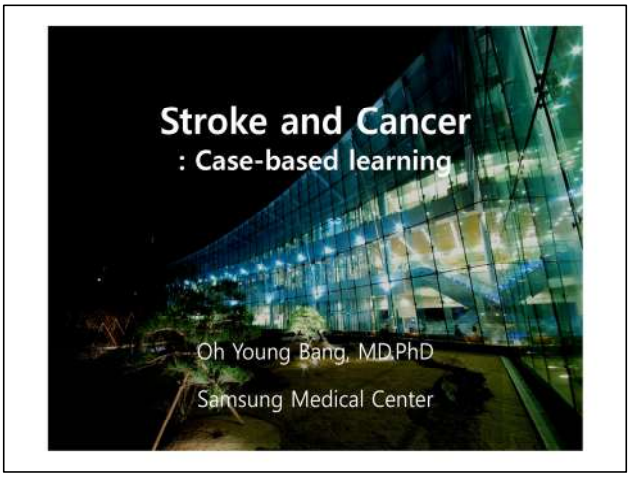
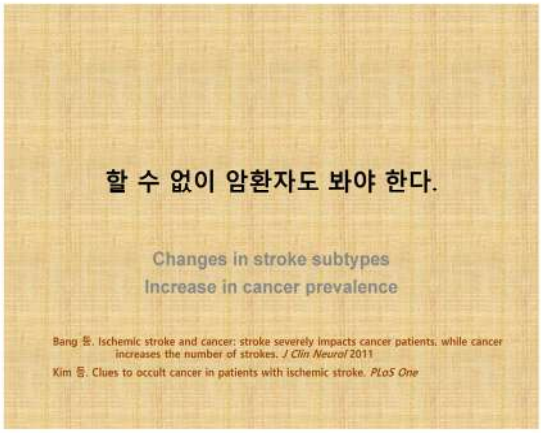
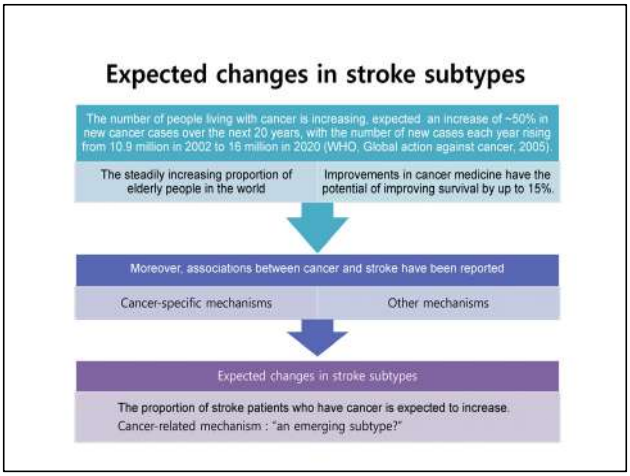
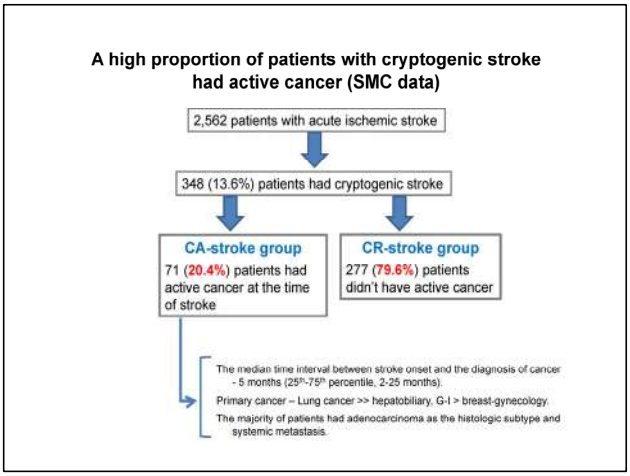
Stroke and cancer : Case-based learning

방 오 영
삼성서울병원









National-wide follow up studies

Sweden *[Zoller B. Eur J Cancer 2012]*

- The risk of ischemic stroke during the 1st 6 months after cancer diagnosis was 1.6, and decreased thereafter, but remained relatively constant after 6 months over time.

Denmark *[Erichsen R. Cancer Epidemiol Biomarkers Prev 2013]*

- The incidence of stroke was increased in colorectal cancer.
- Excess risks attenuated over time and were no longer beyond 1 year.

U.S.A. *[Navi BB. Ann Neurol 2015]*

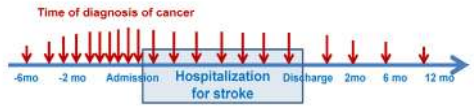
- The incidence of stroke was increased in most cancer types.
- Excess risks attenuated over time and were no longer beyond 1 year.

Taiwan *[Chen PC. Stroke 2011]*

- The incidence of stroke was 1.5 times higher in the lung cancer.
- The risk of stroke is at the highest after the diagnosis of lung cancer.

