Breast, Colon, and Lung Cancer

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General Information

It is anticipated that 70% of all cancer diagnoses by the year of 2030 will be in patients =>65.

Increasing cancer with age

- Some cancer are thought to develop over a long period of time through the accumulation of several damaging genetic events occurring over time.
- DNA repair mechanisms decline with age, especially those without functioning cell cycle checkpoints.
- Telomere shortening and increased epigenetic gene silencing with age.
- Decline in the function of the cellular immune system with age.

Ethnic Differences

- African Americans have the highest cancer incidence and mortality rates (10% higher than Whites, and 50% higher than Hispanic or Asian Americans)

- African Americans have shorter survival times at all stages of diagnosis (30% higher than Whites, and Twice as high as Hispanic and Asian Americans)

Breast cancer

Risk Factors for Breast Cancer

- Gender
- Age
- Race
- Diet (High in fat/calories)
- Early onset menses and late menopause
- Late or no pregnancies
- Family history (BRCA1, BRCA2)
- Dense Breasts
- Alcohol Consumption
- Hormone Supplementation

Age

- Worldwide – 1/3 of breast cancer cases are seen in patients >65 years old, in more developed countries, this number is higher – about 40%
- More favorable tumor biology with age:
  - Increased hormone sensitivity
  - Lower grader and proliferative indices
- Later stage with age (large tumors and more advanced)
- Older individuals less likely to be treated accordingly to treatment guidelines.
- Heterogeneity of population and under-representation in breast cancer clinical trials.

Race

- African-Americans tend to have more aggressive breast cancer. In terms of higher percentage of triple negative disease (negative for ER, PR, and Her-2 Neu)

- Even when matched by age and stage, African-American women have a worse outcome.

Alcohol

- Women who consume 3-9 drinks/week have a 50% higher risk of breast cancer than women than consume less than 3 drinks/week

- Alcohol changes the way estrogen is metabolized leaded to higher estrogen levels.

Screening (Mammography)

- Most recommends screening to begin at age 50, and an individual decision between age 40-49, but screening may be indicated in women <40 with a genetic predisposition, prior cancer, strong family history, prior biopsy with a high-risk lesion or prior chest radiation.
- Limitations in mammography in dense breasts and specific types of lesions, such as invasive lobular and uncalcified DCIS. MRI as an adjunct to mammography may be appropriate in women with a >20% lifetime risk of breast cancer
- Risks of screening: anxiety and consequences of false positives (biopsy).
- In women over the age of 75, breast cancer screening should occur if the life expectancy if over 10 years and in consultation with their primary care provider.

Localized Breast Cancer

- Breast conservation surgery (lumpectomy) with postoperative radiation is the standard of care for all ages.
- Total mastectomy is an option for those that are not candidates for lumpectomy and/or radiation, and is a consideration especially in patients with very large primary lesions.
- If there is no clinical lymph node involvement, sentinel lymph node sampling is just as accurate as a full axillary dissection without the toxicity.
- In very selected individuals over the age of 70 with low risk features undergoing lumpectomy, adjuvant radiation therapy can be omitted, if they will be receiving adjuvant hormone therapy.
- Individuals without adjuvant radiation therapy have a higher local-regional recurrence rate but similar overall survival.

Adjuvant Hormone Therapy

- Two options exist: Tamoxifen or Aromatase Inhibitors.
- Even older frail patients tolerate hormone therapy.

- Aromatase inhibitors (block conversion of androgen to estrogen, Anastrozole, Letrozole, Exemestane) are the first line treatment in women with ER+ tumors (at least 5 years, maybe up to 10 years).
  - Side effects include: joint pain, hot flashes, sexual dysfunction, vaginal dryness, **increase rate of bone mineral loss**.
- Tamoxifen (selective estrogen receptor modulator) – agonist in bone/uterine tissue, antagonist in breast tissue.
  - Side effects include: **thrombo-emoblic disease, increase risk of uterine cancer,** hot flashes, vaginal discharge/bleeding, and sexual dysfunction.

Chemotherapy

- Neo-adjuvant
- Adjuvant
- Metastatic Disease

- The NCCN believes that the best management of any patient with cancer is a clinical trial, which would benefit from being offered to older individuals. Studies have should that one of the reasons for under-representation of older individuals on clinical trials is that they are not offered to older patients.

Adjuvant Chemotherapy in the Elderly

- Could be considered in very health older individuals with ER/PR+ Her2-Neu negative biology with a very high recurrence score based on 21 gene RT-PCR or the presence of lymph node metastasis (chemo first then hormone therapy).
- In women who have ER/PR- Her-2Neu+ disease, adjuvant chemotherapy + Trastuzumab is considered standard.
- Adjuvant chemotherapy can also be considered in individuals with triple negative breast cancer, especially if tumor>1cm or with nodal involvement.

