v#1

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Navigating Patients With Lung Cancer

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Early Detection Options

- Lung Screening Programs:
  - Based on the National Lung Screening Trial (NLST) reported in 2011, which compared two ways of detecting lung cancer: low-dose helical computed tomography (CT) — often referred to as spiral CT — and standard chest X-ray
  - The study findings reveal that participants who received low-dose helical CT scans had a 15 - 20% lower risk of dying from lung cancer than participants who received standard chest X-rays. This is equivalent to approximately 3 fewer deaths per 1000 people screened in the CT group compared to the chest X-ray group over a period of about 7 years of observation (17.6 per 1000 versus 20.7 per 1000, respectively)
  - Current or former cigarette smokers within the past 15 years, 55 - 74 years of age, with at least 30 pack-years of smoking [Pack-years = packs per day x number of years smoking]. Participants must have had no symptoms or signs of lung cancer or other serious medical conditions, and be medically fit for surgery

Follow – Up Medical Care. NIH/NCI. Cancer.gov. February 2018.

Incidental Nodule Findings

- Some programs have been created to function independently of the lung screening program, while others dovetail findings from one to the other.
- These programs follow patients who have had lung nodules found on X-rays or scans done for reasons other than being “high risk.”
  - Pre-op Scans
  - Calcium Scoring Scans
  - Emergency Room/Trauma X-rays or Scans

Following Our Patient

- **Meet “Lorraine”**
  - She is 67 years old, never smoked, not aware of being around other high-risk factors like radon, asbestos, coal mines, etc.
  - She comes to her PCP complaining of not being able to shake off this cold she has had for over a month.
  - Chest X-ray reveals bibasilar patchy atelectasis and a possible semi-solid nodule measuring 8mm in the RLL.
  - Next step: Biopsy if possible or rescan in 3-6 months post antibiotic therapy?
    - Would there be a difference if the nodule was in the RUL vs. the RLL?

Following Our Patient

- **Time from scan to biopsy?**
- Biopsy reveals an adenocarcinoma, moderately differentiated
- Scan shows that the nodule now measures 1.0 cm (increase in size in 6 months)
- Next Steps?
  - PET/CT for clinical staging
    - Nodule is avid at 7
    - No other signs of metastatic spread evident

Biomarkers for Lung Cancer

	Phase 1	Phase 2	Phase 3	Phase 4	Phase 5
Candidates	Discovery/ Prediction	Assay Validation	Retro-longitudinal Study	Prospective Screening	Cancer Control
Autoantibodies (early CDT-test)	X	X	X	X	
C4d Protein	X	X	X		
Serum MicroRNA	X	X	X	X	
Plasma MicroRNA	X	X	X	X	

Sozzi, Boeri (2014)

Some are considered experimental, but are proving to be approximately 80% accurate compared to tissue testing. Other research is following the possibility of saliva testing for biomarkers.

Following Our Patient

- **Multidisciplinary Team to include:**
  - Pulmonary
  - Surgery
  - Medical Oncology
  - Radiation Oncology
  - Social Work
  - Nutrition
  - Nurse Navigator
  - Patient & Family/Support

Standards of Care

- Surgery: based on cell type, size, and location – as well as co-morbidities
  - Mediastinoscopy
  - VATS
  - Segmentectomy
  - Lobectomy
  - Pneumonectomy
- Chemotherapy: based on cell type and staging
- Radiation Therapy: based on cell type, staging, and location – as well as available equipment
  - Lung cancer candidates for **SBRT** are patients with small tumors — five centimeters or less — who are poor candidates for surgery due to the risk of functional deficit. Patients whose tumors are located centrally or close to airways or the heart have sometimes been considered poor candidates for SBRT due to higher complication rates
  - External beam radiation therapy
  - Brachytherapy (internal radiation therapy)

