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# TEI INDEX MIGHT BE THE UNIQUE ECHOCARDIOGRAPHIC PARAMETER THAT DETECTS HYPERVISCOSITY SYNDROME: A CASE REPORT

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***Abstract:*** Hyperviscosity syndromes are disorders of infrequent prevalence in which changes of rheological characteristics cause increased resistance to blood flow, endothelial dysfunction, tissue ischemia and bleeding. Signs of hyperviscosity syndrome become clinically overt at the point of 4 centipoise units. We present a case of patient with hyperviscosity syndrome due to Waldenstrom's macroglobulinemia with negative records on earlier cardiovascular illnesses. Laboratory diagnostic and standard echocardiography did not show any deviation towards increased cardiovascular risk, heart failure or ischemic heart disease. However, unique clinically significant change that could be indirectly related to hyperviscosity syndrome was found with the myocardium performance index (MPI). Tei-index showed median value of 0.75 corresponding to severe grades of myocardial dysfunction earlier described in the literature for other entities. Comprehensive roles of rheological changes in relation to echocardiography, pathophysiology of myocardial performance and cardiovascular continuum might be interesting point for further investigations.

***Key words:*** hyperviscosity syndrome; Waldenstrom's disease; echocardiography; myocardium performance index (MPI); Tei-index.

## INTRODUCTION

Hyperviscosity syndromes are rare disorders in which changed rheological characteristics cause increased resistance to flow of blood (1). Hyperviscosity syndrome symptoms become clinically overt at the point of 4 centipose units. Usual symptoms include tiredness, lightheadness, neurological complaints or bleeding (2). Mildly increased viscosity is usually seen with policytemia or dehydration, in most cases with no serious adverse health effects. Pathologically increased viscosity could be found with Waldenstrom's macroglobulinemia and the plasma cell abnormalities as multiple myeloma (2). We present a case of patient with hyperviscosity syndrome due to Waldenstrom's macroglobulinemia and negative earlier medical history for cardiovascular illness. We aimed to address echocardiographic changes that might be due to alternated rheological characteristics of the hyperviscosity syndrome.

## CASE REPORT

A 57 year old female with hyperviscosity syndrome due to Waldenstrom's disease referred to outpatient clinic for routine cardiovascular checkup. There was no history of chest pain suggestive for angina and no usual cardiovascular risk factors other than mild grade arterial hypertension. In the period of previous year she did not take the antihypertensive therapy due to lower blood pressure values. Body mass index was of normal type and there were no changes in weight. Patient reported only the stiffed nose sensations and had no neurological complaints. There were no signs of heart failure and no elements for ischemic chest pain or acute coronary syndrome.

Stress ECG test did not reveal changes in the ST segment induced by exertion, while pulse and blood pressure dynamics were in age and gender adjusted physiological range. There were no signs of atherosclerotic lesions in the carotid, vertebrobasilar or peripheral arteries using Doppler ultrasound.

Chemotherapy with fludarabine and chlorambucil was scheduled by hematologist to be started in the course after cardiovascular exam.

### Diagnostics

**Echocardiography:** Echocardiography was performed on Toshiba "Artida" applying the PST30BT 3 MHz cardiology transducer (3).

LVEDD 49.3 mm; LVESD 31.3mm, LVPWd 9.4mm, IVSD 12.4mm, EDV 114.4 ml, FS 36.5%; EF 66.1% (Teichholtz) 63% (Simpson bi-plane), CI 3.6 l/min/m2; HR 75 bpm, CO 5.670 l/min. Aorta: bulbus diameter 33 mm, systolic separation 17m, Vmax 1.39 m/s, peak gradient 7.8mmHg. Transmitral flow: E 0.80 m/sec, A 0.65 m/sec, E/A 1.23, E-DCT 208 msec. PAPS 30mmHg. Morphology of heart valves without pathological signs. Doppler measurements verified trivial grade of mitral and tricuspid valve insufficiency. Heart chambers diameters, volumes and wall thicknesses

