2008년 산학협동연구비

The Relation of Circadian Blood Pressure Variation to Left atrial function evaluated using tissue Doppler and Strain imaging

Division of Cardiology
The Catholic University Medical College

박찬석, 윤호중, 조은주, 임상현, 정해억, 김희열, 전희경, 승기배, 김재형

Backgrounds (I)

- Hypertension and Left atrial function
  - Essential hypertension deteriorates LA functions

Nagano R et al. Hypertension 1995;26:815–9

  - Chronic hypertension

: Increased in LA volumes, decrease in LA passive emptying function, increase systolic pump function

Erol MK et al. Acta Cardiol 2002;57:323–7

- Non-dipper Hypertension
  - Higher risk of cardiovascular disease and increased incidence of target organ damage

Imai Y et al. Blood Press Monit 2001; 6:335–9

Backgrounds (II)

- LA function
  - Measured with Doppler velocities differentially influenced by loading conditions

Hoit BD et al. Circulation 1992;86:651-9

  - Doppler tissue imaging (DTI)
    : Can evaluate global and segmental atrial function
    : Cannot distinguish between intrinsic myocardial motion and that produced by passive translatory motion due to the effects of tethering.

Thomas L et al. Heart 2007;93:89-95

Backgrounds (III)

- Left atrial phasic volume in Hypertensive
  - ↑ LA active emptying volume, LA active emptying fraction
  - ↓ LA passive emptying volume, LA passive emptying fraction

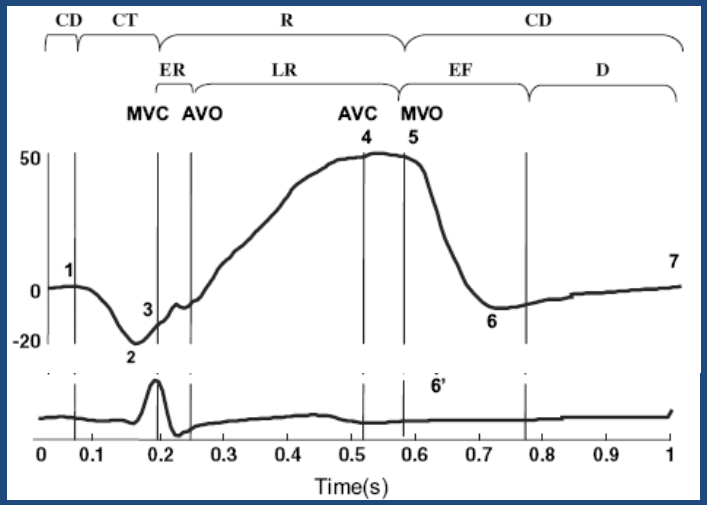
  → *More obvious in non-dipper hypertensive*
  - Atrial reservoir and booster pump functions

  → *Increase more prominent in non-dipper hypertensives*

Aydin M et al. Int J Cardiol 2004;96:419-24

Backgrounds (IV)

- LA strain



- *MVC: mitral valve closure, AVO: aortic valve opening, AVC: aortic valve closing, MVO: mitral valve opening*
- **CT: contractile period (1, onset; 2, peak ε; 3 end**)
- **R: reservoir period (3, onset; 4, peak ε;5, end)**

