



Dr. Ralph Aye
The Role of Surgery in the Management of Non-Small Cell Lung Cancer (NSCLC)
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Intro GRACE, the Global Resource for Advancing Cancer Education, is pleased to provide the following presentation on the Role of Surgery in the Management of Non-Small Cell Lung Cancer, by Dr. Ralph Aye, Thoracic Surgeon Program Leader in the Thoracic Oncology Division at Swedish Cancer Institute in Seattle, WA . Dr. Aye spoke at the GRACE Non-Small Cell Lung Cancer Patient Forum in Seattle in September of 2009, a program supported by OSI Pharmaceuticals and Swedish Cancer Institute.

Dr. Aye: As you may know, lung cancer is grossly underrepresented in our country in terms of public awareness, in terms of funding for research and treatment in relation to the magnitude of problem that it is as a national health problem. And we thank you for taking the time to get involved and come and get yourselves informed, to go out and make other people aware and would encourage you to get involved and to bring other people back with you

So my talk is with regard to lung cancer as it relates to surgical treatment. And this pretty common scenario: we usually start with an abnormal x-ray, either because of symptoms or because the nodule's been discovered incidentally and we have a series of questions: what is it and how do we manage it? And surgery is one of our first thoughts as he mentioned and that's because historically for early disease, surgery has offered the best chance of a cure. It's certainly not a guarantee of a cure. But that's where we start in our questions and there are a variety of issues that come up--which operations should be done, what approach and what are the consequences of surgery.

We really need tissue in order to establish what the nodule is. And there are a variety of ways of doing that and he covered that. But the point I would make is that sometimes we don't know what the nodule is until we take it out surgically. And in that case, it's important to have done all the ground work in terms of the staging, in terms of the pulmonary function testing, evaluating the individual to be sure that once we establish the diagnosis, we're also prepared to provide the appropriate treatment at that time which may mean a larger lung resection than just taking the nodule out.

Staging was covered a bit, and that's critically important with regard to the decision about surgery. We want to know is this a localized nodule, is it confined to the chest and if so, does it involve lymph nodes or surrounding structures. And there is a threshold at which we say this is no longer something where we should be considering surgery either up front or at any time. But in brief, we have small nodules with negative nodes; we have larger nodules or nodules that involve localized lymph nodes within the lung. We have involvement of more centralized nodes or tumors that invade surrounding structures. And we have tumors that have spread outside the chest. And surgery is entirely appropriate in this case and usually in this case, this is a big gray zone, and this is almost a never for surgery.

We start with non-invasive staging imaging tests, CT, PET. Brain is the most common site for spread of cancer outside the chest, so that's a commonly used imaging. The PET CT has really become the workhorse for lung cancer. It provides a tremendous amount of information. Having done those studies, we move on to invasive staging. He already mentioned mediastinoscopy. This is an operation which is done in the operating room under anesthesia. A small incision is made in the base of the neck and then a hollow tube is passed into the space in front of the airway and that's where the lymph nodes are where the cancer can spread to. And so we're looking at whether any nodes are involved and which nodes are involved. sometimes the best way to get to those is with a parasternal biopsy, which means an incision along the side of the sternum to get at lymph nodes that we can't get with mediastinoscopy. And endobronchial ultrasound, a wonderful alternative to mediastinoscopy. And the two are working hand in hand and we're, since it's a relatively new technology, we're still feeling our way as to which modality to use when and how to use them to complement each other.

So, then the question is, is the tumor removable if it's localized within the chest. Is it something we can get out? And there are two aspects to that question. One is can we get it out safely? In other words, are the risks of the operation appropriate for the potential benefit? And the second is, does it make sense from a cancer standpoint? There are some situations where we can remove a tumor, but there isn't much of evidence that it would provide any benefit, removing major blood vessels, removing the esophagus and structures such as that. Whereas removing a part of the lining around the heart and removing part of the chest wall, although it adds to the magnitude of the operation, is something that could be done usually fairly well tolerated and has a reasonable chance of providing a survival benefit.