Stroke as the first manifestation of concealed cancer

- Thrombosis is the second leading cause of death in cancer patients *[Pruemer J. Am J Health Syst Pharm 2005]*
- Up to 10% of previously undiagnosed malignancies will present with thrombosis *[Lee AY. Hematol Am Soc Hematol Educ Program 2006]*
- Work up of hidden malignancy in patients with cryptogenic stroke and suspected coagulopathy revealed hidden malignancies. *[Kwon HM. J Neurol Sci 2007] [Kim, Bang. et al. PLoS ONE 2012]*



[Kim, Bang. et al. PLoS ONE 2012]

심지어는 암이 발견되기 전에 뇌졸중으로

- Thrombosis is the second leading cause of death in cancer patients [68]
- Up to 10% of previously undiagnosed malignancies will present with thrombosis [69].

68 Pruemer J. Prevalence, causes, and impact of cancer-associated thrombosis. Am J Health Syst Pharm 2005; 62:S4–S6.

69 Lee AY. Thrombosis and cancer: the role of screening for occult cancer and recognizing the underlying biological mechanisms. Hematol Am Soc Hematol Educ Program 2006:438–443.

Kwon HM, Kang BJ, Yoon BW. Stroke as the first manifestation of concealed cancer. J Neurol Sci 2007;258:80-83

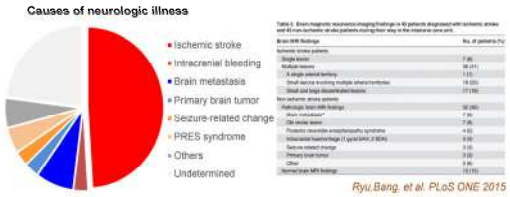
Stroke often underdiagnosed in cancer patients

Data of cancer center ICU

88 patients underwent brain MRI for altered mental status in 55 (63%), hemiparesis in 28 (32%), and seizure in 20 (23%).

Usual practice in oncology: CE-MRI → add DWI

In critically ill patients with cancer, cancer-related stroke is much more prevalent than other causes of neurological involvement, including metastasis.



Ryu,Bang. et al. PLoS ONE 2015

암환자에서 뇌졸중이 의심될때 여러가지 감별해야 한다.

Cancer-unrelated stroke (conventional mechanism)
Cancer-related (coagulopathy) stroke
Cancer treatment-related stroke
Stroke mimic conditions

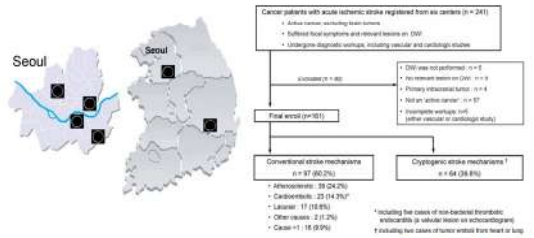
Kim 등. Ischemic stroke in cancer patients with and without conventional mechanisms: a multicenter study in Korea. *Stroke* 2010

Stroke in Cancer patients : Cancer-related mechanism?

- The characteristics of stroke in cancer patients were largely unknown.
- Previous studies reported that the stroke patterns and vascular risk factors in cancer patients were not significant different when compared with the non-cancer population (Zhang et al., 2006) (Chaturvedi et al., 1994) (Zhang et al., 2007).
- On the contrary, others reported that embolism not including cardiac origin was the most common cause of ischemic stroke in cancer patients (Cestari et al., 2004).

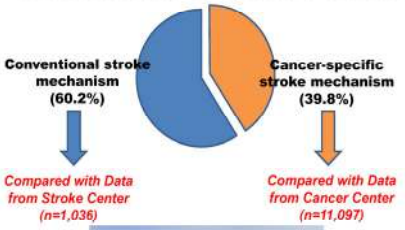
Stroke in Cancer Patients without Conventional Mechanisms: A Multicenter Study

Objective : to assess the prevalence and characteristics of stroke involving mechanisms possibly related to cancer.



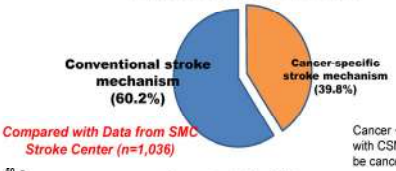
Kim, Bang, et al. Stroke 2010

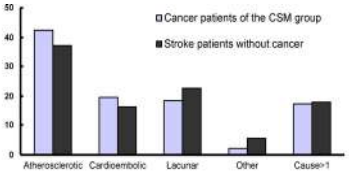
Characteristics of Stroke & Cancer



Kim, Bang, et al. Stroke 2010

Stroke mechanisms





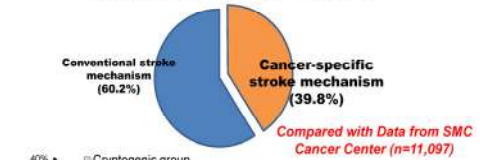
Cancer + stroke patients with CSMs were unlikely to be cancer-related origin

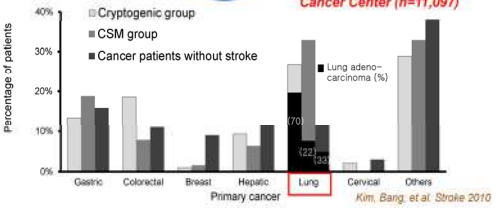
← the mechanisms of stroke in those patients were not different from stroke patients without cancer.

