



# The Role of MDCT in Detection of Vasospastic Angina

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# Introduction

- Classical angina
  - Attack is **induced by exertion** and relieved by rest or NTG administration, and is associated with transient **ST depression**.
  - Pathogenesis: increased myocardial oxygen demand in the presence of fixed organic stenosis of epicardial coronary arteries.
- In 1959, Prinzmetal et al. described a new form of angina pectoris "**variant** form of angina pectoris"
  - The attack **occurred at rest** (not induced by exertion), and is associated with **ST elevation**.
- **Spasm** of epicardial coronary artery was documented angiographically in early 1970s,
  - **coronary spasm** was established as the cause of variant angina.

# Definition of coronary spasm

- **Reversible focal constriction** of a segment or segments of coronary artery such as to **cause restriction of coronary blood flow** and myocardial ischemia
- It may read to not only angina pectoris, but **also various ischemic disease**, including acute myocardial infarction and sudden cardiac death
  - Thus, **variant angina** is only one aspect or wide spectrum of myocardial ischemic syndrome caused by coronary spasm
- Now called as "**vasospastic angina**"  
(variant angina ≠ vasospastic angina)

# Pathogenesis of coronary spasm

- **Endothelial cell dysfunction**
  - Spasm induced by **endothelium-dependent vasodilators** (Ach, ergonovine, serotonin, histamine..), and released by endothelium-independent vasodilator (nitrate).
  - Polymorphisms of eNOS gene
- Hypercontractility of coronary smooth muscle
- **Circadian variation**
  - Spasm occurs at from **midnight to early morning**;  
increased vagal tone, hyper-reactivity to sympathetic stimulation
- Chronic low-grade inflammation
  - Smoking, Alcohol, metabolic abnormalities.

# Epidemiology of coronary spasm

- **15~40%** in patients who complained of chest pain
- **Men** > female
- 40~70 years of age (post-menopausal women)
  
- Frequency has become less frequent:
  - Use of CCBs (HTN, ischemic heart disease) or other medications (aspirin, statin, ACEi..),
  - Decreased smokers.

# Diagnosis of coronary spasm

- **Not necessarily easy;**
  - Not induced by exercise, occurs at rest from midnight to early morning.
  - Attack is transient and unpredictable.
- Noninvasive Diagnosis
  - Standard 12-lead ECG during attack, Holter monitoring, Exercise testing, Hyperventilation testing..
  - **Less sensitive** than pharmacological test
    - Waters et al. [Circulation 1983;67:310-5]

TABLE 2. Comparison of ECG Changes During Ergonovine, Cold Pressor and Exercise Tests

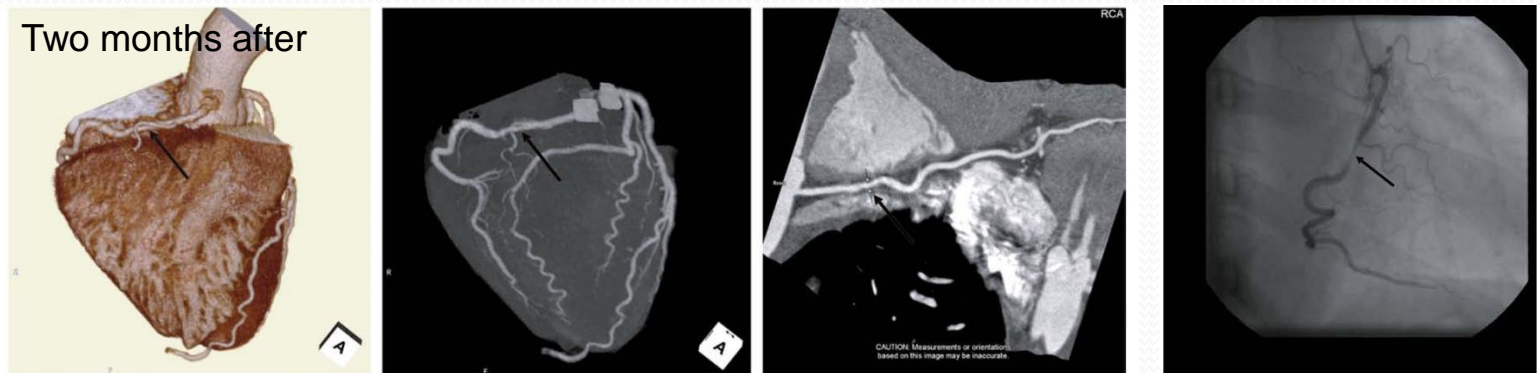
	Ergonovine test	Cold pressor test	Exercise test
ST elevation	32 (94%)	3 (9%)	10 (29%)
Pseudonormalization of T waves	0	2	4*
ST depression	1	0	9†
No ECG changes	1	29	11
Total	34	34	34

# Spasm provoking test

- **Ach**(acetylcholine) and **Ergonovine** tests are most often used
  - Positive response: transient occlusion (>90%) of coronary artery with signs and symptoms of myocardial ischemia (angina/ST changes)
- Usually safe, however a number of **complications** may occur
  - With invasive coronary angiography, use pharmacologic agent
    - Hypertension, hypotension, abdominal cramps, nausea, vomiting, other nonspecific complications
    - **Potential risk** of severe myocardial ischemia or ventricular fibrillation

# Coronary CT angiography

- Coronary CT angiography (CCTA) using MDCT has been widely used as noninvasive imaging technique for evaluation of coronary artery disease.
- There are a **few cases** with spontaneous coronary artery spasm which occasionally detected by CCTA.
  - **Ota et al.** [Int J Cardiol. 2011]  
41-year-old male without overt risk factors (non-smoker) suddenly complained of severe chest pain.





# Coronary CT angiography

- The most published papers about coronary spasm in CCTA were case reports, and only **two original articles** published.
  - Ito et al. In vivo assessment of Ergonovine-induced Coronary artery spasm by 64-slice multislice computed tomography. *Circ Cardiovascu Imaging* 2012;5:226-232
  - Kang et al. Coronary vasospastic angina: assessment by multidetector CT coronary angiography. *KJR* 2012;13:27-33
- ➔ Retrospectively reviewed the characteristics of spasm site (matched with provoking site) on CCTA.