Resectability is somewhat relative. It depends on the individual patient and their physical and emotional characteristics. And it depends upon the experience and interest of the surgical team. This is an example of a tumor invading the thoracic vertebra, which is typically considered unresectable because we can't remove the spine without causing paralysis. But our team has a spine surgeon who trained with a specialized group in Paris and has learned to be able to remove parts of the spine and reconstruct it with this hardware. This patient had a tumor that did not appear to have spread elsewhere but was involving the spine, and so this operation was done.

The similar question comes up when lymph nodes are involved. If the nodes are involved within the lung, that's N1 disease and is still considered frequently to be resectable. If lymph nodes in the center part of the chest -- mediastinum -- are involved, that's a big gray zone and some of those patients could be considered for surgery but more often it's not a good domain for surgical resection.

Along with the question of resectability is whether the individual will tolerate the operation that would be required. We have an old sort of rule of thumb for thoracic surgeons which is if the person can tolerate, can climb one flight of stairs, they can tolerate a thoracotomy having the chest opened. If they can climb two flights of stairs, they can tolerate having a lobe resected. And three flights for pneumonectomy. And it does get at the issue that this is not just about how well someone breathes; its all about how their heart and their lungs function together—

the whole cardiorespiratory system; how fit they are and to some extent motivation. We see people coming in who really don't have a good social support system; they're not very motivated. And we have evidence that they don't do as well with surgery, and so that's one of the factors.

In addition, when we operate on the lungs, we also stress the heart. And so we frequently get a cardiac evaluation as well. If the person has some underlying heart disease, we'll probably discover it after a lung operation. We'd rather find out about that before an operation.

Is surgery the best option? For early stage disease it usually is, for a person who is fit enough to withstand it, but as the patient's other health issues mount up, if they have multiple other health issues as the staging of the tumor advances, we move into an area where surgery may not be the best choice and there are certainly other choices which are going to be discussed today. Radiation therapy really has made dramatic strides in terms of its interaction with computerized imaging. Radiofrequency ablation is a heat treatment that basically cooks the tumor. Cryosurgery is just the opposite, it freezes the tumor. Those are both local treatments. Chemotherapy is systemic treatment. And comfort care is an appropriate decision for people with lung cancer and it takes all these factors into consideration.

There's been some discussion about Stage. I don't think I'll get into that in too much detail. The overall survival after surgery for lung cancer is approximately 50%, but it does depend entirely on Stage. This slide is from experience with a large screening trial and I put it up to show that with early Stage small lesions, the cure rates go way up. And so the screening is a controversial subject, but in this screening trial, these were all bona fide lung cancers, invasive cancers confirmed by an international pathology panel and for resected Stage I lesions, the five-year survival actually projected ten year survival was 92%.

In terms of what operations should be done, the lung is built like a tree. The two major branches are the right lung and the left lung, and then there are lobes which are the next major divisions within the lung, in this case the left upper lobe and the left lower lobe. And then smaller branches within that which are called segments; and so on. The appropriate cancer operation is one that confers a good survival benefit taking the least amount of lung tissue necessary. Wedge resection is just wedging out the nodule. A lobectomy is taking out that entire portion either the upper half or upper third of the lung or lower third, what have you. Pneumonectomy is to take the entire lung. And this is determined by anatomic considerations as, just like a tree, the closer we go to the main trunk, the more branches have to be removed. But it's also determined by some cancer aspects. A wedge is a small operation easily tolerated. But based on the data we have now is probably not a good cancer operation for most people who can tolerate the bigger operation.

There was randomized study back in the 1980s that showed this. It was three times higher local recurrence rate if less than a lobectomy was done. And a higher cancer mortality rate also. However, this was 20 years ago. The tumors were larger. It was when CT scans weren't quite as good. The operations were mostly wedges rather than anatomic segmentectomies. And there's been increasing evidence since then that for smaller cancers being discovered on screening and the

fact that we're seeing what are called ground glass opacities, minimally invasive lung cancers now which often could be multifocal that perhaps we should relook at the question of doing less than a lobectomy because it has the lower risk to the patient if we do less and we preserve lung tissue.