← These patients should be treated according to the stroke subtypes, such as atherosclerotic, lacunar, etc.

Kim, Bang, et al. Stroke 2010

Characteristics of Cancer





Kim, Bang, et al. Stroke 2010

Characteristics of Cancer

Factors to be considered

1. Primary cancer & pathologic type
   - Adenocarcinoma, especially lung cancer *[J Am soc Echocardiogr 2000;13:878-881] [Neurology 2004;62:2025-2030]*
   - *NBTE is reported most commonly in patients with adenocarcinoma, esp. mucin-producing carcinomas of the lung or GI, and lymphoma*
2. Extent of tumor
   - 30.4-47% had metastatic disease *[Acta Neurol Scand 2006;114:378-383]*
   - 52% in cancer-related stroke and 18% in stroke with incidental cancer *[Kim, Bang, et al. Stroke 2010]*
3. Active cancer

   Definition) *[NEJM 2003;349:146-153]*
   1. Within 6 months after diagnosis of cancer
   2. Any cancer treatment, recur or metastasis

Characteristics of Stroke

- DWI pattern of multiple vascular territories and D-dimer >1.11 g/mL were independently associated with the cryptogenic group.

	CSM group (n=92)	Cryptogenic group (n=69)	Odds for cryptogenic group	
			OR (95%CI)	*P*
Risk factor profiles				
Age	70.4±9.9	63.0±11.0		
Hypertension	58 (63.0%)	21 (30.4%)		
Diabetes	26 (28.3%)	8 (11.6%)		
Ischemic heart disease	8 (11.6%)	7 (13.0%)		
Distant metastasis	21 (24.4%)	32 (54.2%)		
DWI patterns				
Single vascular territory	77 (79.4%)	19 (29.7%)	Reference	
Multiple vascular territories	20 (20.6%)	45 (70.3%)	**11.16 (3.74–33.28)**	**<0.001**
Laboratory findings				
D-dimer levels of 1.11 g/mL	29 (39.7%)	45 (81.8%)	**10.55 (3.29–33.84)**	**<0.001**

The AUC for cancer-related stroke according to the presence of DWI pattern of multiple vascular territories or D-dimer levels of >1.11 μg/mL was 0.781 (95% CI, 0.715-0.838).

Kim, Bang, et al. Stroke 2010 Bang, J Clin Neurol 2011

Characteristics of Stroke

The clinical, radiological, & laboratory findings may help to identify patients with cancer-related stroke mechanisms.

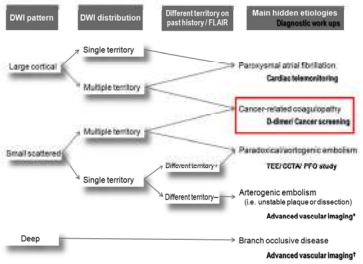
1. DWI patterns of multiple lesions involving multiple arterial territories.
2. Laboratory findings suggesting coagulopathy,
   - D-dimer level (a plasmin-derived degradation product of cross-linked fibrin)

D-dimer levels	Vascular territory involved	
	Multiple	Single
>1.11 (μg/ml)	Conventional 9.8% Cryptogenic **56.4%**	Conventional 3.9% Cryptogenic **25.5%**
≤1.11	Conventional 15.7% Cryptogenic 10.9%	Conventional **70.6%** Cryptogenic 7.3%

Kim, Bang, et al. Stroke 2010

Characteristics of Stroke

Evaluation of cryptogenic stroke



Bang, et al. Stroke 2014.

- Among subjects with cryptogenic stroke and no cancer at the time of stroke
  - 22 patients with D-dimer over the cut-off values.
  - 10 patients had multiple lesions in multiple vascular territories on DWI
- We underwent workup for hidden malignancy during hospitalization, and occult cancer was ultimately found in all the patients.