# In Vivo Assessment of Ergonovine-Induced Coronary Artery Spasm by 64-Slice Multislice Computed Tomography

Tsuyoshi Ito, MD; Mitsuyasu Terashima, MD; Hideaki Kaneda, MD; Kenya Nasu, MD; Mariko Ehara, MD; Yoshihisa Kinoshita, MD; Tatsuya Ito, MD; Masashi Kimura, MD; Nobuyoshi Tanaka, MD; Maoto Habara, MD; Etsuo Tsuchikane, MD; Takahiko Suzuki, MD

- Retrospectively reviewed a total of **296 plaques in 199 patients**
  - with clinically suspected coronary spastic angina **without significant stenosis** (>75%) who underwent both ergonovine provocative testing and MDCT.
- Spasm provoked (+): **46 sites in 43 patients (22%)**
  - CCTA: **All 46 sites had a coronary plaque**
  - **No coronary spasm occurred at the normal coronary segment in CCTA.**

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**Table 3. Comparison of CT Findings Between Spasm and Nonspasm Groups**

	Spasm Group	Nonspasm Group	<i>P</i> *
No. lesions	46	250	
Calcification			<0.01
Noncalcified	44 (96)	47 (19)	
Spotty calcification	2 (4)	120 (48)	
Large calcification	0 (0)	83 (33)	
Attenuation			<0.01
Low	3 (7)	54 (22)	
Intermediate	43 (93)	70 (28)	
High	0 (0)	126 (50)	
Remodeling			<0.01
Positive	3 (7)	96 (38)	
Intermediate	12 (26)	126 (50)	
Negative	31 (67)	28 (11)	

Data are presented as n (%), unless otherwise indicated.

- **Noncalcified** plaque,
- **Intermediate** attenuation (53.8~130HU) plaque ,
- with **negative remodeling** is more frequent in spasm group.

# Coronary Vasospastic Angina: Assessment by Multidetector CT Coronary Angiography

Koung Mi Kang, MD<sup>1</sup>, Sang Il Choi, MD<sup>1</sup>, Eun Ju Chun, MD<sup>1</sup>, Jeong A Kim, MD<sup>1</sup>, Tae-Jin Youn, MD<sup>2</sup>, Dong Ju Choi, MD<sup>2</sup>

<sup>1</sup>Division of Cardiovascular Imaging, Department of Radiology, <sup>2</sup>Division of Cardiology, Department of Internal Medicine, Cardiovascular Center Seoul National University Bundang Hospital, Gyeonggi-do 436-707, Korea

- Retrospectively analyzed both ergonovine test and CCTA findings of **53 patients** with clinically suspected vasospastic angina
- Spasm provoked (+): **25 patients**
  - CCTA:
    - **12 patients** : **no definite plaque with negative arterial remodeling**
    - **7 patients: normal**
    - **6 patients:** insignificant stenosis
      - 3 noncalcified plaque, 2 mixed plaque, 1 calcified plaque

# Coronary Vasospastic Angina: Assessment by Multidetector CT Coronary Angiography

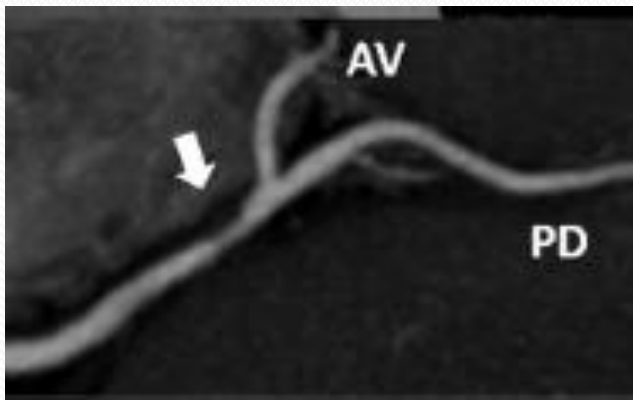
Koung Mi Kang, MD<sup>1</sup>, Sang Il Choi, MD<sup>1</sup>, Eun Ju Chun, MD<sup>1</sup>, Jeong A Kim, MD<sup>1</sup>, Tae-Jin Youn, MD<sup>2</sup>, Dong Ju Choi, MD<sup>2</sup>

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- **Significant stenosis with negative remodeling, but no definite plaque**: characteristic finding on CCTA.(12 patients/25 patients)
  - Sensitivity 48%, specificity 100%, PPV 100%, NPV 68%.
- Limitation
  - High specificity with relatively **low sensitivity** for diagnosis of vasospastic angina.

# Coronary CT angiography

- Limitation or bias factors of CCTA:
  - **Low sensitivity**
    - Coronary spasm is usually occurs in the early morning (rarely during the day time)
    - Routinely use of sublingual vasodilator during CCTA
  - **Spatial and temporal resolution**
    - **Spasm vs True stenosis with invisible (fatty) plaque.**



*Circ Cardiovasc Imaging. 2012;5:226-232*

**“ Non calcified plaque  
with negative remodeling”**



*KJR 2012:13:27-33*

**“ No definite plaque  
with negative remodeling”**

# Coronary CT angiography

- We speculate that ..
  - **Sensitivity** ↑
    - Acquisition of **CCTA in the early morning** may increase the sensitivity of spasm detection.
    - Acquisition of **CCTA without vasodilator** may increase the sensitivity of spasm detection.
  - **Spasm vs True stenosis with invisible (fatty) plaque.**
    - Acquisition of **CCTA during a intravenous (IV) vasodilator injection** may provide fully dilated coronary artery image.





# **Double acquisition of CCTA with/without intravenous vasodilator injection for diagnosis of vasospastic angina. – Pilot study**

**Eun-Ju Kang<sup>1</sup>, Moo Hyun Kim<sup>2</sup>, Dong Hyun Lee<sup>2</sup>, Ki-Nam Lee<sup>1</sup>**

**<sup>1</sup>Department of Radiology, Dong-A University, College of Medicine, Busan, Korea**

**<sup>2</sup>Department of Cardiology, Dong-A University College of Medicine, Busan, Korea**

***ASCI 2014***



# Purpose

- The purpose of our study was to evaluate the feasibility of **double acquisition of CCTA with/without IV vasodilator injection** for diagnosis of vasospastic angina.

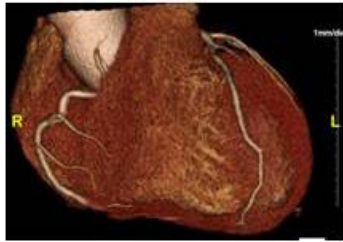
# Material and methods; Subjects

- **20 consecutive patients** with clinically highly suggestive of vasospastic angina.
  - 15 male, 5 female
  - Mean age,  $60 \pm 9$  years (range, 43–84 years)
  - Exclusion criteria were;
    - On coronary artery angiography (CAG): Significant fixed atherosclerotic stenosis ( $> 50\%$  lumen diameter)
    - On CCTA: Calcium score  $> 400$  or inadequate for analysis of coronary artery.
- The definition of vasospastic angina is based on invasive coronary angiography with positive **ergonovine provocation test**

# CCTA Scan Protocol

## \* Diagram of Scan acquisition

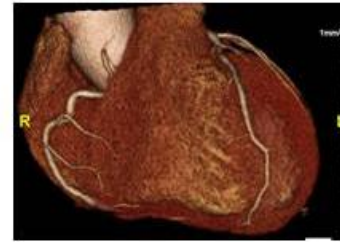
Baseline CT  
(at early morning)



Within 1~ 7 days



IV nitrate CT \*



\* IV nitrate CT protocol

Continuous injection of IV vasodilating agent (isosorbide dinitrate 2 mg/hr)



