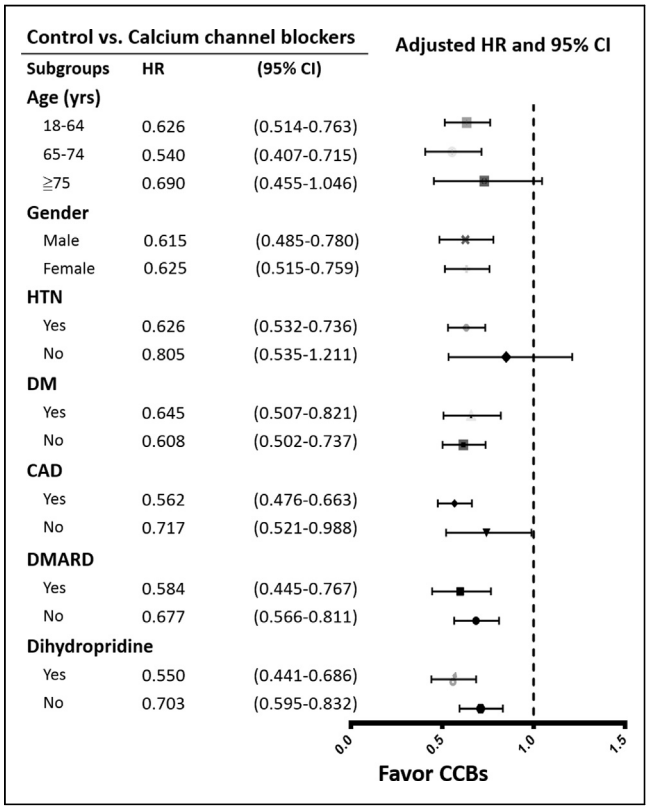

CONCLUSION Therapy of CCBs is associated with a lower risk of MI among patients with RA. Hence, use of CCBs may be a compelling indication for patients with RA and hypertension.

TCTAP A-136

Prevalence of Heparin-induced Thrombocytopenia According to 4T Score in Single Institution of Korea from Large Scale Database

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BACKGROUND Heparin-induced thrombocytopenia (HIT) occurs in 0.5-5%of patients treated with heparin The HIT incidence is high in Korea, approximately 1-10%. HIT is an immune disease, occurring when HIT antibodies (HIT-Ab) target heparin bound to platelet factor 4 (PF-4). The complex composed of HIT antibodies, heparin and PF-4 causes platelet activation leading to thrombocytopenia and thromboembolism. The incidence of HIT depends on the heparin form administered. In patients treated with unfractionated heparin (UFH), HIT develops in 1-3% of the cases and, if accompanied by thrombosis, is followed with the mortality rate of up to 30%. In contrast, the incidence of HIT is <1% when using low molecular weight heparin (LMWH). Various complications (deep vein thrombosis, disseminated intravascular coagulation, pulmonary embolism) are the main danger associated with HIT. Therefore, platelet count should be monitored after heparin administration and early diagnosis and prevention of HIT are important. However, diagnosing HIT is not easy, as other causes of thrombocytopenia need to be excluded.

METHODS This is a retrospective study from a large-scale retrospective cohort study conducted on patients over 18 years old in the Seoul St. Mary's hospital in Korea from January 2009 to December 2014. Patients who have injected heparin more than 96 hours was enrolled. Unfractionated heparin (UFH), dalteparin sodium, enoxaparin sodium, nadroparin calcium, or fondaparinux sodium were included. Those who had received a surgery within 72 hours after heparin injection were excluded. Patients who have Platelet counts before and after heparin included. To evaluate the probability of HIT, the study used 4T scoring. "Acute thrombocytopenia" was defined as platelet count decreased by >50% and nadir ≥20,000/mm^3 (2 points), and 2 points was added when onset timing was between day 5-day 10 after administration of heparin. To exclude other causes of thrombocytopenia, those who were diagnosed as hepatic necrosis, infective endocarditis, paroxysmal nocturnal hemoglobinuria, et al were excluded (2 points). Due to the limitation of EMR data, it was impossible to check new thrombosis, but the three scoring system (acute thrombocytopenia, timing onset, and other causes) above already got 6 points which are equivalent to the high score of HIT.

RESULTS 6,046 patients were enrolled from 18,405 patients who prescribed heparin for the first time during the study period because of the availability of platelet count. Among the total of 6,046 patients, HIT occurred 641 cases (10.6%, 641/6,046). The UFH showed the highest rate of incidence with 13.9% (559/4,030), while dalteparin had 11.5% (13/113) and enoxaparin had 3.9% (69/1760). No HIT occurred in Fondaparinux and Nadroparin. As the result of multivariable logistic regression analysis, the dalteparin (HR=0.55, p=0.036) and enoxaparin (HR=0.40, p<0.001) showed relatively low HIT incidence rate, comparing the UFH. In the case of UFH, HIT had the tendency to equally occur in day 5-10 after the first Heparin medication, whereas with dalteparin, the occurring rate was 76.9% (10/13) in day 8-10 and with enoxaparin, the rate was 66.7% (46/69) in day 5-day 7.