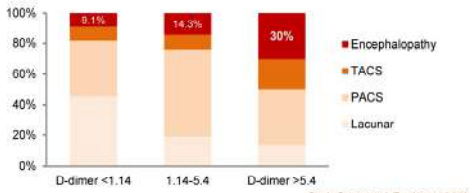
No.	Sex	Age	D-dimer levels (μg/mL)	DWI pattern (territory)	Occult cancer	Primary cancer type	Systemic metastasis	Adeno-carcinoma
1	F	65	2.43	Single	-			
2	M	69	2.51	Single	-			
3	M	70	2.58	Single	-			
4	M	50	2.63	Single	-			
5	M	68	2.87	Single	-			
6	F	76	2.97	Single	-			
7	M	72	3.09	Single	-			
8	F	78	3.09	Single	-			
9	F	79	3.11	Single	-			
10	F	65	3.24	Multiple	Yes	Lung	No	Yes
11	M	76	3.61	Single	-			
12	F	48	4.83	Multiple	Yes	Lung	No	Yes
13	F	72	7.33	Single	-			
14	F	90	8.21	Multiple	Yes	G-I	Yes	No
15	F	71	10.48	Multiple	Yes	Lung	No	No
16	F	68	13.40	Multiple	Yes	G-I	Yes	No
17	F	69	15.88	Multiple	Yes	Lung	Yes	Yes
18	M	71	16.41	Multiple	Yes	G-I	Yes	Yes
19	F	68	17.89	Single	-			
20	M	75	25.20	Multiple	Yes	G-I	Yes	Yes
21	M	61	60.00	Multiple	Yes	G-I	Yes	Yes
22	F	61	66.89	Multiple	Yes	Hepatobiliary	Yes	Yes

Kim, Bang, et al. PLoS ONE 2012

Characteristics of Stroke

- Early identification of stroke in cancer patients – Very rare
  Mostly out of therapeutic time window (even several days)

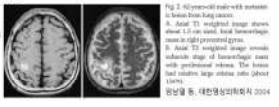
← Stepwise or progressive deficits rather than abrupt onset.
← Reasons for consultation : encephalopathy > focal deficits.



Seok, Bang, et al. Eur Neurol 2012

Stroke mimic conditions

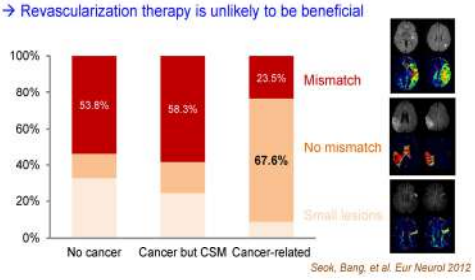
- Metastasis로 오인되기도
  - 이는 atypical presentation을 보여 stroke을 의심하지 않고 post-stroke parenchymal enhancement를 보이는 것을 metastasis로 오인하는 경우
  - 암환자에서는 가급적 official reading을 받도록
    - In Johns Hopkins hospital, 11 (4.9%) of 224 patients discharged with a diagnosis of brain tumor were initially thought to have had a stroke. *[J Neuro-oncol 1999]*
- DDx point
  - Sx: focal Sx with step-wise progression > seizure or headache
  - Ring enhancement vs. petechial hemorrhage and enhancement in stroke
  - Brain swelling by vasogenic edema:
    - edema > hemorrhage in size
    - spared gray-white matter margin
  - MR spectroscopy for NAA, lactate peak



Characteristics of Stroke

- Patients with cancer-related stroke were more likely to have no mismatch pattern (p=0.015)

→ Revascularization therapy is unlikely to be beneficial



Seok, Bang, et al. Eur Neurol 2012

암환자에서의 stroke work ups

Work ups for stroke mechanisms
Work ups for coagulopathy

Suk 등. Coagulopathy and embolic signal in cancer patients with ischemic stroke. *Ann Neurol* 2010
Kim 등. Clues to occult cancer in patients with ischemic stroke. *PLoS ONE* 2012
Kim 등. Tissue factor-bearing microparticle in cancer patients with acute ischemic stroke.
Bang 등. Cancer cell-derived extracellular vesicles are associated with coagulopathy causing ischemic stroke via tissue factor-independent pathway. *PLoS ONE* 2016

Work ups for stroke in cancer patients

- MRI
  - Diffusion (& perfusion if applicable) MRI
  - Enhanced MRI to r/o metastasis (get official reading)
  - MRA
- Cardiac work ups
  - TTE
  - TEE (often contraindicated)

TEE for rule out NBTE를 고려할 수도 있으나, 암환자에 검사를 시행하는데 있어서 어려움이 있으며 (bleeding prone by coagulopathy, poor condition), 또한 NBTE 역시 coagulopathy의 일종으로 치료가 동일해 굳이 감별해야 하는지에 대해 회의적이다.