BP check per every 2 minutes



Systolic/Diastolic BP 10 mmHg ↓

CT scan start

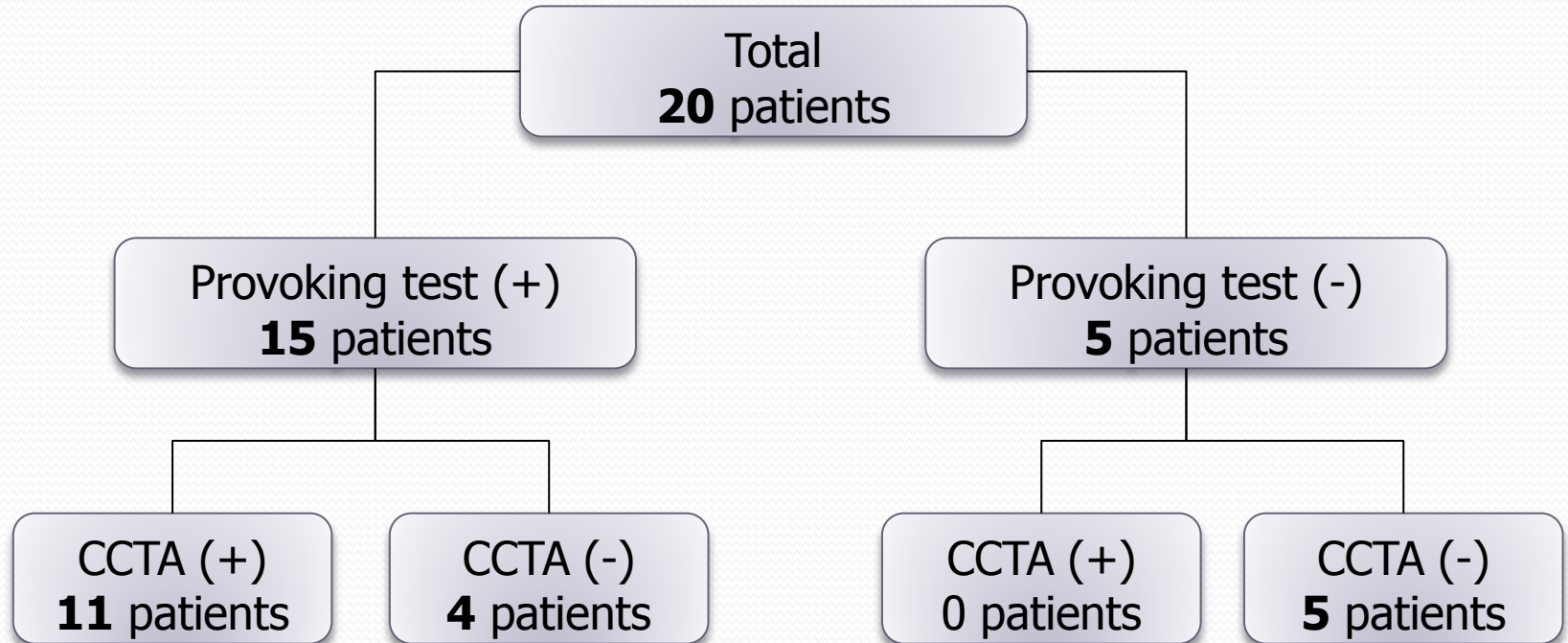
# Post processing and analysis

- We analyzed the curved MPR image and cross-sectional images of coronary arteries on **baseline CT** and **IV nitrate CT**
- We used **positive criteria** of vasospastic angina on CCTA as followings:
  - i) **Significant stenosis with negative remodeling but no definite evidence of plaques**, that **completely dilated** on IV nitrate CT,  
or
  - ii) **Diffuse small diameter (< 2 mm)** of a major coronary artery **with beaded appearance**, that **completely dilate** on IV nitrate CT.

# Statistical Analyses

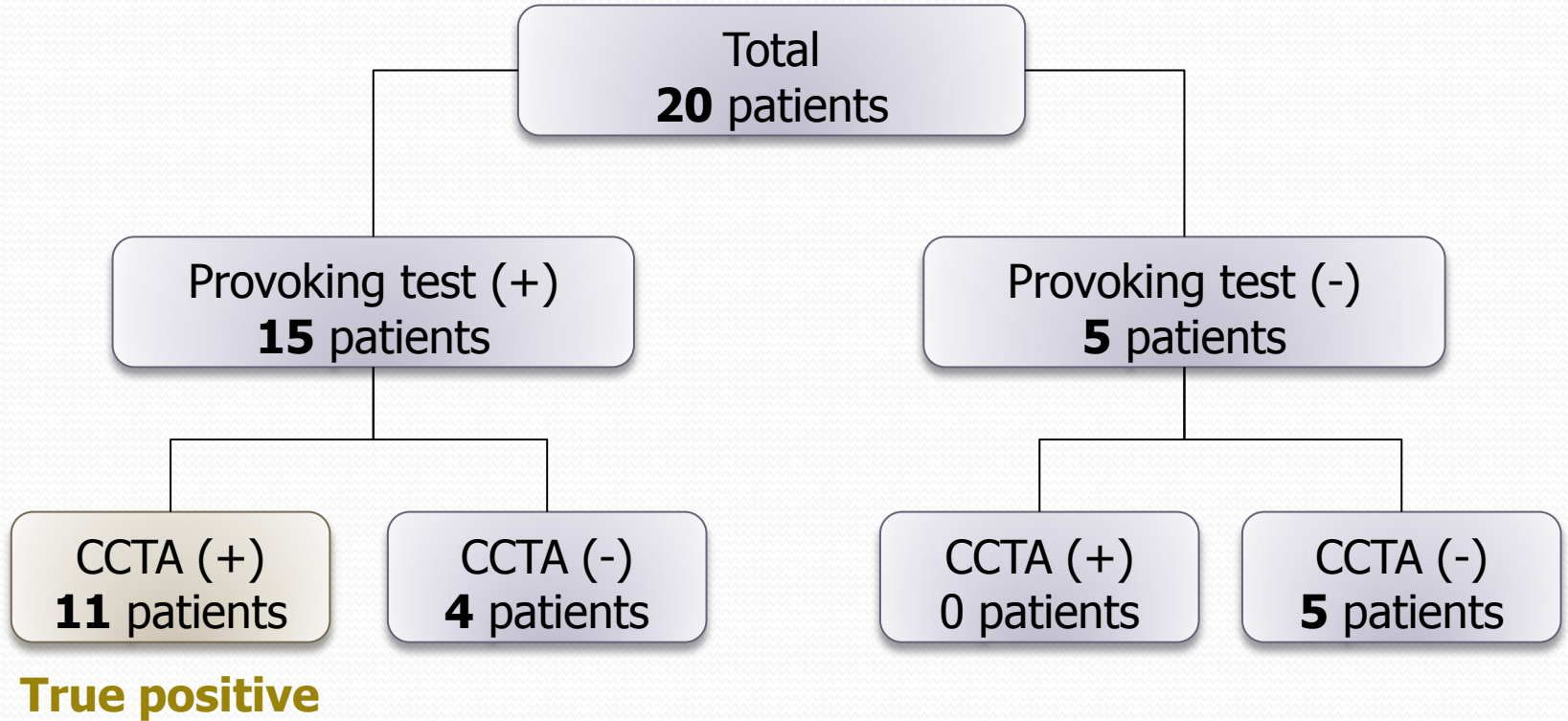
- We determined the diagnostic performance of CCTA findings of vasospastic angina using **ergonovine provocation test** with CAG as a **reference standard**.
  - Firstly, right-side CAG was performed
  - → provocation (+): nitroglycerin was subsequently injected
  - → provocation (-): left-side CAG was performed
- We evaluated the diagnostic performance of CCTA..
  - Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were evaluated.

