Pregledni članak / Review article

Uloga ehokardiografije u dijagnozi plućne hipertenzije

Role of echocardiography in diagnosis of pulmonary hypertension

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SAŽETAK: Plućna hipertenzija (PH) je progresivni proces koji vodi do preopterećenja desne klijetke (DK), hipertrofije, dilatacije i zatajenja DK. U slučajevima s kroničnim zatajivanjem srca, ovo je stanje povezano s težim simptomima i lošijim ishodima.

Transtorakalnu ehokardiografiju treba učiniti u slučaju sumnje na PH, a pretragom se može utvrditi nekoliko varijabli povezanih s hemodinamikom desnog srca. Nekoliko varijabli je važno za procjenu funkcije DK, koji mogu biti razlogom lošeg ishoda: dimenzije i volumeni desne pretklijetke i klijetke, promjene funkcionalnog područja, sistolički pomak trikuspidnog prstena (TAPSE), indeks miokardne performanse, veličina i kolapsibilnost donje šuplje vene, S brzina procijenjena tkivnim Doplerom, a dodatne informacije mogu se dobiti primjenom naprednih ehokardiografskih tehnika, kao što su deformacija, postotak deformacije te 3D-ehokardiografija. Procjena PH temeljena na Doppler ehokardiografiji nije pogodna za procjenu blage, asimptomatske PH. Ehokardiografija se može preporučiti kao alat za probir kod određenih bolesti, praćenje PH te procjenu indiciranosti kateterizacije desnog srca.

KLJUČNE RIJEČI: plućna hipertenzija, funkcija desne klijetke, ehokardiografija.

SUMMARY: Pulmonary hypertension (PH) is a progressive process that leads to right ventricular (RV) overload, hypertrophy, dilatation and RV failure. In cases with chronic heart failure, this condition is associated with more severe symptoms and worse outcomes.

Transthoracic echocardiography can give several parameters which correlate with right heart haemodynamics, and should be performed in a case of suspected PH. Several parameters are important for estimation of the RV function, which can be reason for poor outcome: right atrial and ventricular dimensions and volumes, functional area changes, tricuspid annular plane systolic excursion (TAPSE), myocardial performance index, inferior vena cava size and collapsibility, S velocity estimated by Tissue Doppler Imaging, and additional information obtained from the advance echocardiograpic techniques, like strain, strain rate, three-dimensional echocardiography. Estimation of PH based on Doppler echocardiography measurements is not suitable for screening of mild, asymptomatic PH. Echocardiography can be recommended as a screening tool for specific diseases, follow up PH, and assessment when right heart catheterization is indicated.

KEYWORDS: pulmonary hypertension, right ventricular function, echocardiography.

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Uvod

Plućna hipertenzija se može se pronaći u više kliničkih stanja, sa specifičnim karakteristikama koje su klasificirane u pet kliničkih skupina u novim Smjernicama Europskog kardiološkog društva za dijagnostiku i liječenje plućne hipertenzije. Ova stanja imaju drugačiju epidemiološke, patološke, genetske ili dijagnostičke karakteristike, ali bolest ima sličnu kliničku ekspresiju i zahtijeva specifično liječenje.

Klinička klasifikacija plućne hipertenzije[1]:

I. Plućna arterijska hipertenzija (PAH): idiopatska PAH, nasljedna PAH, uzrokovana lijekovima i toksinima, PH povezana s bolestima vezivnog tkiva, portalna hipertenzija, urođene bolesti srca, kronična hemolitička anemija, itd.;

Introduction

Pulmonary hypertension can be found in multiple clinical conditions, with specific characteristics, which were classified into 5 clinical groups in the new European Society of Cardiology Guidelines for the diagnosis and treatment of pulmonary hypertension. These conditions have different epidemiology, pathology, genetics, diagnostic features, but the diseases have similar clinical expression and need a specific treatments.