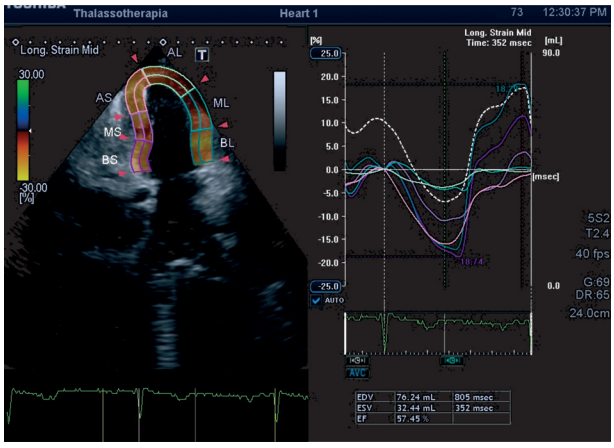


***Figure 1.*** *Longitudinal strain imaging.*

*Figure shows longitudinal strain deformation analysis from four chamber apical view*

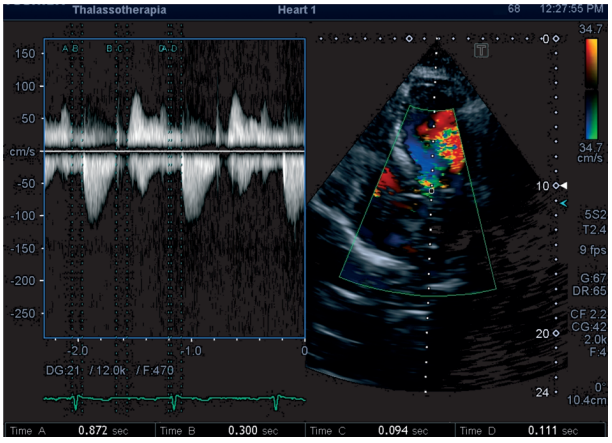


***Figure 2****. Transmitral flow continuous Doppler imaging.*

*Figure shows continuous Doppler imaging from four chamber apical view. Myocardial performance index calculated using formula MPI = (ICT + IRT) / ET. MPI — Myocardial performance index; ICT — isovolumic contraction time(time C); IRT — isovolumic relaxation time (time D); ET — ejection time (time B). MPI = 0.68*

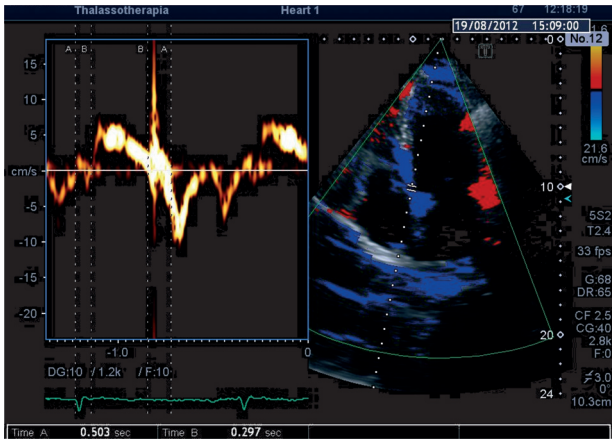


***Figure 3.*** *Power Doppler transmitral flow*

*Figure shows timings (Time a. and b.) in power Doppler of mitral valve motion from four chamber apical view. Myocardial performance index calculated using formula MPI = (a –b) / b. MPI = 0.75.*

were within the physiological ranges. Myocardia motion showed no pathological disturbances, synchronous contractions confirmed by strain rate imaging and no signs of left ventricle systolic dysfunction (Figure 1).

**Myocardium performance index (MPI)-Tei index** calculation was done according to accustomed formula; (isovolumic contraction time + isovolumic relaxation time) / ejection time and considered in referral range if it was ≤ 0.39 ± 0.05 (4). Estimated median MPI-Tei index of our patient was 0.77. Measurements showed variations in relation to the approach: 0.68 using continuous Doppler flow measurement (Figure 2). and 0.75 by power weighted transmitral tissue Doppler (Figure 3).

## DISCUSSION

Perspective of echocardiography imaging in relation to the rheological characteristics of the blood has not been systematically appraised. We expected that alternated rheological changes might stem or influence the alternations of blood flow and myocardial wall motion physiology. Prevalence of Waldenstrom's disease is expected to be approximately 3 x $10^{-6}$, subsequently it is rather difficult to gain the significant number of population for additional compares (5).