# Results



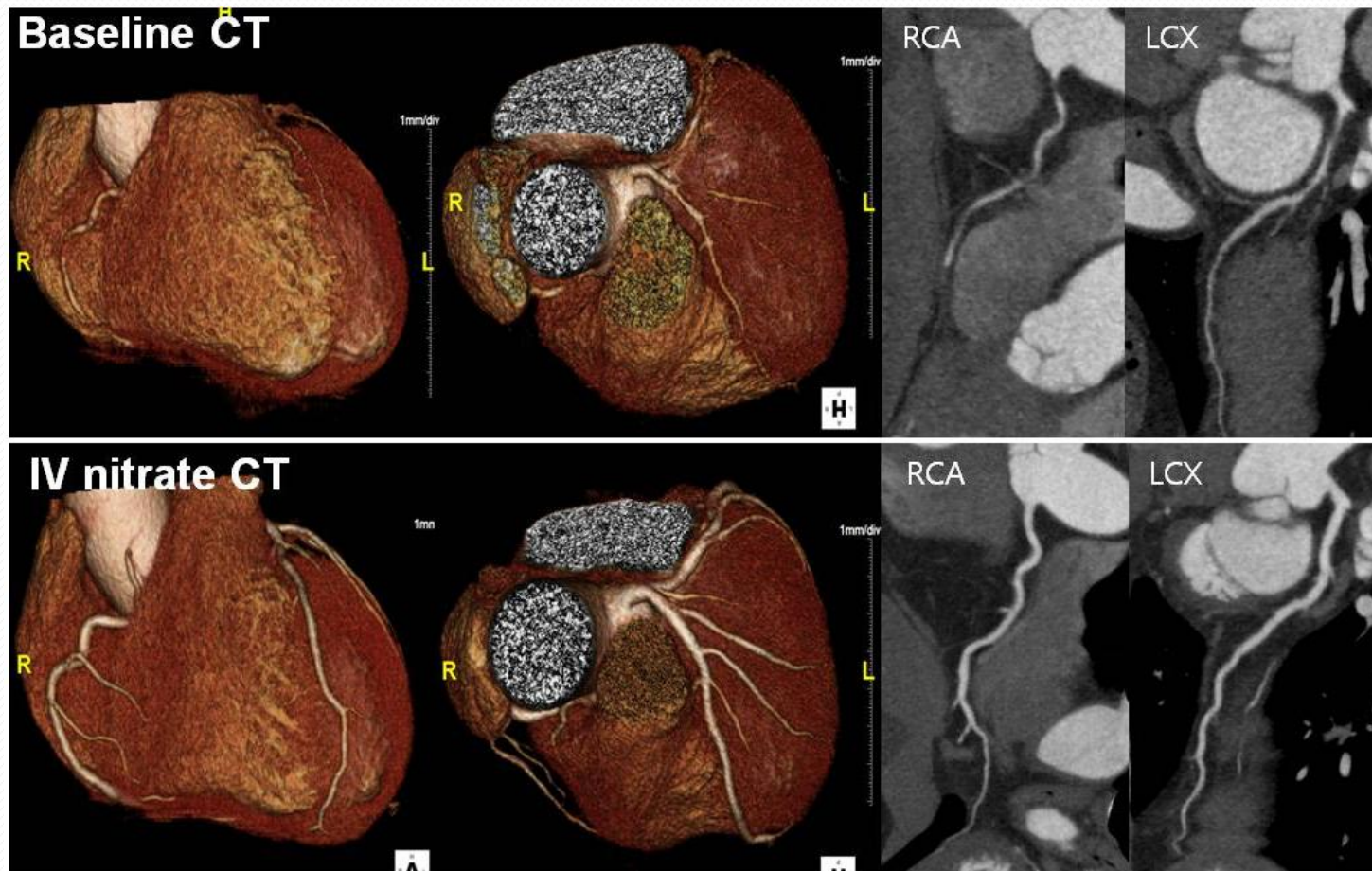
- Diagnostic performance of CCTA
  - Sensitivity 73%, specificity 100%, PPV 100%, NPV 56%

# Results





# Representative case: True positive-1



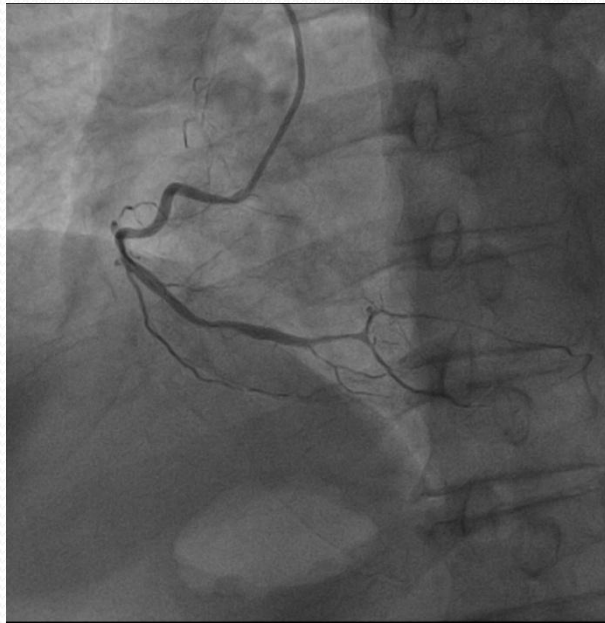
**Case 1.** A 67 year old male patient presented with intractable recurrent chest pain.