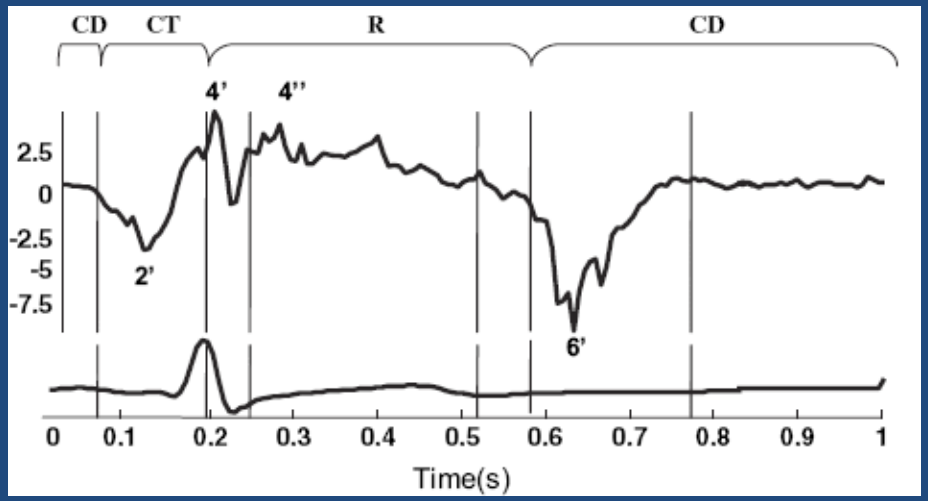
  ER: early reservoir period, LR: late reservoir period
- **CD: conduit period (5, onset; 6, peak ε; 7, end of LA wall deformation during diastasis)**

  EF: early ventricular filling, D: diastasis

Sirbu et al. EJE 2006;7:199-208

Backgrounds (V)

- LA strain rate



- *MVC: mitral valve closure, AVO: aortic valve opening, AVC: aortic valve closing, MVO: mitral valve opening*
- **CT: contractile period (2', peak SR)**
- **R: reservoir period**
  ER: early reservoir period (4' peak SR), LR: late reservoir period (4" peak SR)
- **CD: conduit period (6', peak SR)**
  EF: early ventricular filling, D: diastasis

Sirbu et al. EJE 2006;7:199-208

Backgrounds (VI)

- LA function using strain and strain rate analysis

Atrial timing	Index	*r* value	P value
Reservoir period (R)	Strain R-LA-EI	0.43	<0.01
Conduit period (CD)	Strain CD-LA-PEF	-0.46	<0.005
Contractile period (CT)	Strain CT-LA-AEF	-0.78	<0.001

LA EI, left atrium expansion index; LA PEF, left atrium passive emptying fraction ; LA AEF, left atrium active emptying fraction

Sirbu C, et al. Eur J Echocardiography 2006;7:199-208

Useful Method for evaluation of LA function

Backgrounds (VII)

- Atrial natriuretic peptide (ANP)
  - Produced by atrial cardiomyocyte in response to atrial stretch

    Rubattu S, et al. Am J Hypertens 2008;21:733-41

  - Elevated in hypertensive patients especially complicating LVH

    Nishikimi T, et al. Hypertension 1996;28:22-30

- Brain natriuretic peptide (BNP)
  - secreted by the ventricles of the heart in response to excessive stretching of cardiomyocytes
  - Useful of diagnosis and prognosis prediction in heart failure patients

    Stein BC, et al. Am Heart J 1998;135:914-23

Objectives

Dipper and Non-dipper Hypertensive patients

- *Evaluation of LA function using tissue image (color Doppler, strain rate, strain)*
  - *ANP and Pro-BNP*

→ Difference of LA function measured by echocardiography and serological markers representing cardiomyocyte stretching by nocturnal BP pattern?

Methods (I)

- Study Period: October 2008 ~ February 2010
- Inclusion Criteria
  - Age: 30-80 years old
  - Diagnosed as essential hypertension for the first time
  - No history of anti-hypertensive medication

Methods (II)

- Exclusion Criteria
  - LVEF less than 50%
  - Past history of myocardial infarction
  - Previously diagnosed as diabetics or took diabetes medication
  - Significant valvular heart disease
  - Significant cardiac arrhythmia such as atrial fibrillation
  - Renal failure patient (Creatinine ≥ 1.3 mg/dL or Creatinine clearance rate ≤ 60 mL/min)

Methods (III)

- Blood Pressure (BP) monitoring
  - Office BP

    Two blood pressures 5 min apart → Mean BP
  - Ambulatory BP monitoring

    Tonoport V (General Electric Medical Systems)