Metastatic Breast Cancer

- In older women with ER/PR+ disease, hormone therapy will have effective palliation unless they are significantly symptomatic at the time of diagnosis.
- There have been a large number of studies that have shown that chemotherapy is safe and effective in older adults.
- Chemotherapy is the preferred 1st line treatment in patients with visceral crisis (pain or high symptom burden due to disease in visceral organs such as the lung and liver).
- Usually single agents, at full dosage are used since the goal is palliation. Vulnerable adults can be started at 75% of the full dosage.

Geriatric Assessment

- Traditional oncology tools, such as the Karnofsky Performance Status (KPS) or Eastern Cooperative Oncology Group (ECOG) performance measures correlate with toxicity from chemotherapy but do not predict outcomes as well as geriatric assessment.

- Many abbreviated versions of geriatric assessment are being evaluated for their ability to predict treatment tolerability.
- Two studies, using tailored assessment tools – CARG scale and CRASH score, demonstrated that the addition of domains from geriatric assessment is more predictive of toxicity than just KPS/ECOG.

- Geriatric assessment is multi-disciplinary and has been shown to be feasible in oncology clinical assessment and cooperative group trials.
- The International Society of Geriatric Oncology recommends geriatric assessment in the older cancer patient prior to any cancer-directed therapy.

Colon Cancer

Risk Factors for Colon Cancer

- Age
- Race/Ethnicity – African-Americans
- Polyps
- Inflammatory intestinal conditions (ulcerative colitis or Crohn's)
- Inherited Syndromes (familial adenomatous polyposis or Lynch Syndrome)
- Family History
- Diet – Low Fiber/High Fat
- Diabetes
- Obesity
- Smoking
- Alcohol
- Prior Radiation therapy

Age

- Third leading cause of cancer and 2nd leading cause of cancer death.
- 90% of cases occur in individuals over the age of 50.
- 2/3 of cases occur in individuals who are =>65 years old.
- The risk of colorectal cancer in someone =>80 with rectal bleeding is about 25%.
- 40% of colorectal cancers arise proximal to the splenic flexure, and <10% are within reach of a digital rectal examination.

Polyps

- Do not usually cause symptoms, but may bleed.
- Classified as either neoplastic (adenomas) or non-neoplastic (hyperplastic).
- 40% of the population over the age of 50 have one or more adenomas.
- Detection and removal of adenomas significantly reduces the morbidity and mortality associated with colon cancer.
- Colonoscopy with endoscopic polypectomy remains the ideal examination for the detection and removal of adenomatous polyps.

Colon Cancer Screening

- U.S. Preventative Services Task Force recommends selective colorectal cancer screening in adults over the age of 75 only if there is an increased risk and screening would be a net benefit.
- Cancer screening should be focused on individuals with a life expectancy of greater than 10 years.
- Even in individuals with a known history of polyps, discontinuation of surveillance should be considered if age>75 if follow-up has been normal or only shown small tubular adenomas.
- Sigmoidoscopy and Colonoscopy are equally effective in screening for colon cancer.

Colon Cancer Screening

- Frequency:
  - Colonoscopy every 10 years, sigmoidoscopy every 5 years
  - If an adenomatous polyp is found on sigmoidoscopy a full colonoscopy is indicated.
  - 3 year colonoscopy interval in individuals with adenomas
    - If a small tubular adenoma may be able to extend to 5 years
    - If a large villous adenoma consider follow-up in 1 year
    - If follow-up is negative an interval of 5 years may be sufficient
  - 1 year follow-up colonoscopy in patient with colon cancer post resection
    - Adenoma or cancer recurrence rate is 25-30% at 3 years
  - Adenomas don't usually bleed and thus a fecal occult blood test is not a sensitive screening test.
  - Other options include: high-sensitivity guaiac fecal occult blood test (yearly), Stool DNA fit (every 1-3 years), CT colonography (every 5 years)

Colonoscopy

- All cases of hematochezia
- Occult GI Bleeding
- Iron-deficiency anemia
- Melena after a negative upper endoscopy

- Note: Right sided cancer typically present with iron deficiency anemia and occult GI bleeding.

Early Stage Treatment

- Surgical excision may be adequate for lesions confined to the colon.

- If regional lymph nodes are involved, post-operative adjuvant chemotherapy (5FU + leucovorin) reduced recurrence by 40-50%. The addition of oxaliplatin improves outcomes for younger patients with stage III disease (unclear in older individuals).