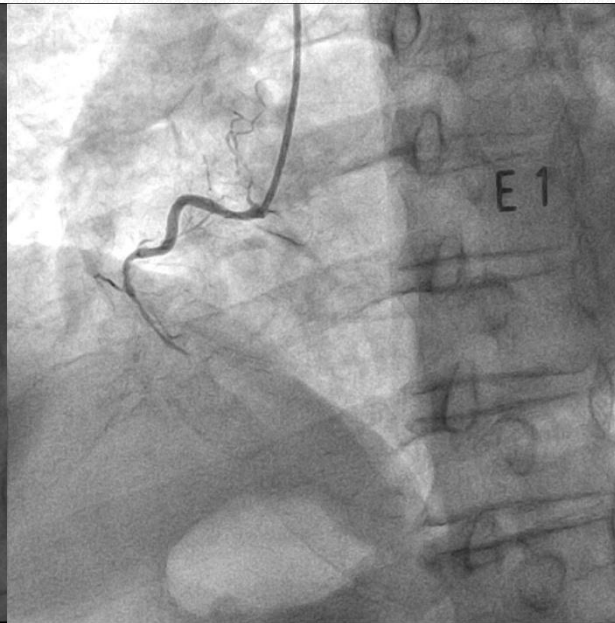
# Representative case: True positive-1

## Provoking test (+) and CCTA (+)

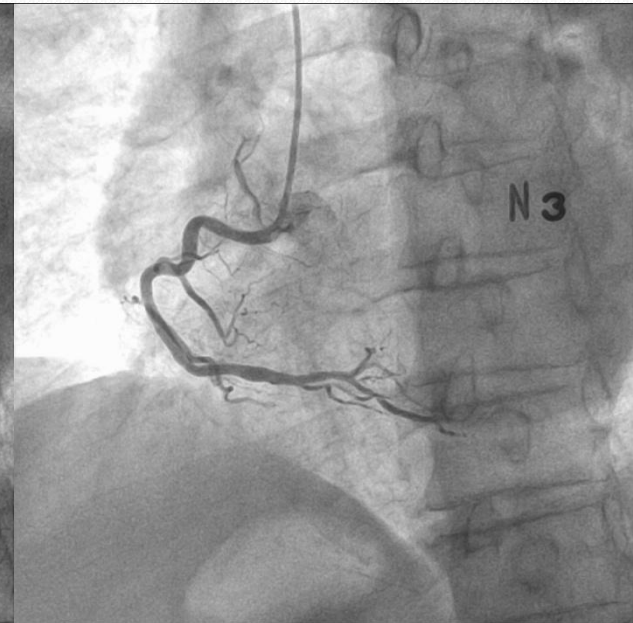
**CAG**



**Ergonovine**



**Nitrate**



**Case 1.** A 67 year old male patient presented with intractable recurrent chest pain.

# Representative case: True positive-2

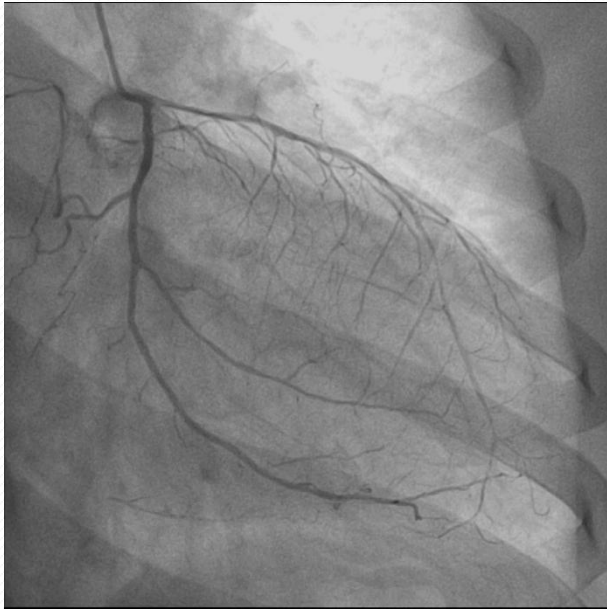


**Case 2.** A 47 year old male patient presented with chest pain.

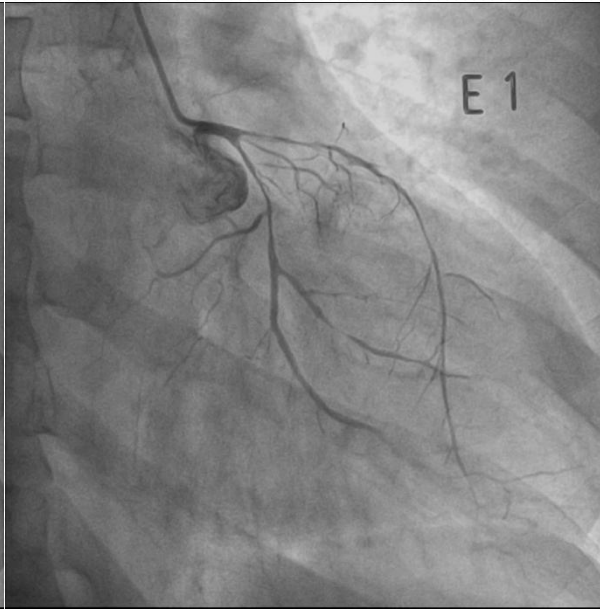