    Daytime BP: From 6:30 AM to 10 PM, every 30 min

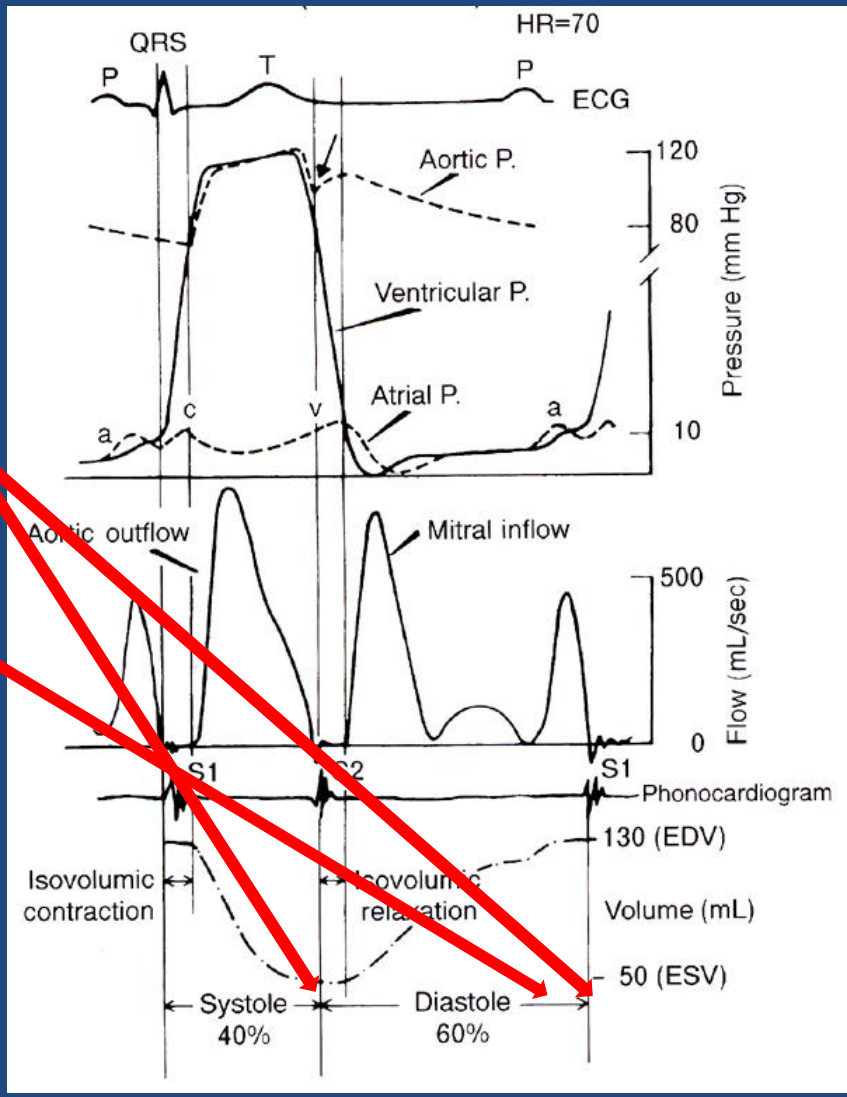
    Nighttime BP: From 10 PM to 6 AM, every 1 hour

    Awakening BP: From 4 AM to 6 AM, every 1 hour
  - Nocturnal dipper

    Both nocturnal SBP and DBP > 10% decrease average daytime blood pressure

Methods (IV)

- Phasic LV volumes
  - LA maximal volume
  - LA minimal volume
  - LA volume at onset of atrial systole



Methods (V)

- Echocardiography
  - Vivid 7 (General Electric Medical Systems)
  - LA volume by area-length method

    LA expansion index

    = (LA maximal volume-LA minimal volume)/LA minimal volume X 100

    LA conduit volume

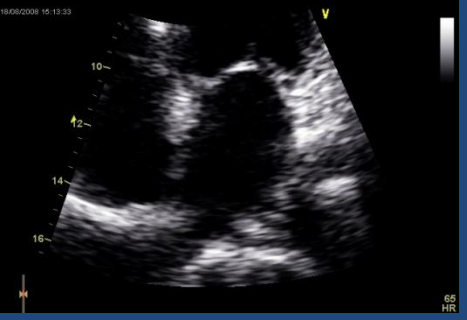
    = LV stroke volume−(LA maximal volume−LA minimal volume)

