cut indication for adjuvant chemotherapy. We didn't find any difference in terms of receiving chemotherapy after surgery between thoracotomy and minimally invasive surgery in our series.

Dr Howington. Have you altered your current approach to informed consent discussions with your patients? So when you're talking to a male patient who has moderate chronic obstructive pulmonary disease and may require an extended resection, is that altered—how you're having the discussion, and weighing, say, chemotherapy and radiation as an option versus surgical resection—particularly if it requires an open approach?

Dr Brunelli. The simple answer is yes. We have incorporated this score to provide more realistic and complete information to patients during consultation—and also during multidisciplinary discussion in tumor boards.

I think it is relevant to balance perioperative risk and long-term survival, especially in high-risk patients. This is the information that patients often ask about, at least in our setting, and what we wanted to develop was a ready-made instrument that could inform the discussion. So yes, we are currently using this instrument to inform shared decision-making and informed consent.

Dr Howington. Again, thank you for an outstanding presentation and for adding to our knowledge and understanding about managing patients with lung cancer. And I appreciate the opportunity to be a discussant.



Dr Benjamin D. Kozower (St Louis, Mo). A huge issue in the United States right now is data fatigue—the amount of data entry that data managers and faculty have to enter is incredible. So you have taken a very different approach. You have a model that is parsimonious using only 6 covariates

to predict your outcomes. Do you recall what percent of the predictive capacity of the total model you have just using these 6 variables?

Dr Brunelli. The reason why we developed the parsimonious model is exactly the one you mentioned. The original Eurolung mortality model included 9 variables, so we thought that this was limiting the participation in the database and in the ESTS accreditation program. For this reason, we wanted to produce an easier, more user-friendly model without losing the predictive ability. In fact, the C-indexes of the parsimonious morbidity and mortality models remained similar to the original ones.

I believe the C-index is approximately 0.78. In any case, it is similar to the original model containing 9 variables. I appreciate by reducing the number of variables we may lose some information, especially in patients with cardiac risk, because there are no cardiac risk variables in the parsimonious model. However, with regard to the larger population-based risk prediction, the 2 models are similar.

Dr Kozower. That's great. With the current pandemic, there is great concern in the quality of data entry and kind of an opportunity for that. Are there any steps being taken by you and your team?

Dr Brunelli. Well, not specifically. We have a data manager now in our unit and in fact, her work is now simplified because we are operating fewer cases at the moment. We are at a very low capacity. We have reduced capacity from 11 surgical theaters a week to only 3. This translates into perhaps 4 or 5 lung resections per week as a team. So, the data entry work is simplified in this regard. In relation to the Covid situation, there is a global registry collecting data on patients operated during this critical period and is UK-based (CovidSurg). We are inputting data in this registry to understand how the cancer pathways have been altered by the Covid situation—and this represents a double entry of data because it's a totally different registry from our institutional one. However, we think it is valuable to understand the changing practice we are undergoing at the moment.



Dr Elliot L. Servais (Burlington, Mass). I did notice that you controlled in your regression analysis for pathologic N and T stage. What I didn't hear is whether you included sublobar resections in this analysis, and also whether there was any control for completeness of resection—maybe

nodal stations harvested, number of nodes, and so forth.

Is there a possibility that somebody who is less fit with a worse Eurolung score undergoes a less aggressive resection, less lymph node harvest, maybe sublobar resection that could affect outcomes?

Dr Brunelli. Yes, we included segmentectomies. These are anatomic resections. We didn't include wedges. The segmentectomies are probably 5%, 7% of the total number of resections in our unit.

Unfortunately, there is no control in terms of number of lymph nodes because we don't collect that information in our database. We collect the type of lymphadenectomy based on the European definition. So systematic dissection versus lobar-specific sampling. Perhaps we can adjust these factors as well to ensure that we control, but at least there is a proper staging when we stratify by pathologic N status. Indeed, these are the data we have at hand.