Metastatic Disease

- A subset of patients with metastatic colorectal cancer with <5 metastatic sites involving the liver and/or lung (oligometastatic disease) can be approached with surgery, stereotactic radiotherapy, and/or ablative strategies with curative intent.
- Age is not a contraindication for surgery. Older individuals can have the same survival benefit as younger individuals.
- In patients with just hepatic metastasis only, hepatic resection can offer a chance at long term survival. However, older patients needs to also be offered perioperative chemotherapy to achieve long-term disease control.

Metastatic Disease

- Chemotherapy, especially with newer agents such as irinotecan and oxaliplatin, can induce partial remission in subsets of patients.

- Survival has increase from an average of 6 months to over 2 years for patients that can tolerate treatment.

- There is a small survival benefit in combination chemotherapy over monotherapy, but in the older adult monotherapy is also a consideration.

Metastatic Disease

- For tumors that have high levels of microsatellite instability (MSI-H) or deficient mismatch repair (dMMR), may benefit for immunotherapy with a PD-1 inhibitor (Pembrolizumab)
- Treatment with oral capectiabine (5FU pro-drug) is an option, but may have a more negative effect on quality of life than infusions 5FU.
- Bevacuzimab (VEGF antibody) improves the overall survival of older adults when used in combination with standard chemotherapy.
- For patients with RAS wild-type tumors, adding monoclonal antibodies to the epidermal growth factor receptor (cetuximab, panitumumab) can improve survival
- Some colon cancers may express Her2, which may make that a target for treatment as well.

Lung Cancer

Leading cause of cancer-related death in Western Countries for both men and women.

Risk Factors for Lung Cancer

- Age (50% of all diagnosed patient are =>70)
- Smoking (also second hand smoke)
  - Cigarettes
  - Cigar and Pipe
  - Electronic Cigarettes
- Asbestos
- Radon
- Air Pollution and Diesel Exhaust
- Radiation
- Inflammatory lung disease

Lung Cancer Screening

- Low Dose CT Screening (every year for three consecutive years) was shown to be effective in a larger randomized trial (National Lung Screening Trial) in high-risk individuals with a lung cancer mortality benefit of 20% and all cause mortality benefit of 6.7%.
  - High risk is defined by the USPSTF as age 50-80 with a =>20 pack year smoking history and currently smoke or quit within the last 15 years.
- The NSLT had only 25% of participants =>65, and none older than 75. Older individuals were more likely to have a false positive screen but also a high prevalence and positive predictive value for cancer.

Lung Cancer

- Two Main Types
  - Non-Small Cell Lung Cancer (NSCLC) comprises at least 80% of all lung cancer
  - Small Cell Lung Cancer
- Most patients present with advanced-stage disease in which the goal of therapy is general palliative.
- Lung cancer is becoming increasing common in older women with one hypothesis being that women are at higher risk than men to develop cancer per unit of tobacco exposure.

Early Stage Disease (Stage I-II)

- Early recognition and surgical resection represent the best chance for a cure, followed by adjuvant chemotherapy (cisplatin-based doublet) if high risk features.

- Stereotactic radiation is a non-surgical alternative for patients who are not candidates for surgery.

Stage III Disease

- Concurrent therapy with chemotherapy and radiation is the standard for younger patients, however many older patients may not be fit enough to undergo definitive chemo-radiation.
- Alternatives in an older patient include sequential approaches or radiation therapy alone.
- In stage IIIA, neo-adjuvant treatment followed by surgical resection can be considered on a case by case basis, benefiting by a geriatric assessment by a multidisciplinary team.

Advanced Lung Cancer (Stage IV)

- Combination chemotherapy with a platinum doublet is the standard treatment of most cases of advanced NSCLC.
- Older individuals (=>70) have been shown in a randomized Phase III study to benefit from doublet therapy (overall survival 10.3 months versus 6.2 months for monotherapy) but toxic adverse events were note more frequently. The performance status of these patients was excellent.
- If the tumor over-expresses PD-L1, first line immunotherapy is an option with better cancer-related outcomes and less toxicity.
- For patients with non-squamous NSCLC, there is a benefit to the addition of Bevacizumab to a platinum doublet.