# Representative case: True positive-2

## Provoking test (+) and CCTA (+)

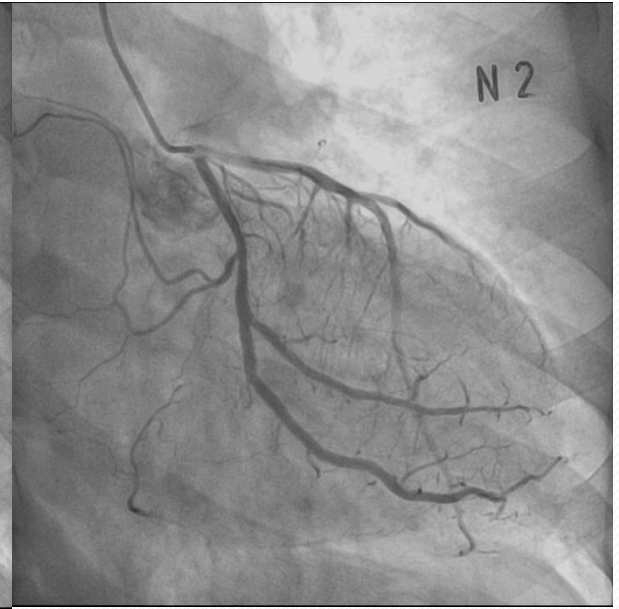
**CAG**



**Ergonovine**

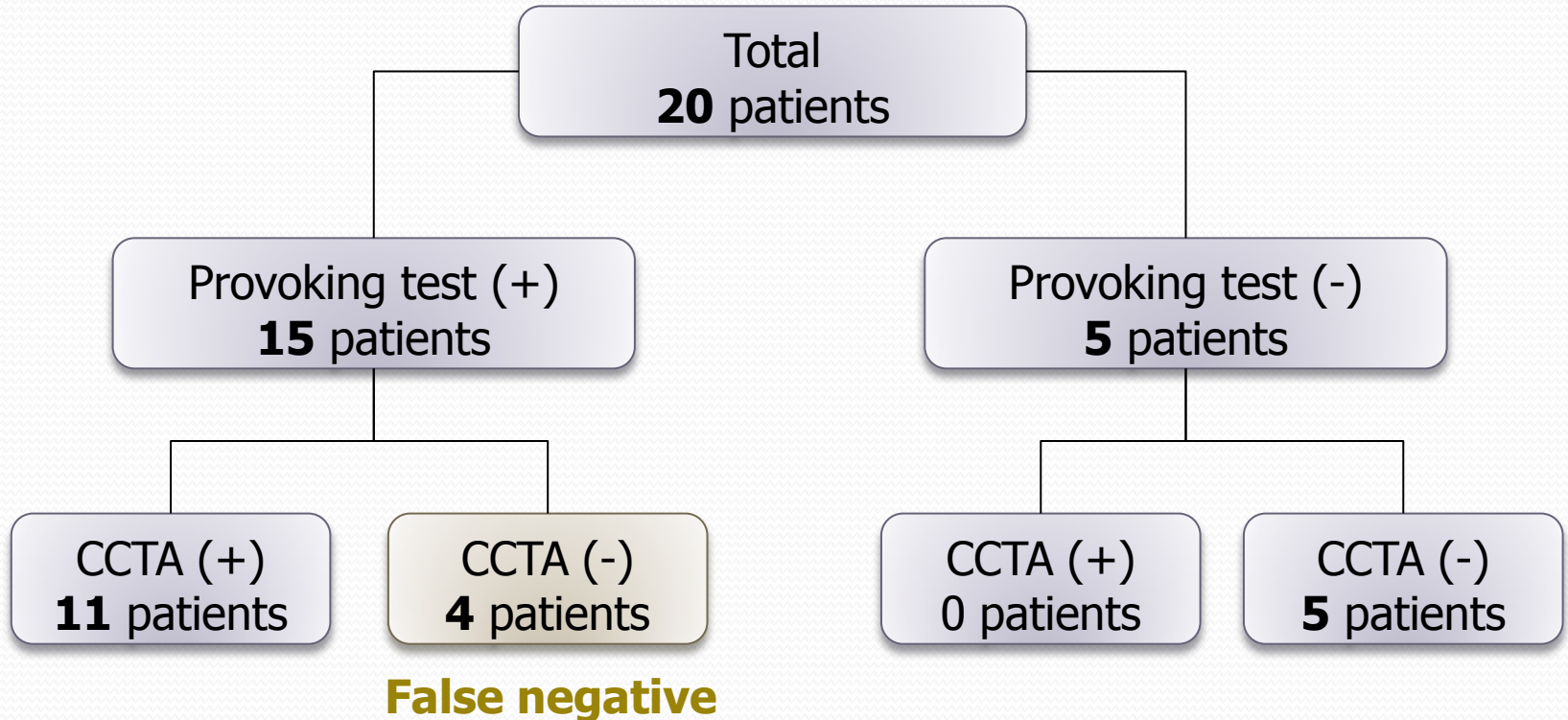


**Nitrate**



**Case 2.** A 47 year old male patient presented with chest pain.

# Results

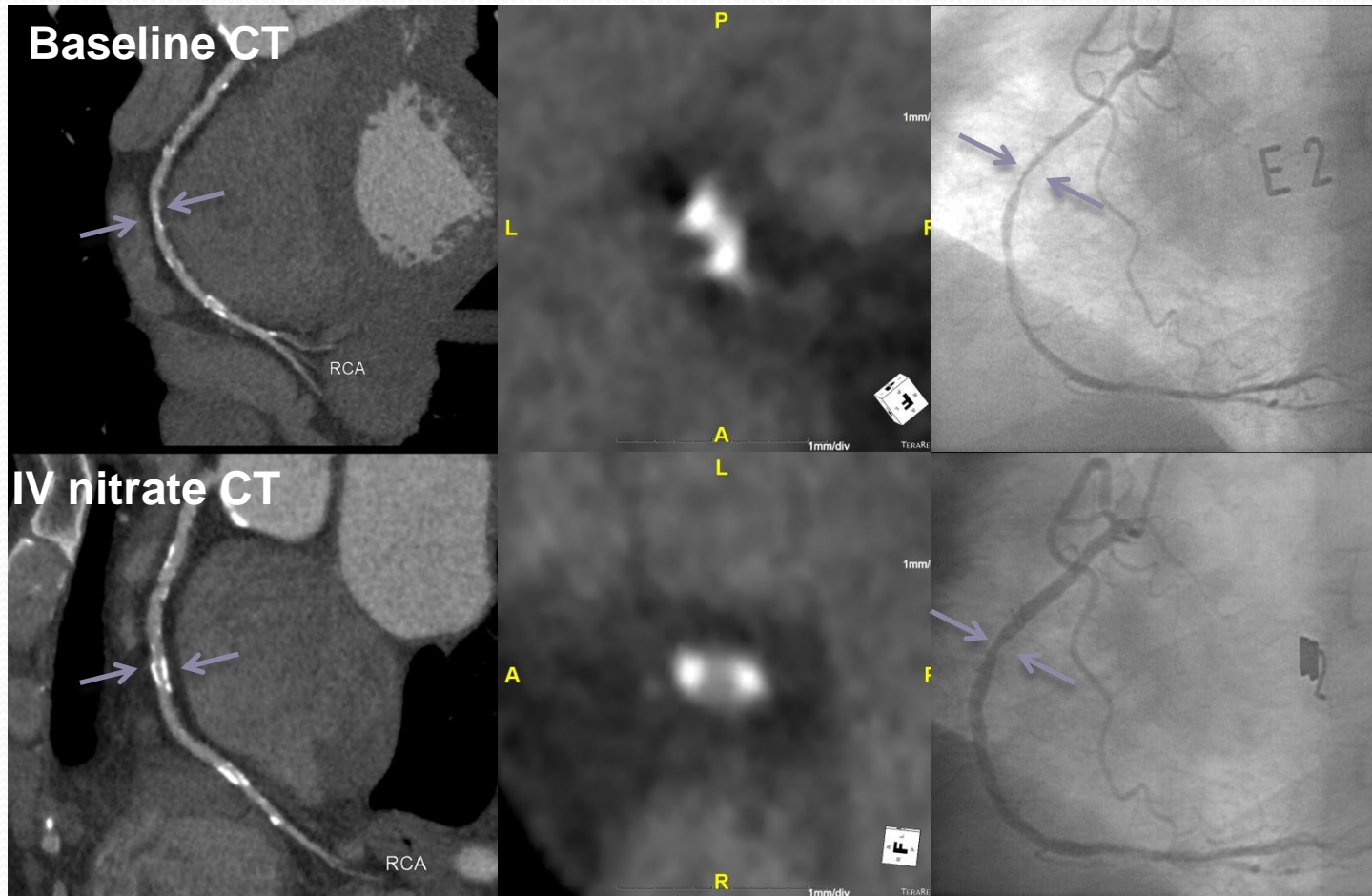


- **1** patient: **calcified plaques** that hid coronary spasm.
- **1** patient: spasm was located at distal RCA that was **too small diameter to evaluated** luminal stenosis on CCTA.
- **2** patients: **negative finding** on both baseline and IV nitrate CCTA.