CONCLUSION HIT occurred in 10.6% according to 4T score, which is a significant number. Also, this study showed a lack of awareness of HIT in clinical practice. Clinicians need to understand HIT when they prescribe heparin and follow-up of patients with platelet count. This study is limited by study design using the 4T score and retrospective study.

TCTAP A-137

Novel Rhynchophylline Analogues as Microvascular Relaxation Agents on the Treatment of Microvascular Dysfunction Leading by Diabetes

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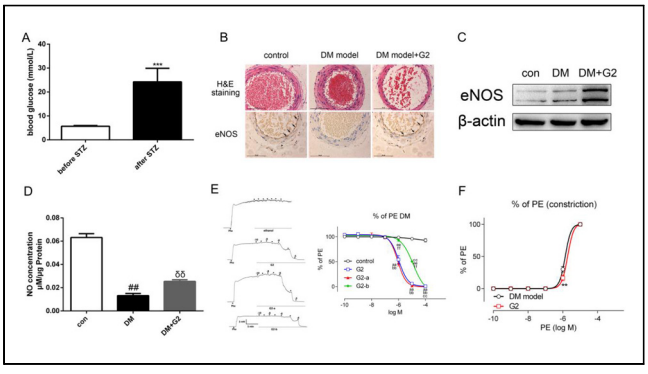
BACKGROUND Cardiovascular disease is part of the main causes of disability and even death throughout the world. Moreover, diabetes mellitus is often associated with complications of various organ systems, of especially microvascular dysfunction. Uncaria rhynchophylla, a traditional Chinese herb medicine, has long been used as an anti-hypertension drug in China for thousands of years. Our group has long devoted to extracting, synthesizing and evaluating indole alkaloids derived from Uncaria rhynchophylla. G2, one of the racemic analog of indole alkaloids we synthesized, exhibited significant vasodilation activity which has, even more, potential than Rhynchophylline in vitro rat thoracic aorta test. After further separation on a choral column, two enantiomers, G2-a and G2-b were obtained from G2. Based on the pharmaceutical preliminary studies on the relaxation of rat thoracic aorta, G2 and its stereoisomers have been chosen as the vascular relaxation agents to further investigate their functions and mechanisms on the treatment of microvascular dysfunction leading to diabetes.

METHODS Diabetic model in Sprague-Dawley rats was induced by intrapulmonary injection of 60 mg/kg streptozotocin (STZ) followed by a gavage of high-glucose solution. After 8 weeks of modeling, diabetes was established by confirming the blood glucose measuring. Then, the diabetic rats were addressed in 20 mg/kg G2 (gavage) for 2 weeks, and mesenteric arteries were taken. Then vessels were placed for vasodilation effects by myograph chambers, eNOS and iNOS levels by western blotting and immunohistochemical staining.

RESULTS To determine whether G2 could restore endothelium function, phenylephrine-induced concentration-dependent contractions and acetylcholine-induced endothelium-dependent relaxations were performed. G2 (20mg/kg) gavage for a week improved EDRs and decreased Phenylephrine-induced concentration-dependent contractions. G2 could protect the vessel from eNOS loss induced by diabetes mellitus, which was vital for artery relaxation.



CONCLUSION Diabetes as a pathological model of endothelium damage to investigate whether the chemicals could still trigger relaxant effects and again to illustrate that whether endothelium-dependent relaxation was involved. G2 could generate vasodilation effects with a right shift curve, indicating endothelium was involved in G2-incduced vasorelaxation.

TCTAP A-138

Impact of mean platelet aggregation degree on long-term clinical outcomes among patients undergoing complex percutaneous coronary intervention