Clinical classification of pulmonary hypertension[1]:

I. Pulmonary arterial hypertension (PAH): idiopathic PAH, heritable PAH, drug and toxins induced, PH associated with

II. Plućna hipertenzija zbog bolesti lijevog srca, zbog sistoličke i dijastoličke disfunkcije lijeve klijetke i valvularnih bolesti srca;

III. Plućna hipertenzija zbog plućnih bolesti i/ili hipoksemije;

IV. Kronična tromboembolijska plućna hipertenzija;

V. Plućna hipertenzija s nejasnim i/ili višestrukim mehanizmima.

Plućna hipertenzija (PH) je hemodinamsko i patofiziološko stanje definirano kao povećanje srednjeg tlaka u plućnoj arteriji (PAP) >25mmHg u mirovanju koja se ocjenjuje kateterizacijom desnog srca. Plućna arterijska hipertenzija definirana je kao kliničko stanje karakterizirano prisutnošću prekapilarne plućne hipertenzije u nedostatku drugih uzroka za prekapilarnu PH, kao što su PH uslijed plućne bolesti, kronična tromboembolijska PH ili druge rijetke bolesti. U svakom kliničkom stanju, PH je prekapilarna, osim PH zbog bolesti lijevog srca koje karakterizira post-kapilarna PH.

Bez obzira na patogenezu nastanka, PH je progresivni proces koji dovodi do preopterećenja desne klijetke (DK), hipertrofije, dilatacije i zatajivanja DK. PH se javlja kao progresivna ozljeda plućne vaskularne mreže koja uzrokuje endotelnu disfunkciju s karakterističnim patološkim značajkama kao što su in-situ tromboza, hipertrofija glatkih mišića, intimalna i adventicijalna proliferacija i vazokonstrikcija. Bolest može biti reverzibilna do nastanka opstruktivnih promjena plućne mikrociruklacije. Napredna vaskularna lezija dovodi do ireverzibilnih promjena plućne vaskularne mreže.

Osim opstruktivnih promjena plućne mikrocirkulacije, stupanj napredovanja ovisi o utjecaju PH na funkciju DK. Nedovoljna prilagodba kontraktilnosti miokarda DK je jedan od važnih razloga za napredovanje zatajivanja srca u kronično prekomjerno opterećenoj DK. Zatajivanje DK dovodi do loše kvalitete života i loše prognoze kod ovakvih bolesnika[1-7].

Procjena plućne hipertenzije ehokardiografijom

Transtorakalna ehokardiografija (TTE) ima središnje mjesto između neinvazivnih postupaka za otkrivanje i procjenu PH. Ehokardiografija može dati važne informacije u otkrivanju PH i otkrivanju etioloških razloga za PH (**Slika 1**). TTE nam također može dati podatke o hemodinamskom utjecaju PH na dimenziju i funkciju DK[8,9].

connective tissue diseases, portal hypertension, congenital heart diseases, chronic haemolytic anaemia, etc.;

II. Pulmonary hypertension due to the left heart diseases, because of systolic and diastolic dysfunction of the left ventricle and valvular heart diseases;

III. Pulmonary hypertension due to lung diseases and/or hypoxaemia;

IV. Chronic thromboembolic pulmonary hypertension;

V. Pulmonary hypertension with unclear and/or multifactorial mechanisms.

Pulmonary hypertension (PH) is haemodynamic and pathophysiological condition defined as an increase in the mean pulmonary arterial pressure (PAP) >25mmHg at rest assessed by right heart catheterization. The term pulmonary arterial hypertension was defined as a clinical condition characterized by the presence of precapillary pulmonary hypertension in the absence of other causes of precapillary PH, such as PH due to lung diseases, chronic thromboembolic PH or other rare diseases. In all clinical condition, PH is precapillary, except for PH due to left heart diseases, characterized by post capillary PH.