# Representative case: False negative-1

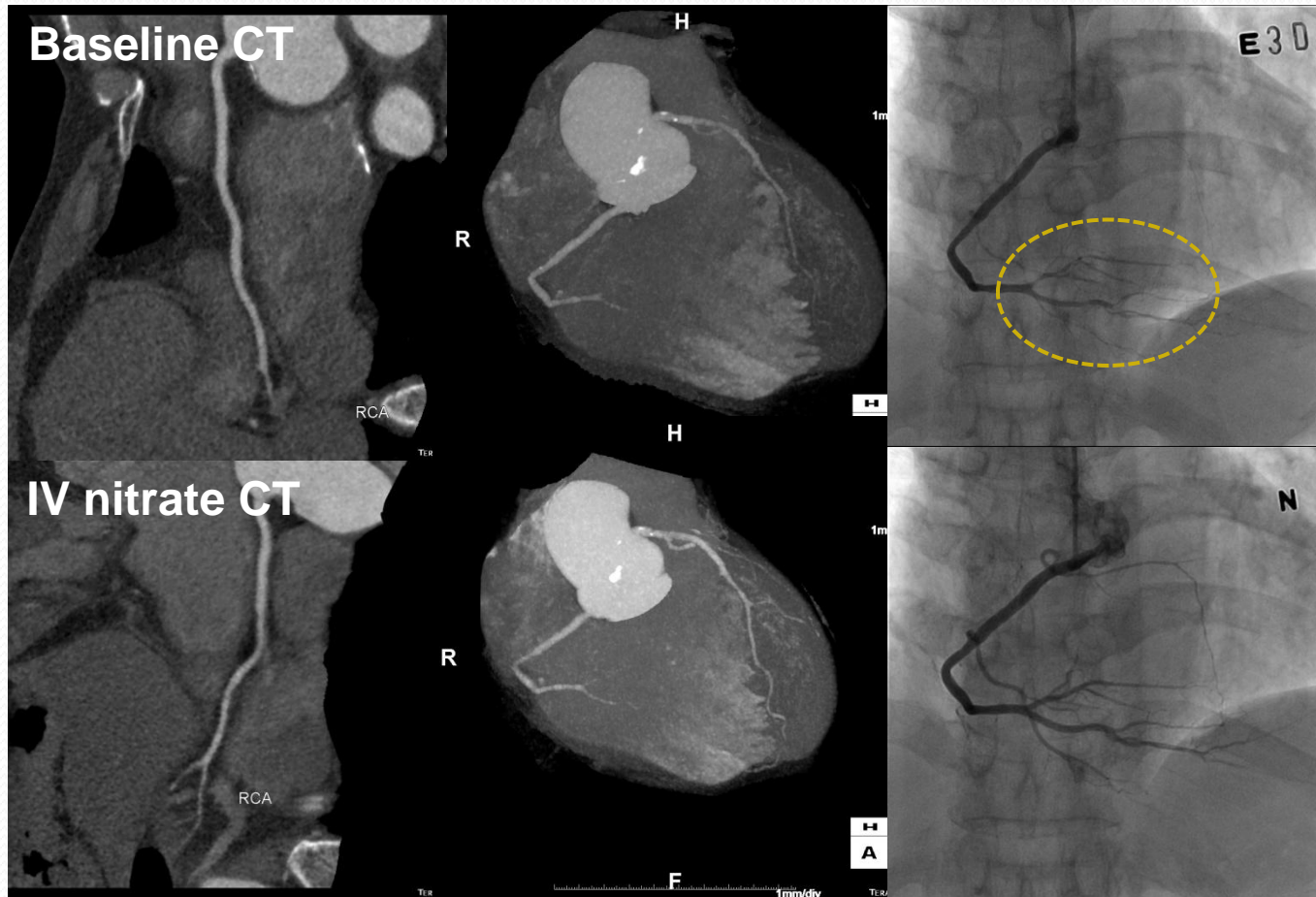
## Provoking test (+) and CCTA (-)