Mild grades of rheological changes could be found in patients with endothelial dysfunction, diabetes, hypercholesterolemia and chronic renal disease (6, 7). Alternated rheological features even might be the in part responsible for chronic disorders born composited noxious effects. However, clinically overt hyperviscosity syndromes are generally occurring due to increased serum immunoglobulins as in Waldenstrom's disease (2). Pathologically increased viscosity of hemato-

logical dissorderseventualy causes significant restrictions of blood flow in the central nervous system or peripheral tissues. Our patient had viscosity of undoubtedly non-physiological range and at the same time did not have any medical record of neurological or cardiovascular disorders. Applied diagnostics tests from conventional cardiovascular backgrounds were all of referral ranges. Standard echocardiographic exam of patient did not find any specific deviation within morphology, systolic or diastolic functions using two dimensional, m-mode or deformation analyzes. Ultrasonic appraisal of left ventricle ejection fraction has showed diagnostic limitations due to lesser sensitivity in detecting acute disease or therapy born changes and differences in regard to calculation methodology applied. We found relatively congruent results of left ventricle ejection fractions in range 57–66% using motion mode analyzes (Teichholtz), volumetric (Simpson bi-plane) and longitudinal strain imaging. Diastolic function is clinically more complex issue with several of disputes; limited in reproducibility and interest variability, mediated through heart frequency, chambers loading hemodynamics and the age of patient. Our patient had normal transmitral flow pattern showing no signs of diastolic dysfunction.

Partiality of systolic and diastolic components in global heart function were effectively overcome by development of myocardial performance index (MPI) by Tei et al (4). Calculation represents summation of termination and commencement time of mitral flow withdrawn from the ejection time, i.e. isovolumic relaxation time and isovolumic contraction time divided by ejection time. Median values of MPI were found to be discriminatory different in patients with heart diseases to healthy individuals, and of relatively unchangeable characteristics within wide range of heart frequencies (8, 9). Preload conditions significantly increase of Tei index in healthy controls in compare to patients that survived the myocardial infarction (10). Afterload is also found to be increasing factor to the MPI (11). Left and right heart performance measured by indexes was significantly intercorrelated after the acute infarction and of prognostic characteristic for reinfarction or heart failure rates for the duration of follow up even to one year (12, 13). Restitution of left ventricle MPI was shown to be of prolonged timeline in compare to one of right ventricle. Index has demonstrated satisfactory levels of correlations with invasive hemodynamic measurements and changes due to chronic heart failure, mitral or aortic valve diseases (14, 15). Sensitivity and prognostic usefulness were also verified in detecting of functional changes caused by acute myocardial infarction or impairments of coronary circulation (13, 16, 17). Significant echocardiographic landmark of hyperviscosity syndrome in our patient was found in myocardial performance index (Tei), that was estimated 0.75 i.e. resembling values of severely impaired structure and function (8, 13, 17, 18). Changes in loading conditions could be considered best responsible for the observed degree of impairment. Earlier study in this manner described greater influence of load characteristics on myocardial performance index, rather than acute changes in ejection fraction or the elasticity of myocardium (19). Although inflow and outflow profiles expectantly seems to be restricted in hyperviscosity syndrome there were no conspicuous changes in conventional transvalvular doppler measurements, systolic or diastolic functions.

Diffuse atherosclerotic process causes endothelial dysfunction and negatively influences function of several organ systems, particularly coronary arteries, peripheral arteries, renal vascular bed, arterial network of the eye. Deficient transport of oxygen to the central nervous system or peripheral tissues becomes particularly underprivileged if associated with chronic atherosclerotic comorbidities. Course of diseases within the cardiovascular continuum seems to be negatively influenced by the increase in blood viscosity (6, 7). Although our patient had no signs of increased cardiovascular risk on laboratory diagnostics, diagnostic accuracy might in this part be less representative due to hyperviscosity (20).

This is the first case addressing relationship of echocardiography measurements to alternated rheological characteristics in patient with Waldenstrom's disease and verified pathological results of the blood viscosity testing (viscosity over 4, as the initial point of hyperviscose syndrome). Myocardial performance index was found to be of severely impaired grade, although there were no signs of earlier cardiovascular diseases and all of conventional diagnostics were within healthy referral ranges.