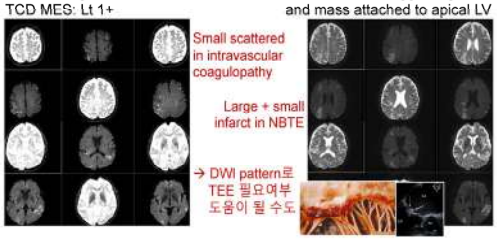
- Laboratory test for coagulopathy
  - **TCD microembolic signal detection**
  - **D-dimer monitoring**

Locally-advanced bladder TCC

s/p RCx/IC (2014-7-9), pT3aN2Mx
metastasis to Lt thigh and liver
s/p RT 55 Gy (2015-12-21 ~ 2016-1-26)

1st stroke (2016-9-11)
N/E: Anomic aphasia
Auditory/tactile extinction
Rt. VFD
TEE: no vegetation
TCD MES: Lt 1+

2nd stroke (2016-9-17)
N/E: Sensory aphasia
Gerstmann syndrome
TTE: irregular-shaped mass like lesions at AoV suggesting NBTE and mass attached to apical LV



Small scattered in intravascular coagulopathy

Large + small infarct in NBTE

→ DWI pattern로 TEE 필요여부 도움이 될 수도

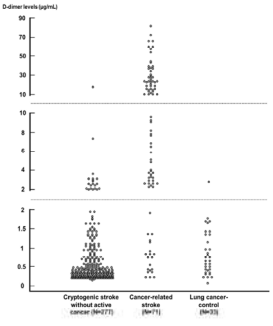
Mechanisms underlying stroke in cancer patients

Cancer-unrelated	Conventional stroke mechanisms Atherosclerosis, cardioembolic, lacunar, etc.
Cancer-related	Coagulopathy : m/c (adenocarcinoma) Intravascular coagulation non-bacterial thrombotic endocarditis (NBTE) Cerebral venous thrombosis, paradoxical embolism by Tumor cell (esp. adenocarcinoma)-derived cytokines or microparticles Tissue factor and cancer procoagulants Cytokines such as TNF-α, interleukins Tumor occlusion : rare Tumor embolism (lung or cardiac [i.e. myxoma]) Intravascular lymphoma (B-cell lymphoma), hyperviscosity (leukemia) Direct tumor-related : rare (metastasis or CNS tumor) Vessel compression or infiltration
Treatment-related	Chemotherapy causing coagulopathy (leukemia, breast cancer, etc) such as cisplatin, methotrexate, l-asparaginase, bevacizumab Radiation or surgery causing vascular stenosis (head & neck cancer, lymphoma) Medical comorbidities, such as fungal infection or infective endocarditis

Ischemic stroke and hematologic malignancy

Mechanism	Pathology	Clinical setting
1. Coagulopathy		
NBTE	Cardiac valvular lesions Arterial thrombosis with infarct	Adenocarcinoma (esp. mucin-producing lung/GI-), lymphoma
DIC	Arterial thrombosis with infarct	Leukemia, breast cancer
Unknown	SSS thrombosis	Leukemia, lymphoma, solid tumor
2. Direct tumor-related		
Skull or dural metastasis	SSS compression or infiltration	Lung or breast cancer, neuroblastoma, lymphoma
Leptomeningeal metastasis	Arterial thrombosis or spasm	Glioma, solid tumor
Parasellar tumor	Arterial thrombosis or invasion	Meningioma
3. Tumor-occlusion		
Intravascular lymphoma	Obstruction of arterial vessels	Lymphoma (Large B-cell > T-cell)
Hyperviscity	Obstruction of arterial vessels	Leukemia
Tumor embolism	Embolic infarct	Lung or cardiac tumor
4. Treatment-related		
Chemotherapy (Cisplatin, MTX, L-asparaginase)	SSS thrombosis Arterial thrombosis with infarct	Leukemia, breast cancer
Radiation-induced	ICA stenosis or thrombosis	Head & neck cancer, lymphoma
Carotid blow-out SD	Carotid ligation with infarct	Head & neck cancer after treatment
5. Infection		
Fungal sepsis	Embolic infarct, Vasculitis	Leukemia, BM transplant

D-dimer level was significantly higher in patients with Cancer-related-stroke than those without canceror Cancer without stroke (both $p<0.001$).



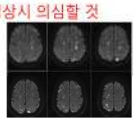
D-dimers are generated when the endogenous fibrinolytic system degrades fibrin, and related to hypercoagulabilty.

D-dimer level is a direct measure of activated coagulation.