    LA passive emptying volume

    = LA maximal volume-LA volume at onset of atrial systole

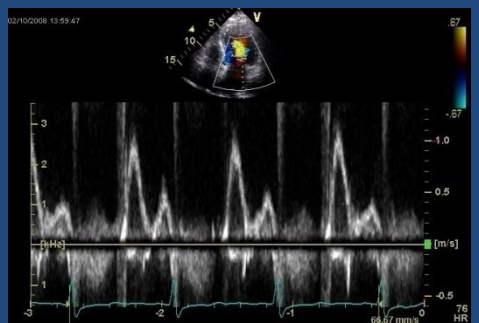
    LA passive emptying fraction

    = LA passive emptying volume/LA maximal volume X 100



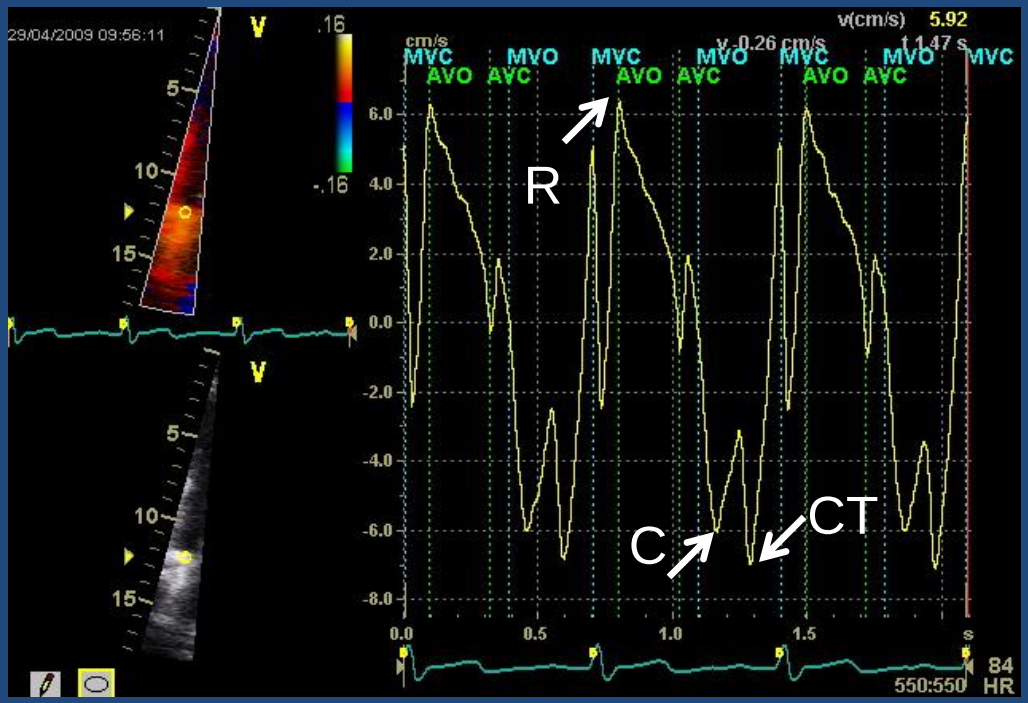
Methods (VI)

- Echocardiography
  - LA active emptying volume
    - = LA volume at onset of atrial systole−LA minimal volume
  - Left atrial active emptying fraction
    - = LA active emptying volume/LA volume at onset of atrial systole
  - Left atrial ejection fraction
    - = Left atrial stroke volume/LA end systolic volume X 100
  - Atrial fraction
    - = A wave VTI / (A wave VTI + E wave VTI) X 100