NCCN Chemotherapy Order Templates. NCCN.org. 2018

Changes in Staging

ANATOMIC STAGE/PROGNOSTIC GROUPING											
2017						2018					
STAGE			T	N	M	STAGE		T	N	M	
Occult Carcinoma			TX	N0	M0	Occult Carcinoma		TX	N0	MO	
								Tis	N0	M0	
0			Tis	N0	M0	0		Tis	N0	M0	
1A			T1a	N0	M0	1A1		T1mi	N0	M0	
			T1b	N0	M0			T1a	N0	M0	
						1A2		T1b	N0	M0	
						1A3		T1c	N0	M0	
1B			T2a	N0	M0	1B		T2a	N0	M0	
2A			T2b	N0	M0	2A		T2b	N0	M0	
			T1a	N1	M0						
			T1b	N1	M0						
			T2a	N1	M0						

Adapted from AJCC Cancer Staging Manual, 8th ed. 2017 - 2018

Changes in Staging (cont'd)

2B			T2b	N1	M0		2B		T1a	N1	M0
			T3	N0	M0				T1b	N1	M0
									T1c	N1	M0
									T2a	N1	M0
									T2b	N1	M0
									T3	N0	M0
3A			T1a	N2	M0		3A		T1a	N2	M0
			T1b	N2	M0				T1b	N2	M0
			T2a	N2	M0				T1c	N2	M0
			T2b	N2	M0				T2a	N2	M0
			T3	N1	M0				T2b	N2	M0
			T4	N0	M0				T3	N1	M0
			T4	N1	M0				T4	N0	M0
									T4	N1	M0

Adapted from AJCC Cancer Staging Manual, 8th ed. 2017 - 2018

Changes in Staging (cont'd)

3B			T1a	N3	M0		3B		T1a	N3	M0
			T1b	N3	M0				T1b	N3	M0
			T2a	N2	M0				T2a	N3	M0
			T2b	N3	M0				T2b	N3	M0
			T3	N3	M0				T3	N2	M0
			T4	N2	M0				T3	N3	M0
			T4	N3	M0				T4	N2	M0
							3C		T4	N3	M0
4			Any T	Any N	M1a		4A		Any T	Any N	M1a
			Any T	Any N	M1b				Any T	Any N	M1b
							4B		Any T	Any N	M1c

Adapted by AJCC Cancer Staging Manual, 8th ed. 2017 - 2018

Changes in Staging

DESCRIPTOR	SEVENTH EDITION	EIGHTH EDITION
T component		
0 cm (pure lepidic adenocarcinoma ≤3 cm total size)	T1a if ≤2 cm; T1b if >2-3 cm	Tis (AIS)
≤0.5 cm invasive size (lepidic predominant adenocarcinoma ≤3 cm total size)	T1a if ≤2 cm; T1b if >2-3 cm	T1mi
≤1 cm	T1a	T1a
>1-2 cm	T1a	T1b
>2-3 cm	T1b	T1c
>3-4 cm	T2a	T2a
>4-5 cm	T2a	T2b
>5-7 cm	T2b	T3

Adapted from AJCC Cancer Staging Manual, 8th ed. 2017 - 2018

Changes in Staging (cont'd)

DESCRIPTOR	SEVENTH EDITION	EIGHTH EDITION
>7 cm	**T3**	**T4**
Bronchus <2 cm from carina	T3	T2
Total atelectasis/pneumonitis	T3	T2
Invasion of diaphragm	T3	T4
Invasion of mediastinal pleura	T3	-
N component		
No assessment, no involvement, or involvement of regional lymph nodes	NX, N0, N1, N2, N3	No change
M component		
Metastases within the thoracic cavity	M1a	M1a
Single extrathoracic metastasis	M1b	M1b

Adapted from AJCC Cancer Staging Manual, 8th ed. 2017 - 2018

Changes in Staging (cont'd)

DESCRIPTOR	SEVENTH EDITION	EIGHTH EDITION
Multiple extrathoracic metastases	M1b	M1c

•Abbreviations: AIS, adenocarcinoma in situ; mi, minimally invasive adenocarcinoma; Tis, tumor in situ.