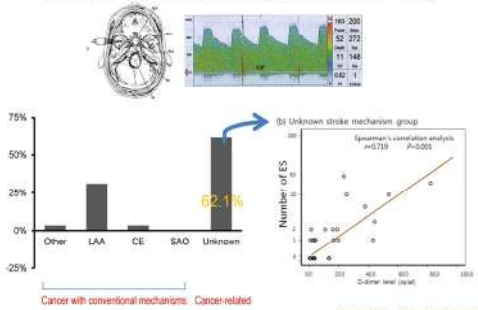
Kim, Bang, et al. PLoS ONE 2012

Hypereosinophilia SD

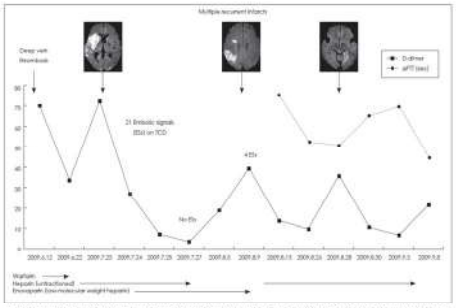
- Leukoproliferative disorder originally described in 1975
- 3 defining features
  1. blood eosinophilia of ≥1500/μL present for more than six months
  2. no other apparent etiologies for eosinophilia, such as parasitic infection or allergic disease
  3. signs and/or symptoms of eosinophil-mediated end-organ dysfunction
- Cancer-related coagulopathy 의심되는데 D-dimer 정상시 의심할 것
- Work ups
  - Bone marrow
  - PDGFRA, PDGFRB, FGFR
  - JAK2 (to exclude Myeloproliferative neoplasm)
  - Chromosome study (DDX. Acute eosinophilic leukemia, CML..)



TCD microembolic signals were detected in cancer-related stroke patients than those with other mechanisms and were associated with a higher D-dimer level or multiple number of lesions on DWI (both $p<0.001$).



Seok, Bang, et al. Ann Neurol 2010



A typical example case showing fluctuating levels of embolic signals and D-dimer that were directly related to the anticoagulation. A 59-year-old woman was diagnosed with bile-duct adenocarcinoma with metastasis and received chemotherapy. She had started anticoagulation for DVT, but stopped due to hemorrhoid bleeding. After that, she developed right hemiplegia. DWI revealed multiple infarcts involving multiple territory, suggesting emboli. TCD revealed embolic signals. During hospitalization, recurrent infarcts with clinical deterioration occurred twice while her D-dimer levels were ≥15 μg/dL. D-dimer levels (red line) were inversely correlated with prothrombin time (aPTT; green line).

Seok, Bang, et al. Ann Neurol 2010

D-dimer

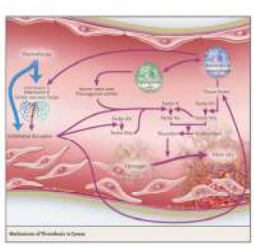
- D-dimers are generated when the endogenous fibrinolytic system degrades fibrin, and related to hypercoagulabilty.

  J of Thromb & Haemost 2006;4:1253-1258
- D-dimer level is a direct measure of activated coagulation and is used in many previous studies as a measure of hypercoagulabilty.
  - PE, DVT, and DIC
- Treatment of cancer, cancer itself, and stroke itself cause the elevated D-dimer levels.
  - In several large series of patients with cancer, an elevated D-dimer can be identified in 30.5 to 90% depending on whether metastatic disease was present or not.
- **Therefore, It can be difficult to attribute a stroke definitively to hypercoagulability based on D-dimer alone.**

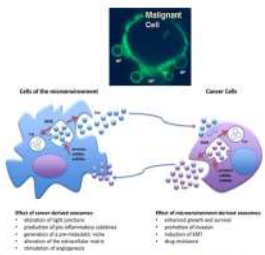
Neurology 2004;62:2025-2030
Semin Thromb Hemost. 1999;25:167-172

D-dimer is a non-specific marker and It can be difficult to attribute a stroke definitively to hypercoagulability based on D-dimer alone.

Cancer cells secrete extracellular vesicles (EVs) as well as soluble factors associated with coagulopathy

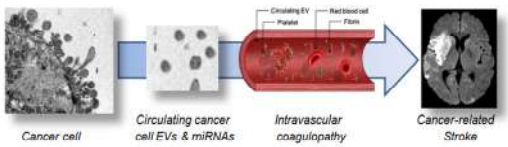


Bick RL, N Engl J Med 2003;349:109-11



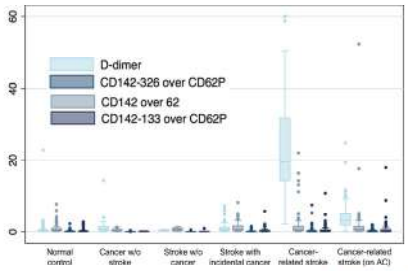
Neviani & Fabbri, Front. Med. 2015

Cancer Cell-derived EVs are associated with Coagulopathy causing Ischemic Stroke via Tissue Factor-independent way



Cancer cell-derived EV levels could add information to D-dimer

D-dimer levels are nonspecific and may change with therapy



Bang, et al. PLoS ONE, 2016

암환자에서의 acute and preventive treatment strategies

Treatment should focus on correction of the coagulopathy rather than revascularization therapy.