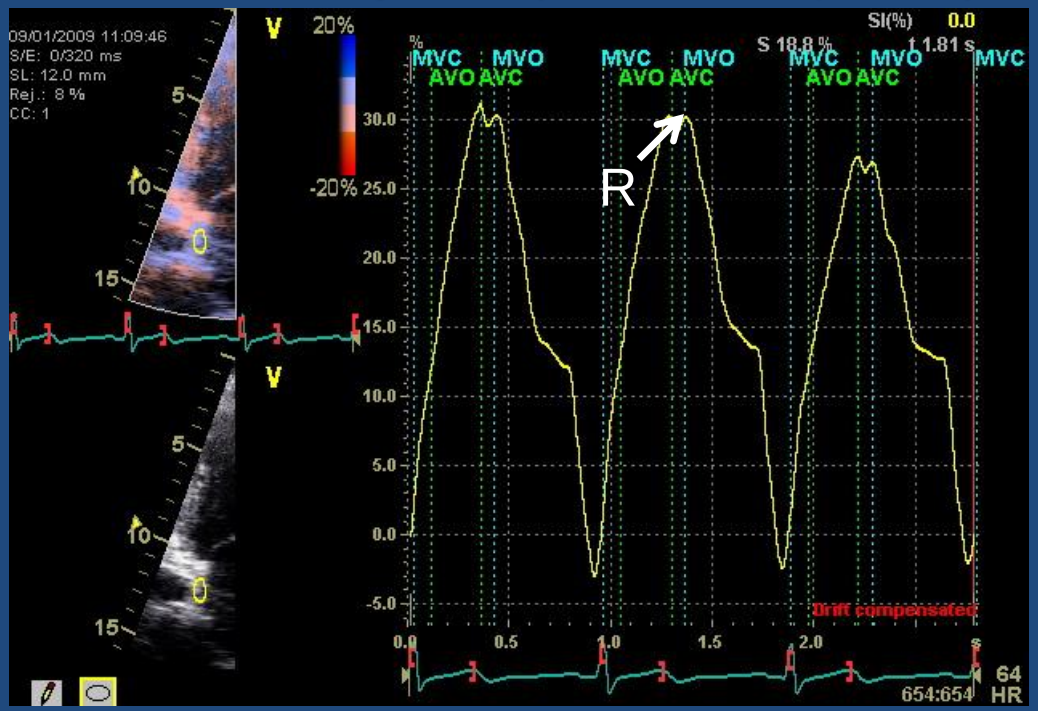
Methods (VII)

- Echocardiography
- Color Doppler tissue imaging
  - Atrial tissue velocities velocity at basal septal, lateral, inferior and ant erior wall of LA during reservoir, conduit and contractile period(apical 4 chamber and 2 chamber view)



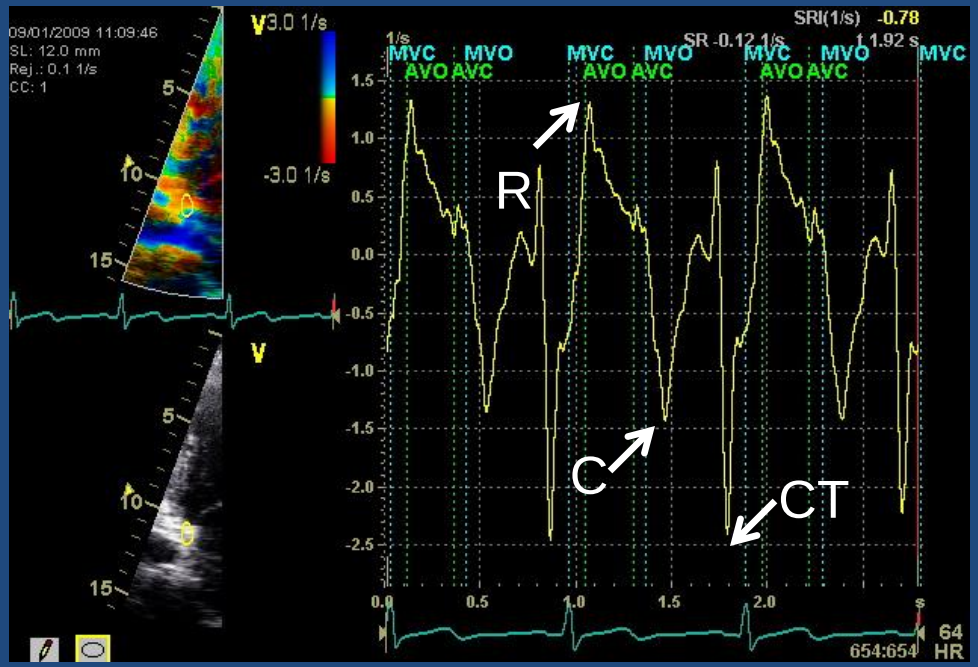
Methods (VIII)