Adapted from AJCC Cancer Staging Manual, 8th ed. 2017 - 2018

Therapeutic Options

- Interventional Pulmonology: using bronchoscopic and/or pleuroscopic techniques including endobronchial ultrasound (EBUS) which uses a bronchoscope with an ultrasound probe to identify lymph nodes and masses outside of the airways or navigational bronchoscopy in which a steerable catheter can be advanced through the bronchoscope and directed to masses that cannot be seen in the airway

- Interventional Radiology: using ablative techniques including radiofrequency ablation, cryoablation, and/or percutaneous ablations

Lung Cancer 101. www.Lungcancer.org/ find_information/publications

Therapeutic Options (cont'd)

- Chemotherapy Options: Combination therapies are being developed and tested continuously
- Immunotherapies: Numerous drugs are being developed and tested, among them are therapeutic vaccines, adoptive cell therapy (i.e. CAR-T) and immune checkpoint inhibitors (anti-PD-L1)
- Photodynamic Therapy: used to treat both early and advanced stages of lung cancer and in combination with surgery. It can preserve pulmonary function, is well tolerated, and is cost-effective in comparison with other treatments
- Proton Therapy: external beam radiotherapy that works by aiming protons onto the target tumor. Because of the accuracy of the beam, proton therapy delivers a higher dose of treatment directly to the tumor, while sparing healthy tissue, which can lead to benefits such as:
  - Improved outcomes and fewer side effects
  - The ability to treat cancerous tumors close to critical organs
  - A greater quality of life during treatment
  - The ability to offer new treatment options for patients whose cancer has recurred

Lung Cancer 101. www.Lungcancer.org/ find information/publications

Following Our Patient

- Lorraine has now had surgery that removed the lower lung lobe
- She has received chemotherapy – not immunotherapy
  - Cisplatin and Docetaxel
- Radiation was not considered at this time
- Follow up Recommendations?

Symptom Management

Summary of Potential Treatment Strategies in Lung Cancer Survivors	
Symptoms	**Recommendations**
Fatigue	Assess for underlying pulmonary disease, depression. Thyroid dysfunction
	Encourage routine physical activities as tolerated
Pain	NSAIDS, opioids, antidepressants, anti-epileptics as needed
	Consider referral to PT
	Early referral to pain management
	Consider nerve blocks for severe pain

Lehto; 2017

Symptom Management (cont'd)

Symptoms	Recommendations
Peripheral Neuropathy	Duloxetine, pregabalin, NSAIDS, opioids
Psychosocial and Economic Issues	Screen for anxiety and depressions routinely
	Screen for comorbidities and socioeconomic issues
	Consider use of antidepressants
	Referral to mental health professionals as needed
	Referral to peer support programs, educational-informational programs as appropriate and available
	Regular assessment of practical and financial concerns

Lehto; 2017

Symptom Management (cont'd)

Symptoms	Recommendations
Tobacco Use	Assess for continued use of tobacco products and dependence
	Combination of support groups and pharmacologic interventions for smoking cessation
	Referral to community-based resources
Respiratory Dysfunction	Bronchodilators as indicated
	Supplemental oxygen as indicated
	Consider referral to pulmonary rehab if available
	Continued assessments for ability to management above

Symptom Management (cont'd)

Symptoms	Recommendations
Lifestyle/Activity	Assess pretreatment and posttreatment activity levels
	Counsel against "staying put"
	Encourage 30 minutes of physical activity/day as tolerated
	Consider referral to physical rehab or pulmonary rehab if available
Preventive Health	Review vaccination history regularly
	Annual flu vaccine
	Pneumonia vaccines as per NCCN and CDC recommendations

Lehto; 2017

Symptom Management (cont'd)

Recurrence/Secondary Malignancy	Surveillance for recurrance with regular evaluations
	Screen for continued tobacco use
	Age appropriate screenings per NCCN and ACS guidelines

Please note that NCCN and ASCO have just come out with a new Patient Education handout on Understanding Immunotherapy Side Effects that is available on line.
www.nccn.org/about/news/newsinfo.aspx?NewsID=1008

Survivorship Recommendations

- Repeat Chest CT at 6 months X2, then annually X3
- Follow-up appointments with surgery and medical oncology every 3 months for 3 years, then every 6 months for 2 years, including review of scans and bloodwork
- Annual follow-up with PCP including bloodwork
- Recommended vaccines

Challenges in Dealing with Patients in this Population

- Social impacts of lung cancer on QOL for patient and family
  - Smoking/tobacco utilization
  - Alcohol usage
  - Are symptoms experienced before/during diagnosis
  - Financial implications of treatment and beyond
  - Work-related issues
    - Time off
    - Insurance coverage
    - Jobs being held during treatment time