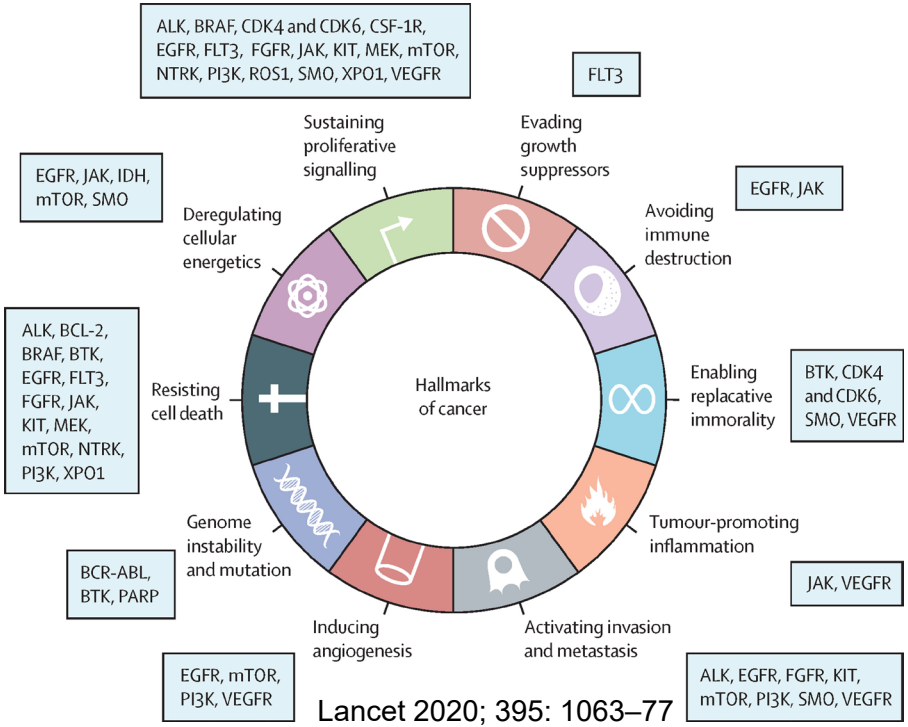
Small Cell Lung Cancer

- Diagnosis exclusive to heavy smoking exposure.
- Often treated with chemotherapy and radiation without surgery.
- Brain metastatic relapse is common and thus paved the way for prophylactic cranial irradiation.

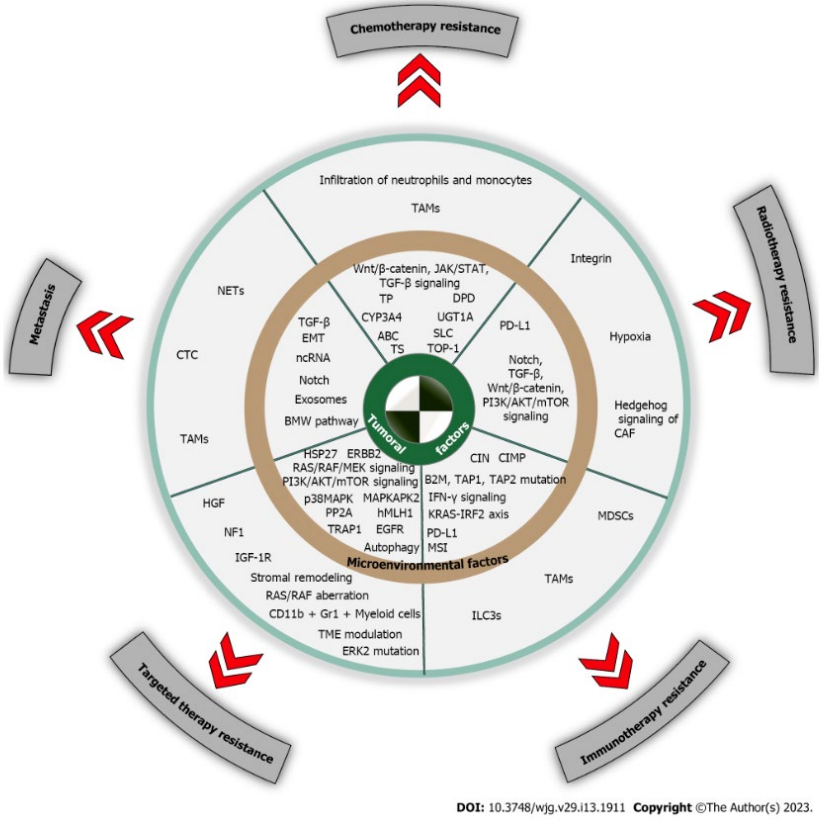
How much does a geriatrician need to know about cancer treatment?

- Compared to classic chemotherapy, newer targeted cancer treatments may be less toxic and tolerable to the older patient.
- Many of these newer drugs have side-effect profiles that require primary care provider awareness:
  - Trastuzumab (Herceptin) for Breast Cancer: **Cardiac Disease**
  - Bevacizumab (Avastin) for Colon Cancer: **Hypertension/GI Perforation**
  - Pembrolizumab (Keytruda) for Lung Cancer: **Hypophysitis**

Cancer Genomics in Advanced Cancer



Lancet 2020; 395: 1063–77



DOI: 10.3748/wjg.v29.i13.1911

World J Gastroenterol. Apr 7, 2023; 29(13): 1911-1941

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