## CONCLUSION

Tei index could be recommended for routine clinical practice because of simplicity, noninvasiveness, increased overall sensitivity. Relatively high negative predictive value seems to rule out severe systemic disease and localized alternations of cardiovascular morphology or function.

### Conflict of interest

None declared

### List of abbreviations

**MPI** — myocardium performance index;
**ECG —** electrocardiography;
**ST —** segment of electrocardiography;

**LVESD —** left ventricle end systolic dimension;
**LVEDD —** left ventricle end diastolic dimension;
**LVPW —** left ventricle posterior wall thickness;
**IVSD —** interventricular septum diastolic thickness;
**V max —** maximal velocity;
**LVEF** — left ventricle ejection fraction (%);
**E —** early ventricular filling velocity (m/s);
**E-DCT —** E wave deceleration time (s);
**A —** late (atrial) filling velocity(m/s);
**PAPS —** pulmonary artery systolic pressure (mmHg).

## Appendix
## (data not shown; remainder diagnostics)

**Complete blood count**: erythrocytes sedimentation rate 135mm/3.6ks, Erytrocyte count 3.48 x $10^{12}$, Hematocrit 0.32, Hemoglobin 110 g/l, Mean corpuscular volume 97 fl, Platelets counts 299 x $10^{9}$, Leucocytes 6.2 x $10^{9}$ (no pathological changes within differential analyzes of white blood cells).

**Biochemistry:** serum glucose 4.6 mmol/l, urea 3.8mmol/l, creatinine 69umol/l, sodium 139 mmol/l, potassium 5.2 mmol/l, alanine aminotransferase (ALT) 25 IU/l at 37'C, aspartate aminotransferase (AST) 24 IU/l at 37'C, gamma glutamyltransferase (GGT) 9 IU/l at 37'C, triglycerides 0.97 mmol/l, total cholesterol 3.86 mmol/l, high density lipoprotein (HDL) 1.13 mmol/l, low density lipoprotein (LDL) 2.36 mmol/l. Urine biochemistry no signs of proteinuria. 24-urine collection no signs of microalbuminuria. Thyroids hormones within the reference range. Blood viscosity 4 centipoise (cP) units.

**Eye fundus:** clear lines the optical nerve papilla. Positive Gunn's shadows (grade III). No signs of bleeding or exudations.

## Sažetak

# TEI INDEKS MOŽE BITI JEDINSTVEN EHOKARDIOGRAFSKI PARAMETAR ZA DETEKCIJU SINDROMA HIPERVISKOZNOSTI: PRIKAZ SLUČAJA

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Sindromi hiperviskoznosti su serije poremećaja koji se retko javljaju, čije promene, reološke prirode, utiču na povećanu otpornost protoka krvi, ispad funkcije endotela, ishemiju tkiva i krvarenje. Znaci sindroma hiperviskoznosti postaju klinički jasni pri vrednostima viskoznosti krvi od 4 centipuaza (cP). Prikazan je slučaj pacijenta sa sindromom hiperviskoznosti krvi kod Waldenstrom-ove makroglobulinemije sa negativnom anamnezom o prethodnim kardiovaskularnim bolestima. Laboratorijska dijagnostika i i standardna ehokardiografija nisu pokazale nikakve znake u smislu povećanog rizika od određenih kardiovaskularnih bolesti, srčanog zastoja ili ishemičnih bolesti srca. Međutim, jedinstvena klinički značajna promena, koja bi indirektno mogla biti u vezi sa sindromom hiperviskoznosti je nađena u MPI indeksu (myocardium performance index). Tei-index je pokazao srednju vrednost od 0,75, ukazujući na ozbiljne stadijume miokardne disfunkcije, ranije opisane u literaturi za druge entitete. Značajna uloga reoloških promena krvi u odnosu sa ehokardiografijom, patofiziologijom rada srčanog mišića i kardiovaskularnim kontinuumom i može biti zanimljiv predmet daljeg istraživanja.

**Ključne reči**: hiperviskozni sindrom, Waldenstrom-ova bolest, ehokardiografija, MPI, Tei-index.

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