Gina Columbus. Onclive.com State of the Science Summit on Advanced Non-Small Cell Lung Cancer. 2017

Challenges in Dealing with Patients in this Population

- Symptoms associated with treatments
  - Pain
  - Fatigue
  - Neuropathy
  - Weight loss and loss of appetite
  - Chronic infections secondary to decreased immune response
  - Paraneoplastic syndromes
    - SIADH
    - Hypercalcemia
    - Blood Clots

Gina Columbus. Onclive.com State of the Science Summit on Advanced Non-Small Cell Lung Cancer. 2017

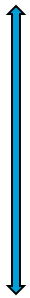
Programmatic Challenges and Champions

- Challenges:
  - Managing the populations we serve – identifying and diagnosing may be easier than follow-up, especially if the patients are not symptomatic.
  - Racial and socioeconomic disparities will continue to play a role in program need versus development. How do we move forward in an environment of financial instability to grow these programs? Ethnic differences versus racial disparities will continue. i.e. “Hispanic” culture encompasses many ethnic differences: Cuban, Latin American, Mexican, Spanish, etc.
  - Health care Insurance issues face the entire country. It does not matter if our service communities are urban, suburban, or rural.
  - Educational deficits do not know physical boundaries.

Gina Columbus. Onclive.com State of the Science Summit on Advanced Non-Small Cell Lung Cancer. 2017

Programmatic Challenges and Champions

- Champions:
  - We need to look towards our communities to identify champions. Who in the community leadership can we work with to get information out regarding the need to identify and treat lung cancer?
  - Who within our health care facilities should be on the “frontline?”



    - Administration
    - Physician Champion – Pulmonologist, Thoracic/Oncologic Surgeon, PCP
    - Nurse Navigators
    - Social Workers

Following Our Patient

- Patient has a complete response and remains NED
- Patient has a partial response. **Next?**
- Patient recurs. **Next?**
- Patient does not respond to treatment. **Next?**


QUESTIONS

LRAD SCORING

- **Category 0 (incomplete)**
- prior CT studies were performed, but are not available for comparison
- lungs are incompletely imaged
- **Category 1 (negative, <1% chance of malignancy)**
- no lung nodules
- lung nodule(s) with specific findings favoring benign nodule(s)
  - complete calcification
  - central calcification
  - popcorn calcification
  - calcification in concentric rings
  - fat-containing nodules

Lung RADS. American College of Radiology. 2018

LRAD SCORING (cont'd)

- **Category 2 (benign appearance, <1% chance of malignancy)**
- solid nodule(s)
  - <6 mm
  - new nodule <4 mm
- subsolid nodule(s)
  - <6 mm on baseline screening
- ground glass nodule(s)
  - <20 mm
  - ≥20 mm and unchanged or slowly growing
- category 3 or 4 nodules that are unchanged for ≥3 months

Lung RADS. American College of Radiology. 2018

LRAD SCORING (cont'd)

- **Category 3 (probably benign, 1-2% chance of malignancy)**
- solid nodule(s)
  - ≥6 mm to <8 mm at baseline
  - new nodule 4 mm to <6 mm
- subsolid nodule(s)
  - ≥6 mm total diameter with solid component <6 mm
  - new <6 mm total diameter
- ground glass nodule(s)
  - ≥20 mm on baseline CT or new

Lung RADS. American College of Radiology. 2018

LRAD SCORING (cont'd)

- **Category 4A (suspicious, 5-15% chance of malignancy)**
- solid nodule(s)
  - ≥8 mm to <15 mm at baseline
  - growing nodule(s) <8 mm
  - new nodule 6 mm to <8 mm
- subsolid nodule(s)
  - ≥6 mm total diameter with solid component ≥ 6 mm to <8 mm
  - new or growing <4 mm solid component
- endobronchial nodule

Lung RADS. American College of Radiology. 2018

LRAD SCORING (cont'd)

- **Category 4B (suspicious, >15% chance of malignancy)**
- solid nodule(s)
  - ≥15 mm
  - new or growing, and ≥8 mm
- subsolid nodule(s)
  - solid component ≥8 mm
  - new or growing ≥4 mm solid component

Lung RADS. American College of Radiology. 2018

LRAD SCORING (cont'd)