**Case 3.** A 60 year old male patient presented with intractable recurrent chest pain.

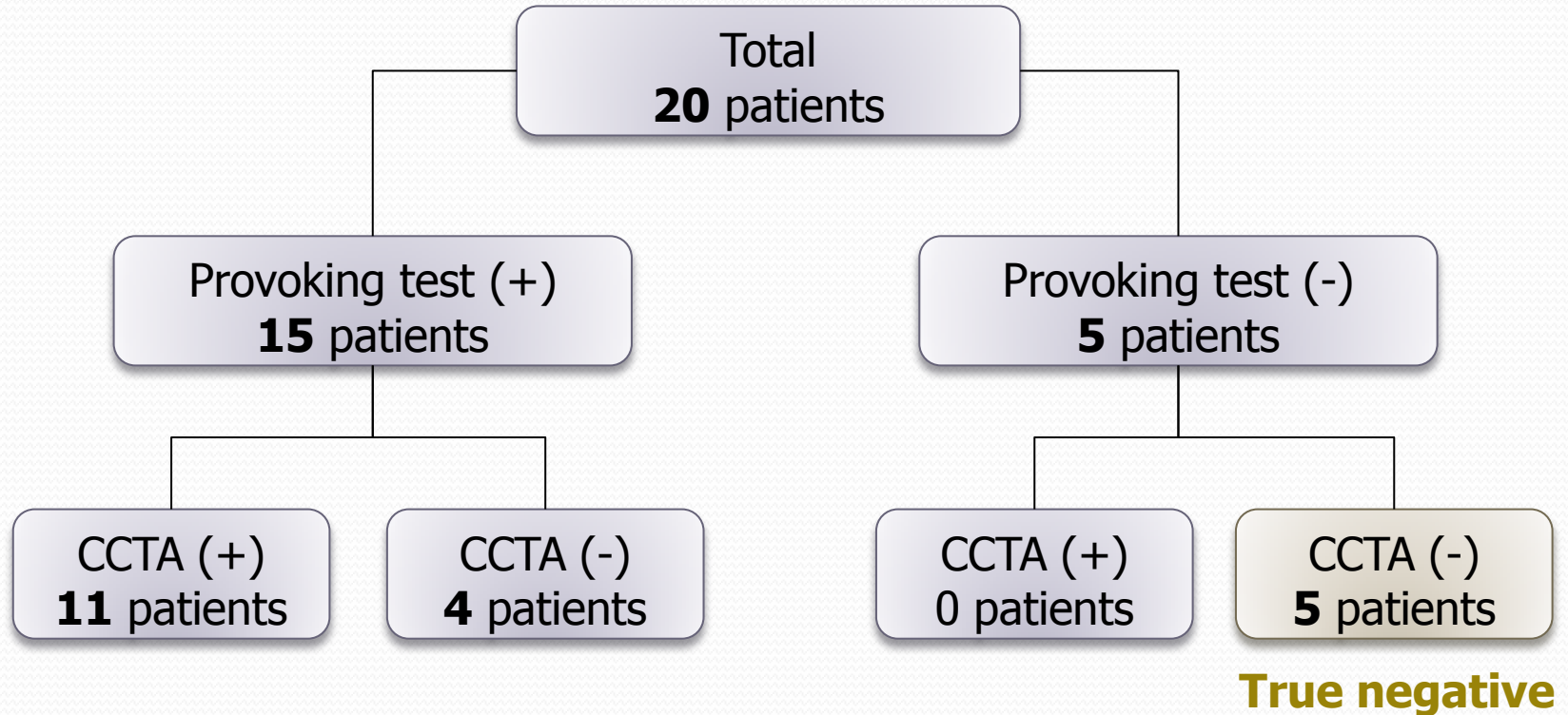
# Representative case: False negative-2

## Provoking test (+) and CCTA (-)



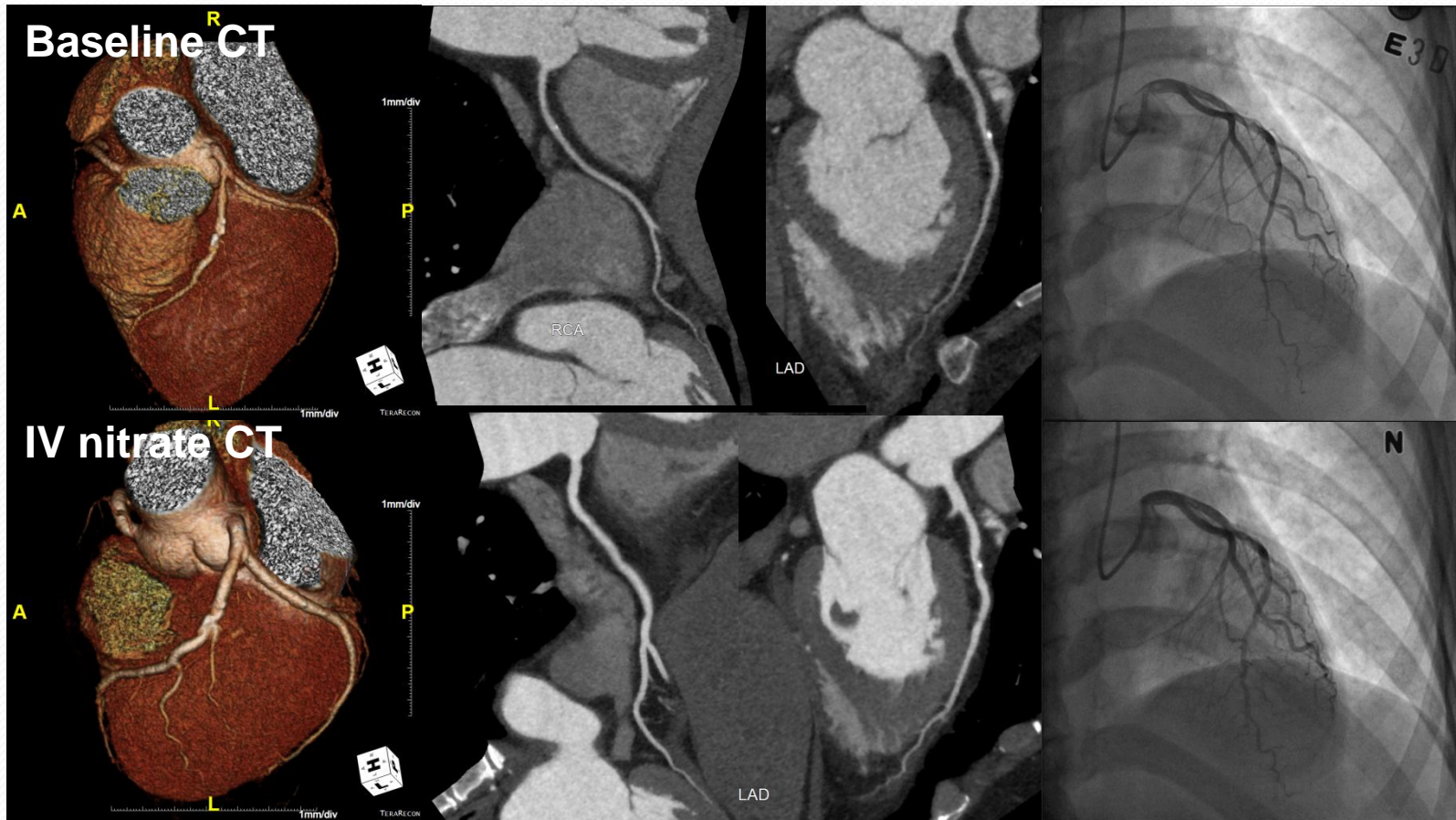
**Case 4.** A 60 year old male patient presented with intractable recurrent chest pain.

# Results



# Representative case: True negative-1

## Provoking test (-) and CCTA (-)



**Case 5.** A 53 year old female patient presented with intractable recurrent chest pain.



# Results

- **Contrast media**

- Total iodinated contrast medium volume: 120 ml (Xenetix 350 mg/ml)
  - Baseline CT 60 ml + IV nitrate CT 60 ml.

- **Radiation dose**

- Mean effective dose (baseline CT + IV nitrate CT):  
**8.3 ± 3.6 mSv (range: 2.9 - 13.5 mSv)**
  - \* Effective dose; calculated using a conversion coefficient for chest and coronary arteries ( $k = 0.014 \text{ mSv/ [mGy}\cdot\text{cm]}$ )

# Limitations

1. Although a high specificity and PPV, **the sensitivity was relatively low (73%)**, it is insufficient to predict variant angina **without provoking test**.
  - **Higher sensitivity** compare with the results of previous literature (sensitivity **48%**, Kang et al. KJR 2012) which produced from retrospective analyze of conventional CCTA.
2. Double acquisition of CCTA per one individual requires **more amount of contrast media and radiation dose**.
3. The sample size of our study was relatively small.

# Conclusion

- We speculate that double acquisition of CCTA with and without IV vasodilator **can increase the sensitivity of vasospastic angina detection.**

# Cons of CCTA in coronary spasm

- Cons
  - **Detection**
    - Spasm is transient and unpredictable.
    - Usually not occurs at day time
  - Relatively **low spatial and temporal resolution** than conventional CAG.
  - Radiation dose, contrast media

# Pros of CCTA in coronary spasm

- Pros
  - Most frequently using primary screening tool of CAD
  - Noninvasive

**Diagnosis of coronary spasm in CCTA X**

# Pros of CCTA in coronary spasm

- Pros
  - Most frequently using primary screening tool of CAD
  - Noninvasive

**Detection of coronary spasm in CCTA 0 (?)**



# Thank you !

**Moo Hyun Kim**, Department of Cardiology, Dong-A University College of Medicine, Busan, Republic of Korea.

**Ki-Nam Lee**, Department of Radiology, Dong-A University College of Medicine, Busan, Republic of Korea.



The 3rd Annual Meeting of

# SCCT KOREA IRC

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February 13 (Fri) - 14 (Sat), 2015

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Early Bird Registration: January 9 (Fri), 2015

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