Regardless of the pathogenesis of occurrence, PH is a progressive process which leads to right ventricular (RV) overload, hypertrophy, dilatation and RV failure. PH occurs as a progressive injury of the pulmonary vascular bed which has produced endothelial dysfunction with the characteristic pathological features like in situ thrombosis, smooth muscle hypertrophy, intimal and adventitial proliferation and vasoconstriction. Disease can be reversible until obstructive changes in pulmonary microcirculation have occurred. Advanced vascular lesion leads to irreversible changes of the pulmonary vascular bed.

Beside the obstructive changes in pulmonary microcirculation, the rate of progression depends on the influence of the PH to the RV function. The inadequate adaptation of the RV myocardial contractility is one of the important reasons for the progression of the heart failure in a chronically overloaded right ventricle. The RV failure leads to poor quality of life and prognosis in this patients[1-7].

Assessment of pulmonary hypertension by echocardiography

Transthoracic echocardiography (TTE) has a central position between noninvasive procedure for discovering and estimation of PH. Echocardiography can give important infor-

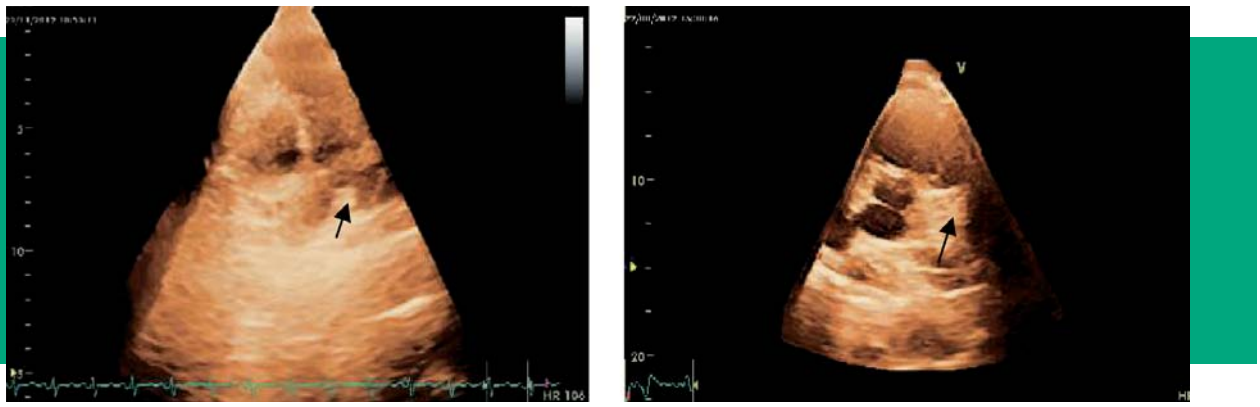

Figure 1. *Threedimensional image which show a thrombus at the bifurcation of the pulmonary artery (left) and a big thrombus just below the pulmonary artery (right) which can be a reason for development of pulmonary hypertension.*

Procjena sistoličkog tlaka plućne arterije (SPAP) temelji se na najvećoj brzini mlaza trikuspidne regurgitacije. Pojednostavljena Bernoullijeva jednadžba se koristi za procjenu PH iz najviše brzine trikuspidne regurgitacije. U formuli, SPAP predstavlja sistolički tlak plućne arterije, pri čemu je Vmax TR predstavlja maksimalnu brzinu trikuspidne regurgitacije dobivenu CW Doppler ehokardiografijom, a RAP je tlak desne pretklijetke. Vrijednost RAP-a je 5-10 mmHg, ovisno o promjeru i respiratornoj varijaciji donje šuplje vene[3] (**Slika 2**).

mation in detection of PH and discovering some of the etiological reasons for PH (**Figure 1**). TTE can also give us information about the hemodynamic impact of the PH on RV chambers and RV function[8,9].