- Echocardiography
- Peak strain measurement
  - Basal septal, lateral, inferior and anterior wall of LA (apical 4 chamber and 2 chamber view)
  - Peak strain of LA at late systole (= reservoir period)



Methods (IX)

- Echocardiography
- Strain rate measurement
  - Basal septal, lateral, inferior and anterior wall of LA (apical 4 chamber and 2 chamber view)
  - Peak strain rate of LA (A-sr) at reservoir, conduit and contractile period



Statistics

- Chi-square test for discrete variables
- Student’s t-test for continuous variables
- Pearson correlation between serological, volumetric and tissue imaging parameter

Result

- Total 40 patients were enrolled
- 20 dipper and 20 non-dipper patients

Patient Characteristics

	Dipper (n=20)	Non-dipper (n=20)	*P value*
Age (years)	48±7	48±10	0.88
Male (%)	65	40	0.11
Current Smoking (%)	40	25	0.31
BMI (kg/m^2)	25.0±2.2	24.1±3.4	0.32
BUN (mg/dL)	14.3±2.9	13.5±2.7	0.37
Creatinine (mg/dL)	0.87±0.18	0.74±0.17	0.03
Total cholesterol(mg/dL)	205±35	203±33	0.91
Triglyceride (mg/dL)	157±74	126±59	0.14
HDL (mg/dL)	50±12	60±29	0.16
LDL (mg/dL)	124±35	118±38	0.60
Urine microalbumin (mg/dL)	12.24±25.58	9.04±11.75	0.62
Uric acid (mg/dL)	5.4±1.2	4.6±0.8	0.02*
hs CRP (mg/dL)	1.73±1.86	1.89±2.58	0.82
Fibrinogen (mg/dL)	258±72	269±67	0.60
ANP (pg/mL)	20.03±24.01	23.19±13.60	0.61
NT-proBNP (pg/mL)	51.64±67.50	71.51±117.15	0.52

Ambulatory Pressure Monitoring

	Dipper (n=20)	Non-dipper (n=20)	*P value*
Office SBP (mmHg)	160±19	162±15	0.70
Office DBP (mmHg)	95±14	99±12	0.44
24-hr average SBP (mmHg)	148±15	152±16	0.31
24-hr average DBP (mmHg)	101±11	102±11	0.76
Daytime SBP (mmHg)	153±15	153±17	0.98
Daytime DBP (mmHg)	105±11	103±11	0.49
Nocturnal SBP (mmHg)	132±15	149±17	<0.01*
Nocturnal DBP (mmHg)	88±11	99±12	<0.01*
Awakening SBP (mmHg)	131±16	150±18	<0.01*
Awakening DBP (mmHg)	88±12	98±12	<0.01*

Echocardiographic parameters (I)

	Dipper (n=20)	Non-dipper (n=20)	*P value*
Septal thickness (mm)	9.8±2.0	9.1±1.8	0.23
Posterior wall thickness (mm)	9.9±1.8	9.4±1.7	0.42
LV end diastolic dimension (mm)	49.4±4.2	49.9±3.0	0.70
LV end systolic dimension (mm)	30.8±3.7	29.8±3.8	0.40
LVEF (%)	65.3±3.6	67.0±4.3	0.18
LV mass index (g/m^2)	93.02±17.71	100.25±20.89	0.25

Echocardiographic parameters (II)