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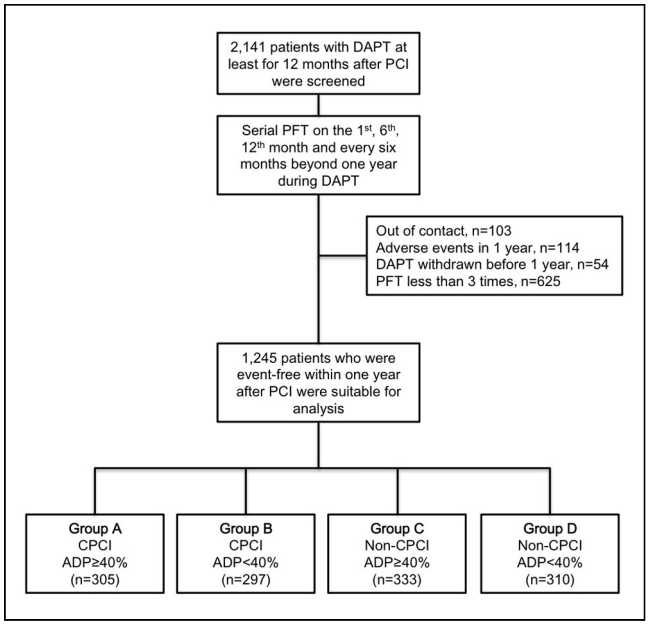
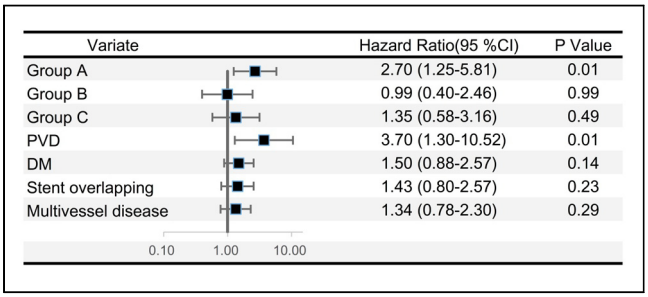
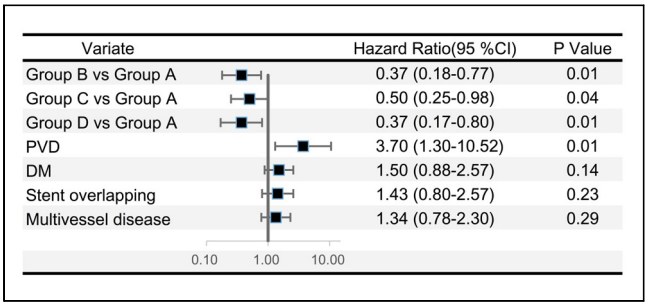
BACKGROUND To evaluate the associationbetween mean platelet aggregation degree and long-term clinical outcomes inpatients receiving complex percutaneous coronary intervention (CPCI).

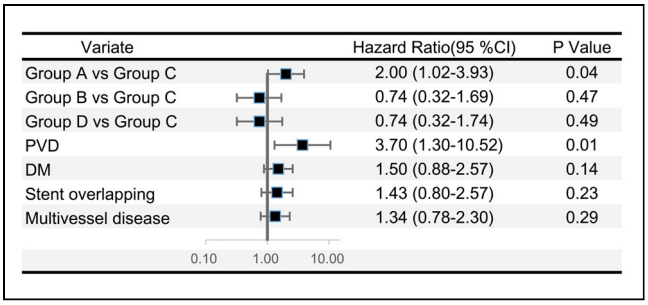
METHODS We screened 2,141 patientsafter PCI and treated with aspirin and clopidogrel. CPCI was defined as aprocedure targeted to at least one of the following: left main disease;bifurcation lesion; ostial lesion; chronic total occlusion and small vesselstenting. Adenosine diphosphate (ADP) -induced platelet aggregation was requiredto be serially measured by light transmission aggregometry at least three timesafter PCI and the mean value was calculated. The population was categorized accordingto the mean ADP degree and presence of CPCI. The primary endpoint was majoradverse cardiovascular and cerebral event (MACCE).



RESULTS Finally, a total of 1,245patients were enrolled and divided into four groups: Group A (CPCI &ADP≥40%), Group B (CPCI & ADP<40%), Group C (non-CPCI & ADP≥40%) andGroup D (non-CPCI & ADP<40%). The median follow-up was 29.9 months. The Cox multivariate analysis suggested that Group A was anindependent risk factor of MACCE (HR 2.70, 95%CI 1.25-5.81; P<0.001). Comparedwith Group A, Group B, C and D were all associated with a lower rate of MACCE. WhenGroup C set as a comparator, Group B and Group D had similar risk of primaryendpoints.







CONCLUSION Patients undergoing CPCI withhigh mean ADP degree were associated with higher risk of MACCE. Serial PFT isof importance in patients receiving CPCI.

TCTAP A-139

Gp130-mediated STAT3 Activation by S-propargyl-cysteine, an Endogenous Hydrogen Sulfide Initiator, Prevents Doxorubicin-induced Cardiotoxicity

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BACKGROUND Doxorubicin (Dox) could trigger a large amount of apoptotic cells in the myocardium, which leads to dilated cardiomyopathy and heart failure. S-propargyl-cysteine (SPRC), a producing agent of endogenous hydrogen sulfide (H_2S), possesses cardioprotective efficacy. However, the specific effect and mechanism of SPRC in Dox-induced cardiotoxicity remain elusive. Given gp130 with its main downstream signaling molecule, STAT3, is involved in cardiac myocyte survival and growth, the present study was performed to elucidate whether SPRC counteracts Dox-induced cardiotoxicity, and if so, whether the gp130/STAT3 pathway is involved in this cardioprotective activity.

METHODS SPRC triggered STAT3 via gp130 in both cultured cardiomyocytes and rodent hearts, determined using siRNA transfection, western blot, co-immunoprecipitation, or/and immunocytochemical analysis.

RESULTS SPRC stimulated the activation of STAT3 via gp130-mediated transduction tunnel *in vitro* and *in vivo*. In Dox-stimulated cardiotoxicity, SPRC enhanced cell viability, reduced lactate dehydrogenase (LDH) release, restored expression of gp130/STAT3-