The estimation of the systolic pulmonary artery pressure (SPAP) is based on the peak velocity of the jet of tricuspid regurgitation. A simplified Bernoulli equation is used to estimate PH from the peak velocity of the tricuspid regurgitation. In formula, SPAP is systolic pulmonary artery pressure, where Vmax of the TR is maximal velocity of the tricuspid regurgitation obtained from CW Doppler echocardiography, and RAP is the right atrial pressure. The value of RAP is 5-10 mmHg, depending on the diameter and respiratory variation of the inferior vena cava[3] (**Figure 2**).

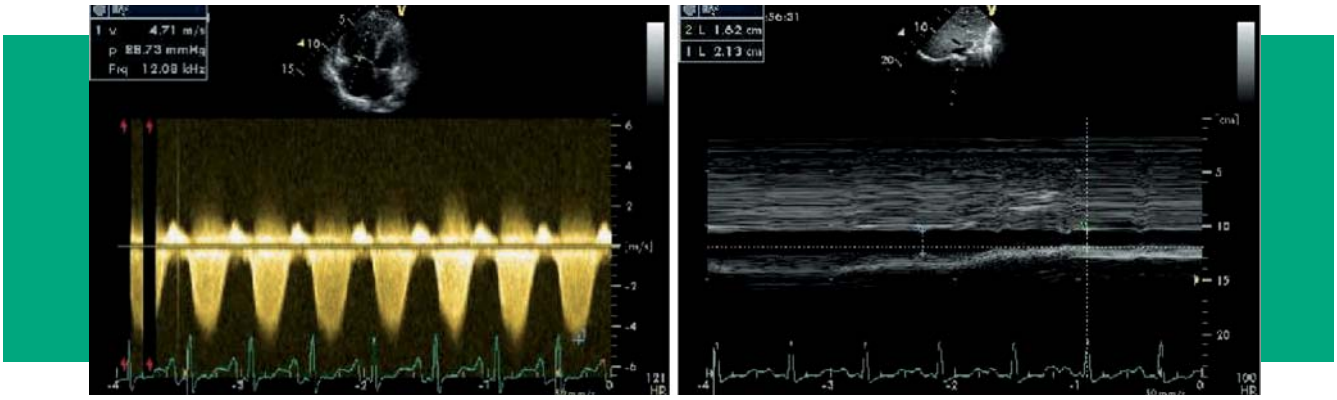

Figure 2. *Continuous wave Doppler on tricuspid valve which show severe tricuspid regurgitation, with maximal velocity of 4.7 m/s (right image); Estimated systolic pulmonary arterial pressure, using Bernoulli equitation and inferior vena cava size and collapsibility (left image) is about 100 mmHg.*

SPAP (mmHg) = 4 (Vmax TR)^2 + RAP

Teška trikuspidna regurgitacija je povezana s malom brzinom mlaza zbog smanjenog transvalvularnog gradijenta između desnog atrija i DK, čime se može podcijeniti PH.

Nadalje, Bernoullijeva jednadžba se može koristiti za procjenu srednjeg plućnog tlaka (srednji PAP) i dijastoličkog plućnog tlaka (DPAP) pomoću brzine plućne regurgitacije (PR) na početku krivulje i na kraju prikazane krivulje Dopplera (**Slika 3**).

SPAP (mmHg) = 4 (Vmax of the TR)^2 + RAP

Severe tricuspid regurgitation is associated with a low jet velocity, because of the reduced transvalvular gradient between RA and RV, and can underestimate pulmonary hypertension.

Furthermore, the Bernoulli equation can be used to estimate the mean pulmonary pressure (mean PAP) and diastolic pulmonary pressure (DPAP) by the velocity of the pulmonary regurgitation (PR) at the beginning of the curve and at the end of the curve (**Figure 3**).

