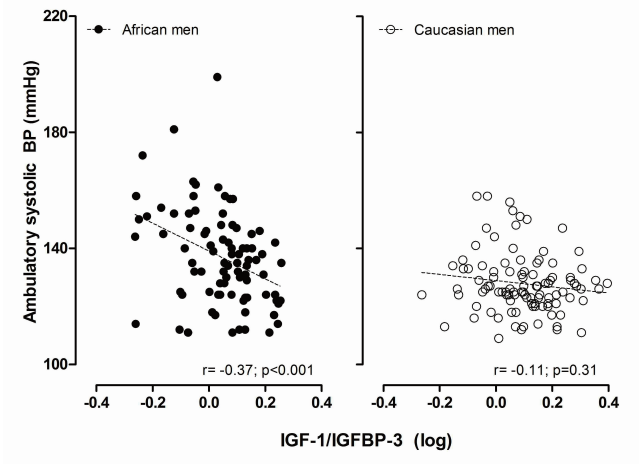
gle, partial and multiple regression analyses confirmed a significant independent association between ambulatory systolic BP and bioavailable IGF-1 only in African men ($R^2$=0.23; =-0.21; p=0.042). cIMT was similar in the ethnic groups (p=0.34), and was only associated with bioavailable IGF-1 in Caucasian men prior to adjustment for -glutamyl transferase.




**Conclusions:** Elevated ambulatory blood pressure of African men is significantly linked to reduced IGF-1 bioavailability. It clearly seems worthwhile to consider recombinant IGF-1 administration as a potential pharmacological tool in cardiovascular medicine to curb the rising prevalence of cardiovascular disease.

## PP.29.417 CHARACTERISTICS OF THE CYP11B2 POLYMORPHISM IN JAPANESE PATIENTS WITH PRIMARY ALDOSTERONISM

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**Background:** Primary aldosteronism (PA) is mostly frequently presented as two subtypes, idiopathic hyperaldosteronism (IHA) or aldosterone-producing adenoma (APA). The CYP11B2 gene encodes a key enzyme of the aldosterone biosynthesis – aldosterone synthase. A polymorphism in the 5' promoter region of this gene at -344T/C alters a putative recognition site for steroidogenic transcription factor-1 (SF-1). Significant association between this polymorphism and aldosterone level had been reported, while controversial results also exsisted. This genetic variant has also been investigated in patients with PA in Italy, showing no association to aldosterone production. On the other hand, this polymorphism distribution in patients with PA subtypes has not been investigated in Japan.

**Objective:** The aim of our study is to identify the distribution of CYP11B2 polymorphism that influences PA subtypes and plasma aldosterone concentration (PAC) in Japanese patients with PA.

**Patients and methods:** We examined totally 56 patients (29 males and 27 females) with PA. Their mean age was 50.9 years old (34-69y.o.) and their diagnosis was confirmed by super-selective ACTH-stimulating adrenal venous sampling for IHA and pathological findings after unilateral adrenalectomy for APA from April 2011 through August 2012. The CYP11B2 -344T/C polymorphism was determined by the analysis of restriction fragment length polymorphism (RFLP).

**Results:** The genotype frequencies of CYP11B2 -344T/C was T/T:75% (21 cases), T/C:21.4%(6 cases), C/C:3.6%(1 case) in 28 APA cases and T/T:46.4%(13 cases), T/C:35.7%(10 cases), C/C:17.9%(5 cases) in 28 IHA cases. PAC (pg/ml) in each PA subtype-genotype was APA-T/T 340±303, APA-T/C 624±396, APA-C/C 124, IHA-T/T 117±37, IHA-T/C 143±31, IHA-C/C 108±36. There was no significant difference in the blood pressure among the PA subtypes or the genotypes.

**Conclusion:** The present study was in agreement with several studies previously conducted in Caucasians, showing association of -344T/C allele with aldosterone level in patients with hypertension. Our study showed the higher frequency of the CYP11B2 T/T genotype in patients with APA than that in Japanese essential hypertensive patients. Further studies of this locus should be performed in large-scale patients to confirm our results and to define the underlying physiological implications of observed association and tumor genesis of APA.

## PP.29.418 HETEROGENEOUS MACHINE LEARNING SYSTEM FOR DIAGNOSING PRIMARY ALDOSTERONISM

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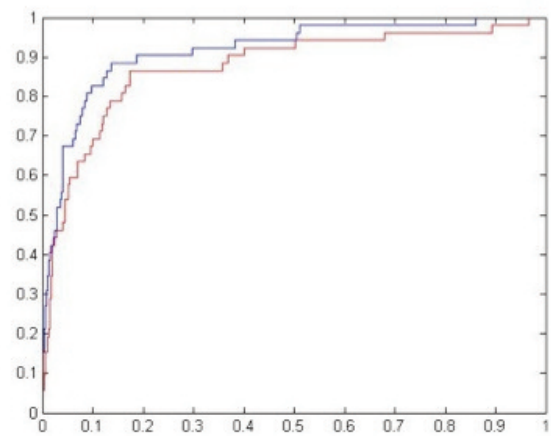
**Objective:** The identification of Primary Aldosteronism (PA) is challenging in that this common cause of curable hypertension often mimics primary (essential) hypertension. Hence, we aimed at developing an improved machine learning method for classification of PA. Since missing values and collinearity are common problems in real-world data, the new method was required to deal with such issues.

**Design and method:** The classifier we propose is an ensemble that integrates, in a nontrivial, hierarchical fashion, different base classifiers, namely: Support Vector Machines, Decision Trees, and a logistic Multivariate Discriminant Analysis (MDA) model. The outputs of the base classifiers are combined by sum rule. The ensemble can handle correlation among variables, via the use of random subspaces; missing values, via the Expectation-Maximization method; imbalance in the training data, via a variant of the EasyEnsemble strategy. The MATLAB code for our classifier is available at http://www.dei.unipd.it
The ensemble is quantitatively evaluated by measuring performance on the dataset from the PAPY study, which comprises 1124 patients (52 PA cases) from 15 specialized hypertension centers; each patient is described by a set of 29 features, which include both demographic and biochemical data. The metric of performance is the Error Under the ROC Curve (EUC). We used a "leave-one-out-clinical", 15-fold cross validation: in each fold, 14 centers are used for training and 1 as the test set.

**Results:** Using the Wilcoxon signed-rank test at 0.05 alpha level our novel classifier (featuring EUC=8.39) considerably outperformed the base classifiers in the ensemble and also the MDA model (EUC=13.70) proposed in 1998 as a standalone classifier for PA. Our classifier exhibited a FPR of ~50% (MDA model: ~90%) when a FNR as low as ~2% was tolerated, corresponding to only 1 PA patient in PAPY dataset.

**Conclusions:** The ensemble method for the classification of PA that was developed features a statistically significant improvement in performance with respect to previous classifiers, and robust to common issues, such as collinearity, missing values, and class imbalance. This increased performance would allow to reduce considerably the number of patients to be subjected to further invasive tests.




## PP.29.419 MARINOBUFAGENIN IN ESSENTIAL HYPERTENSION AND PRIMARY ALDOSTERONISM: A CARDIOTONIC STEROID WITH CLINICAL AND DIAGNOSTIC IMPLICATIONS

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