So there is another randomized trial nationally which is listed at the bottom, and this is for smaller tumors, less than two centimeters randomized to a lobectomy versus less than a lobectomy. And this is a patient who entered that trial. Now, none of us like to be guinea pigs and this patient's struggled with this question, should I be entered in this national trial? This is a small nodule that she'd had for two years that had been followed. It was discovered incidentally. And it had this sub-solid, you see this sort of hazy appearance around the outside and it hadn't changed a lot in terms of its size, but it had started to fill in a little bit. So we were pretty sure it was a cancer and she had a needle biopsy that confirmed that it was. It was in a good location for doing less than a lobectomy and still doing a pretty good cancer operation. And she entered the trial and was randomized to a sub-lobar resection and had a basal segmentectomy performed with a thoracoscopic approach. And I say that because this is how we make our advances in knowledge is through these trials. And its important to support those to the extent that we're able to.

How should the operation be done? The gold standard has been an open thoracotomy which is usually made up under the arm. We spread the ribs, we were able to get hands and instruments inside the chest and perform an operation under direct vision and this is certainly the standard that other operations are measured against. We now can do a lot of this work with a videoscope, and we can do the same standard operations that we've done with open surgery. Its been pretty well shown that there is less pain, that there's a shorter hospital stay, quicker return in pulmonary function and overall physical function. But there have been some concerns raised about whether it's a good cancer operation and it's not an easy operation technically. So it's not available in the hands of every surgeon. And there are still legitimate questions being asked about it.

We've had a large experience with that. We compared a hundred patients who underwent the thoracoscopic approach with a hundred who had the open approach. The survival was no different at five years and we feel that it is a good cancer operation when done appropriately.

But the bottom line is the best approach is the one that can be done competently in the hands of a competent thoracic surgeon. And so I wouldn't get too hung up on that question.

Robotics is being used as well. That's even more of a question mark at this time and hasn't been widely used.

So what about risk and recovery issues? Typically the operation lasts about two to four hours. Hospital stay is in the range of three to five days. One of the big bugaboos with lung surgery is persistent air leak. The lung is covered by a membrane called the pleura. When we operate we violate that membrane and so frequently there's an air leak from the lung into the space around the lung and we need to leave tubes in the chest until that air leak stops. Typically it stops in a couple of days; but sometimes particularly in emphysematous patients it will go on

quite a bit longer. And so that's the big unknown in terms of hospital stay. The average is 3-5 days. Usually 3-6 weeks off work; there are a lot of variables in that. Pain medicine as you see listed. There is definitely a loss of lung function. The lung does not grow back, but the remaining lung and the heart and the whole cardiorespiratory system can make up for that loss of lung function and, so, after a lobectomy, the typical loss of function would be approximately 15%. And of course, for removal of the entire lung it's going to be higher, but still tolerated for a fit individual. There are a variety of risks every operation carries some risks. There are pain issues, anesthetic reactions, the risk of cardiac events as I mentioned, prolonged air leak, blood clots that can travel through the lungs, and so forth.

Overall mortality risk for a major lung resection is between 1% and 10%. One percent for a lobectomy is pretty much the standard. For a pneumonectomy its higher, between 5% and 10%.

Is additional therapy required? For a small tumor, usually not, and you see size limits. I routinely refer patients to an oncologist after surgery if the tumor is larger. If they've had any nodes that are involved and if there are close margins. In other words, if we're not sure we got every cell in the area where maybe it was stuck to part of the chest wall or the mediastinum, then we may want to consider radiation. And again, consider clinical trials.

Follow-up, somewhat controversial and it's based on evidence, but it's sort of a common sense approach. CT scans are used a lot for follow-up and our practice is to get a baseline CT at four months because the anatomy has been changed by the operation and we want to get a new CT to be used as a comparison for future CTs for any changes. And PET scans are used selectively depending upon the Stage at diagnosis and treatment. Chest x-rays are used fairly frequently as well. And of course part of it is just following up the patient after surgery.

I commend you for being here to raise awareness about lung cancer. Thank you.