- **Category 4X (suspicious, >15% chance of malignancy)**
- category 3 or 4 nodules with additional features or imaging findings that increase the suspicion of malignancy
- includes:
  - spiculation
  - ground glass nodule(s) that double in size in 1 year
  - enlarged regional lymph nodes
- **Modified categories**
- [X]**S** (e.g. "3S") if there is a clinically significant or potentially significant non-lung cancer finding
- [X]**C** (e.g. "3C") for a patient with a prior diagnosis of lung cancer who returns to screening

Lung RADS. American College of Radiology. 2018

Recommended Follow-up

- **Category 0:**
  - comparison with prior studies before assignment of Lung-RADS classification
- **Category 1:**
  - continue annual screening with LDCT
- **Category 2:**
  - continue annual screening with LDCT
- **Category 3:**
  - 6 month follow-up with LDCT
- **Category 4A:**
  - 3 month follow-up with LDCT
- PET/CT may be used if there is a ≥8 mm solid component

Lung RADS. American College of Radiology. 2018

Recommended Follow-up

- **Category 4B and 4X:**
- chest CT with or without contrast, as appropriate
- PET/CT and/or tissue sampling depending on the probability of malignancy and comorbidities (PET/CT if solid component ≥8 mm)
- **Practical Points**
- nodule measurement should be in lung windows
- nodule average diameter is rounded to the nearest whole number
- only a single measurement is necessary for round nodules
- "growth" is an increase in size of ≥1.5 mm
- assignment of a Lung-RADS status is based on the most suspicious nodule
- category 4B management is based on multiple factors including overall patient status and patient preference

College of Radiology 2018

Fleischner Criteria Changes from 2017 to 2018

- Primary tumor — Major changes between the seventh and the eighth editions include the following:
- **T1 changes –** New stage groupings divide T1 tumors into T1a (≤1 cm), T1b (>1 to ≤2 cm), and T1c (>2 to ≤3 cm)
- **T2 changes –** T2 tumors have a size cutoff of 5 cm now, rather than 7 cm. Involvement of the main stem bronchus, regardless of distance from carina, is now T2 rather than T3. Both partial and total atelectasis/pneumonitis are now T2
- **T3 and T4 changes –** Tumors greater than 5 to less than or equal to 7 cm are now T3 instead of T2; tumors greater than 7 cm now fall into a new T4A grouping. Diaphragm invasion is now T4 rather than T3
- A new stage category has been developed for T3 and T4 tumors, which are now classified as stage IIIC when accompanied by contralateral lymph node (N3) involvement

Fleischner Criteria Updates. RSNA Radiology. July 2017.

Fleischner Criteria Changes

- Regional lymph nodes — Although N descriptors from the seventh edition consistently predicted prognosis and were carried forward in the eighth edition, an exploratory subclassification of pathologic N1 and N2 disease based on the number of involved nodal stations and individual nodes was proposed:
- pN1 – Involvement of ipsilateral intrapulmonary, peribronchial, or hilar lymph nodes
- pN1a: Single station metastasis
- pN1b: Multiple station metastasis
- pN2 – Involvement of ipsilateral mediastinal or subcarinal lymph nodes
- pN2a1: Single N2 station without concurrent N1 station involvement (skip metastasis)
- pN2a2: Single N2 station with concurrent N1 involvement
- pN2b: Multiple N2 station metastasis

Fleischner Criteria Updates. RSNA Radiology. July 2017.

Fleischner Criteria Changes

- Metastasis — In the eighth edition of the TNM staging system, metastatic disease continues to be classified as M1a if it is limited to the chest (cases with pleural/pericardial effusions, contralateral lung or pleural nodules, or a combination of these factors)
- If not confined to the chest, there is now a new category, M1b, designating a single extrathoracic metastasis, which is distinguished from M1c, in which there are multiple metastatic lesions (in one or multiple organs)
- These changes led to the designation of stage IVa disease, in which disease is limited to either intrathoracic metastatic involvement or a single extrathoracic metastasis, versus stage IVb disease, in which multiple extrathoracic metastases exist. It is intended that this degree of precision will ultimately help guide treatment options for oligometastatic disease

Fleischner Criteria Updates. RSNA Radiology. July 2017.

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