Suk 등. Clinical presentation and ischemic zone on MRI in cancer patients with acute ischemic stroke. *Eur Neurol, 2012*

Lee 등. Clinical presentation and ischemic zone on MRI in cancer patients with acute ischemic stroke. *Eur Neurol, 2012*

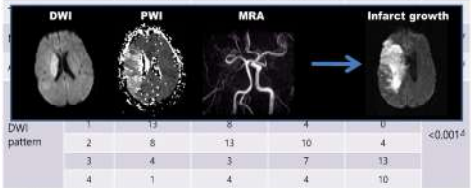
Jang 등. Comparison of enoxaparin and warfarin for secondary prevention of cancer-associated stroke. *J Oncol 2015*

Acute Treatment

- The use of thrombolytics within the therapeutic time window is not contraindicated in cancer patients under the current guidelines for acute stroke therapy.
- However, the response to thrombolysis may differ between stroke patients with and without cancer.
  1. Patients with the target mismatch profile ↓
  2. Outside therapeutic time window (progressive > sudden onset) ↑
  3. Life expectation ↓
- Strategies for stroke treatment in cancer patients should focus on correction of the coagulopathy rather than recanalization.

MRI and TCD

	D-dimer Quartile (Coagulopathy)				*P*
	Q1	Q2	Q3	Q4	
MRA-DWI mismatch	10 (66.7%)	13 (61.9%)	7 (31.8%)	6 (23.1%)	0.001[a,b]
PWI-DWI mismatch	8 (61.5%)	11 (64.7%)	11 (55.0%)	7 (30.4%)	0.035[a,b]
DWI pattern	1	13	8	4	0	<0.001[c]
	2	8	13	10	4	
	3	4	3	7	13	
	4	1	4	4	10	



[a] Pearson Chi-Square test
[b] Linear-by-linear association test
[c] Fisher's Exact test
[d] Small artery disease or posterior circulation infarction patients were excluded

Acute Treatment

- Current standard for treatment for VTE in cancer patients
  - Long-term low molecular weight heparin (LMWH)
  - Non-vitamin K antagonists (NOACs)
- For cancer-related stroke – No established standard
  - UF-heparin
  - Fondaparinux (**Arixtra™**)
  - LMWH
    - Enoxaparin (1mg/kg sc. q12h)
    - Dalteparin (200 unit/kg sc. qd)

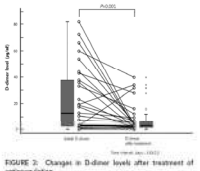
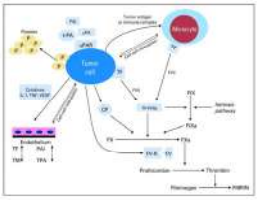


FIGURE 2: Changes in D-dimer levels after treatment of anticoagulation.

NCCN guideline 2013

Chronic Management

- Duration of anticoagulation
  - Minimum 3 months
  - Indefinite anticoagulation, if active cancer or persistent risk factor
- LMWH is preferred over warfarin
  - NOACs (in case with DVT)
  - Warfarin has limitations
    1. Direct stimulation of cancer procoagulant to Factor X
    2. INR prolongation in advanced cancer
    3. Drug interaction with chemoagent
    4. Inability to monitor INR in advanced cancer
    5. High GI bleeding risk

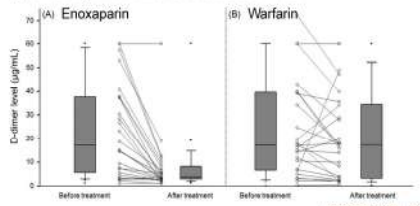


Kuderer NM, J Clin Oncol 2009

LMWH vs. Warfarin

- Data of 79 patients with cryptogenic stroke with active cancer
- Blood samples for measuring the initial and follow-up D-dimer levels were collected at admission and a median of 8 days after admission, respectively.

Figure. Changes in D-dimer levels after treatment:



Jang, Bang, Kim. J Onocol 2015

LMWH vs. Warfarin

- Data of 79 patients with cryptogenic stroke with active cancer
- During the mean follow-up period of 4.9 months, recurrent strokes were noted in only 1 (3.4%) patient treated with enoxaparin and in 8 (16.0%) patients treated with warfarin.
- Time to recurrence was usually within 2 months of the initial event, and most patients had D-dimer levels that were >10μg/mL and an INR >2.0.

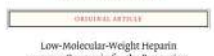
Multiple regression analysis: Independent predictors of D-dimer ≥10 μg/mL.

	Estimated OR (95% CI)		*P*
	Univariable	Multivariable	
Treatment			
Enoxaparin	Reference	Reference	
Warfarin	6.72 (1.92-23.58)	12.95 (2.89-57.94)	0.001
Systemic metastasis	6.96 (0.80-60.53)	18.73 (1.69-207.48)	0.017
Adenocarcinoma	3.58 (0.86-14.87)	2.41 (0.43-13.44)	0.314

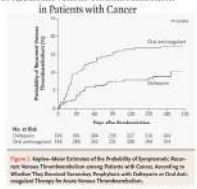
Jang, Bang, Kim. J Onocol 2015

2013 American Society of Clinical Oncology Clinical Practice Guideline Updates

For long term anticoagulation, LMWH for at least 6 months is preferred because of improved efficacy over VKAs. VKAs are an acceptable alternative for long-term therapy if LMWH is not available.