	Dipper (n=20)	Non-dipper (n=20)	*P value*
E wave (cm/s)	60.3±12.4	67.6±13.7	*0.09*
A wave (cm/s)	61.5±14.6	69.9±15.8	*0.09*
E/A ratio	1.03±0.31	1.03±0.38	0.99
Deceleration time (ms)	190.9±41.6	193.5±30.1	0.82
IVRT (ms)	84.1±15.8	82.3±12.7	0.80
A duration (ms)	145.8±16.8	144.5±16.9	*0.09*
Peak septal S' (cm/s)	6.70±1.19	6.77±1.06	0.83
Peak septal E' (cm/s)	6.89±1.99	6.89±1.82	1.00
Peak septal A' (cm/s)	8.09±1.22	8.57±1.49	0.27
Septal E/E'	9.23±2.56	10.30±2.76	0.21
Peak lateral S' (cm/s)	8.19±2.49	8.06±2.04	0.85
Peak lateral E' (cm/s)	9.08±2.58	9.34±2.41	0.75
Peak lateral A' (cm/s)	8.85±1.84	9.21±2.11	0.57
Lateral E/E'	6.97±1.87	7.57±1.99	0.34

Echocardiographic parameters : LA function

	Dipper (n=20)	Non-dipper (n=20)	*P value*
LA maximal volume (ml/m^2)	27.35±4.31	31.66±6.05	0.01*
LA minimal volume (ml/m^2)	10.62±2.78	10.82±2.59	0.81
LA volume at onset of atrial systole (ml/m^2)	16.83±3.08	19.98±4.69	0.02*
LA expansion index	165.87±43.80	199.42±51.40	0.03*
Conduit volume (ml/m^2)	21.43±6.51	17.05±5.80	0.03*
LA passive emptying volume (ml/m^2)	10.52±3.17	11.68±3.59	0.29
LA passive emptying fraction (%)	38.17±8.30	36.70±8.40	0.58
LA active emptying volume (ml/m^2)	6.21±1.45	9.16±3.28	<0.01*
LA active emptying fraction (%)	37.34±7.81	45.35±8.91	<0.01*
LA ejection fraction (%)	61.39±6.45	65.60±6.29	0.04*
Atrial fraction (%)	40.64±6.48	41.47±6.54	0.69

Tissue Velocity measured by color Doppler tissue imaging of LA

	Dipper (n=20)	Non-dipper (n=20)	*P value*
Reservoir Septal (cm/s)	5.23±1.00	5.36±0.85	0.66
Lateral (cm/s)	6.24±1.98	6.62±1.59	0.51
Inferior (cm/s)	5.73±1.52	5.56±1.17	0.70
Anterior (cm/s)	6.38±1.87	6.34±1.62	0.94
Average (cm/s)	5.89±1.40	5.97±1.05	0.85
Conduit Septal (cm/s)	-5.36±1.42	-5.22±1.33	0.75
Lateral (cm/s)	-6.53±2.24	-6.92±1.65	0.53
Inferior (cm/s)	-5.50±1.56	-5.34±1.89	0.76
Anterior (cm/s)	-6.67±2.25	-6.75±1.91	0.90
Average (cm/s)	-6.01±1.75	-6.06±1.56	0.94
Contractile Septal (cm/s)	-6.66±1.14	-6.85±1.47	0.66
Lateral (cm/s)	-6.95±1.77	-7.68±1.89	0.21
Inferior (cm/s)	-7.44±1.10	-7.66±1.46	0.60
Anterior (cm/s)	-8.05±1.31	-8.46±1.89	0.43
Average (cm/s)	-5.90±0.91	-6.28±1.15	0.25

Strain indices of longitudinal deformation for LA wall

	Dipper (n=20)	Non-dipper (n=20)	*P value*
Septal strain (%)	18.23±6.13	19.45±5.13	0.50
Lateral strain (%)	20.21±6.87	24.46±7.13	0.06
Inferior strain (%)	24.04±7.21	28.82±9.27	0.08
Anterior strain (%)	22.55±6.35	26.93±9.44	0.09
Average strain (%)	***21.26±4.23***	***24.91±5.20***	***0.02****