ORIGINAL ARTICLE

Low-Molecular-Weight Heparin versus a Coumarin for the Prevention of Recurrent Venous Thromboembolism in Patients with Cancer



NEJM 2003;349:146-153

Nadroparin for the prevention of thromboembolic events in ambulatory patients with metastatic or locally advanced solid cancer receiving chemotherapy: a randomised, placebo-controlled, double-blind study

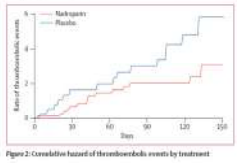


Figure 2: Cumulative hazard of thromboembolic events by treatment

Lancet Oncol 2009; 10: 943–9

Efficacy and Safety of Anticoagulant Therapy for the Treatment of Acute Cancer-Associated Thrombosis: A Systematic Review and Meta-Analysis

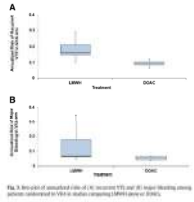
LMWH should be used for the treatment of acute cancer-associated thrombosis.

Our results are consistent with the current recommendations favoring the use of LMWH monotherapy for the treatment of cancer-related thrombosis

NOACs can't be recommended until trials comparing NOAC vs. LMWH are conducted

Therefore, the available data show that NOACs hold promise in the treatment of cancer-associated thrombosis but are underpowered for demonstrating superiority or non-inferiority against VKA, a regimen known to be inferior to LMWH.

Considering that cancer patients enrolled in the NOAC studies have a lower risk of recurrent VTE and major bleeding than those in LMWH trials. they were selected to be more like non-cancer patients in the DOAC studies



M. Carrier et al. / Thrombosis Research 134 (2014) 1214–1219

NOAC use

- NOAC use to prevent recurrent venous thromboembolism

Cancer patients in EINSTEIN-DVT/PE

Lancet Haematol. 2014;1:e37–46

Limited evidences from RCTs of NOAC in cancer patients

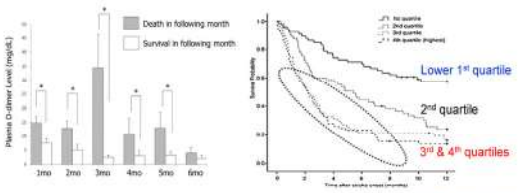
- In phase III trials, all 4 NOACs were noninferior and probably safer than conventional therapy (LMWH followed by warfarin).
- A proportion ranging between 2.5% and 9.4% of patients included in the Phase III trials with NOACs had cancer

JACC 2016;67:1941-55

Importance of effective correction of hypercoagulability in survival

Successful correction of hypercoagulability was protective for 1-year survival in anticoagulated patients in the 3-4th quartiles of pretreatment D-dimer levels (adjusted HR 0.26, 95% CI 0.10–0.68, p=0.006).

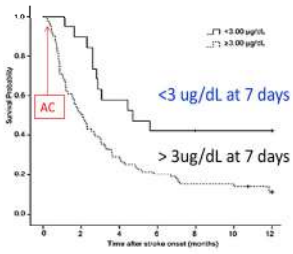
Stroke severity was not independently associated with mortality.

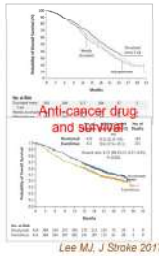


Lee MJ. J Stroke 2017

Importance of effective correction of hypercoagulability in survival

After AC, patients showing rapid improvement in coagulation level
(defined as <3 ug/dL at 7 days)
→ Better survival, especially within 1 year after stroke Dx





Lee MJ. J Stroke 2017

Conclusions and Perspectives

- Stroke with cancer-specific mechanisms occurred in large number in cryptogenic stroke.
  - With the increase in the number of people living with cancer, this type of stroke could become one of the prevalent stroke subtypes in the future.
- The characteristics of cancer-related stroke are very distinct from those of conventional stroke.
  - Embolism caused by cancer-related coagulopathy is the main mechanism underlying cancer-related stroke.
  - The characteristics of cancer-related stroke are very distinct from those of conventional stroke.
  - Laboratory findings (especially, D-dimer and TCD microembolism) and DWI lesion patterns were helpful in the differentiation of stroke mechanisms and also valuable in monitoring the effects of treatment in cancer patients.

- Anticoagulant use may be helpful particularly in patients where coagulation abnormality is the principle mechanism of stroke
  - Considering the characteristics of the presenting symptoms (i.e., encephalopathy), the ischemic zone assessed by MRI (i.e., relative lack of ischemic penumbrae), and a higher rate of recurrent embolism, treatment should focus on correction of the coagulopathy rather than revascularization therapy.
  - Longitudinal follow up data are needed to identify proper anticoagulants in those patients
  - Like DVT, further studies are needed for the standard of care for treatment of stroke and specific biomarkers for coagulopathy
- Although many new beginnings have been made in the field of cancer-associated thrombosis in the past decade, much learning awaits.