Strain rate indices of phasic longitudinal deformation for LA wall

	Dipper (n=20)	Non-dipper (n=20)	*P value*
Reservoir Septal SR (s^{-1})	1.16±0.32	1.33±0.36	0.13
Lateral SR (s^{-1})	1.23±0.37	1.51±0.59	0.08
Inferior SR (s^{-1})	1.48±0.30	1.76±0.48	0.03*
Anterior SR (s^{-1})	1.28±0.34	1.50±0.54	0.13
Average SR (s^{-1})	***1.29±0.23***	***1.52±0.27***	***0.01****
Conduit Septal SR (s^{-1})	-1.12±0.34	-0.97±0.40	0.21
Lateral SR (s^{-1})	-1.76±0.58	-1.46±0.41	0.07
Inferior SR (s^{-1})	-1.47±0.45	-1.27±0.34	0.13
Anterior SR (s^{-1})	-1.55±0.42	-1.44±0.61	0.49
Average SR (s^{-1})	***-1.47±0.35***	***-1.28±0.26***	***0.06***
Contractile Septal SR (s^{-1})	-1.48±0.36	-1.53±0.61	0.08
Lateral SR (s^{-1})	-1.10±0.53	-1.54±0.36	0.01*
Inferior SR (s^{-1})	-1.38±0.29	-2.02±0.51	<0.01*
Anterior SR (s^{-1})	-1.08±0.34	-1.80±0.65	<0.01*
Average SR (s^{-1})	***-1.38±0.24***	***-1.68±0.32***	***<0.01***

Pearson coefficient between ANP, NT-proBNP, and volumetric indices

	NTproBNP	ANP
LV mass index	0.410**	0.360*
LA volume index	0.463**	0.347*
LA expansion index	0.047	-0.017
Conduit volume	-0.085	0.050
LA passive emptying volume	0.386*	0.182
LA passive emptying fraction	0.114	-0.040
LA active emptying volume	0.150	0.197
LA active emptying fraction	-0.078	-0.004
LA ejection fraction	0.012	-0.019
Atrial fraction	-0.078	0.093

**: $p<0.05$, **: $p<0.01$*

Pearson coefficient between ANP, NT-proBNP, and strain indices

	NTproBNP	ANP
Septal	-0.229	-0.401*
Lateral	-0.048	-0.122
Inferior	-0.031	-0.091
Anterior	-0.097	-0.028
Average	-0.134	-0.206

**: p<0.05, **: p<0.01*

Pearson coefficient between ANP, NT-proBNP and SR indices

	NTproBNP	ANP
Reservoir Septal	0.200	0.241
Lateral	0.059	0.056
Inferior	-0.216	-0.194
Anterior	-0.273	-0.277
Average	-0.107	-0.089
Conduit Septal	-0.152	-0.021
Lateral	-0.113	-0.113
Inferior	0.157	0.038
Anterior	-0.186	-0.099
Average	-0.117	-0.080
Contractile Septal	0.138	0.050
Lateral	0.014	0.042
Inferior	-0.221	-0.083
Anterior	0.178	0.035
Average	0.041	0.042

**: p<0.05, **: p<0.01*

Summary

- In Non-dipper hypertension patients
  - Exaggerated increase of LA expansion index, LA active emptying volume and LA active emptying fraction
  - LA strain rate during reservoir and atrial systole
  - LA strain during reservoir period

    → Significantly increased compared to Dipper HTN
  - No difference in finding of LA tissue velocity measured by color Doppler tissue imaging

- NT-proBNP and ANP
  - Correlated with LV mass index and LA volume index
  - Only LA strain measured at septal wall correlated with ANP

Conclusion

- Reservoir and booster pump function of LA is exaggerated from very early stage of hypertension of non-dipper patients
- This finding is consistent when measured by conventional volumetric or deformation imaging methods
- Strain rate and strain imaging is useful and more simple method for the evaluation of LA function