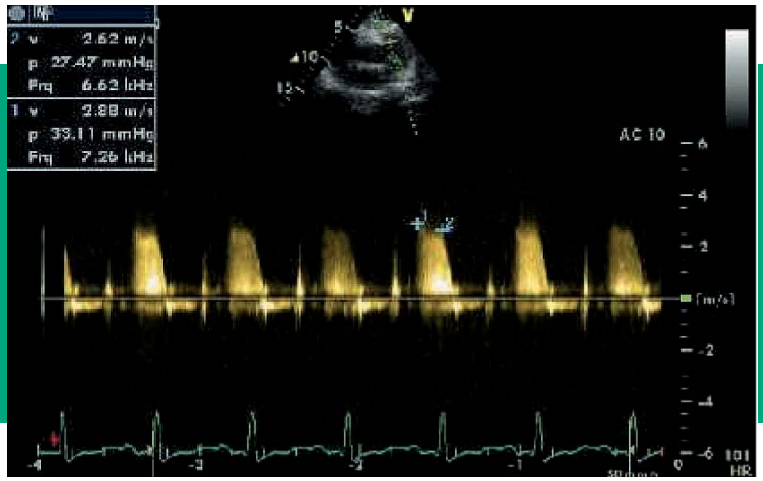

Figure 3. *Continuous wave Doppler on pulmonary regurgitation in patient with pulmonary hypertension, which can be used to estimate mean and diastolic pulmonary pressure.*

Srednji PAP (mmHg) = 4 (V na početku krivulje PR)^2 + RAP

DPAP (mmHg) = 4 (V na kraju krivulje PR)^2 + RAP

U ESC smjernicama postoje definirani kriteriji za otkrivanje prisutnosti PH na temelju najveće brzine TR i Dopplerom izračunatog plućnog arterijskog tlaka u mirovanju[1]:

1. Ehokardiografska dijagnoza — mala vjerojatnost PH (klasa I, razina B)

— brzina TR <2,8 m/sec, SPAP <36 mmHg i bez dodatnih ehokardiografskih varijabli koje upućuju na PH

2. Ehokardiografska dijagnoza — moguća PH (klasa II, razina C)

— brzina TR <2,8 m/sec, SPAP <36 mmHg, prisutnost dodatnih ehokardiografskih varijabli koje upućuju na PH

— brzina TR <2,9-3,4 m/sec, SPAP <37-50 mmHg, s ili bez dodatnih ehokardiografskih varijabli koje upućuju na PH

3. Ehokardiografska dijagnoza — vjerojatna PH (klasa I, razina B)

— brzina TR <3,4 m/sec, SPAP <50 mmHg, s ili bez dodatnih ehokardiografskih varijabli koje upućuju na PH

4. Doppler ehokardiografije prilikom opterećenja nije preporučena za probir PH (klasa III, razina C).

Procjena PH temeljena na mjerenju Doppler ehokardiografijom nije pogodna za ispitivanje blage, asimptomatske PH. Ako je ehokardiografska dijagnoza PH moguća, bez simptoma i čimbenika rizika za plućne arterijske hipertenzije, preporuča se ehokardiografsko praćenje (klasa I, razina C), međutim, ako postoji prisutnost simptoma i povezanih stanja ili faktora rizika za plućnu arterijske hipertenziju, može se razmotriti kateterizacija desnog srca (klasa IIb, razina C)[1].

Ehokardiografija se može preporučiti kao alat za probir za ocjenu PH zbog bolesti pluća (klasa I, razina C), detekciju PH u simptomatskih bolesnika s bolestima jetre i/ili kandidata za transplantaciju jetre (klasa I, B razina) te za otkrivanje PH u simptomatskih bolesnika s bolestima vezivnog tkiva (klasa I, razina C)[1].

Ehokardiografija je i jedna od metoda za praćenje uspješnosti terapije. Procjena pomoću TTE se mora učiniti prije terapije, 3-4 mjeseca nakon početka terapije ili promjena i u slučaju kliničkog pogoršanja.

Važnost procjene funkcije desne klijetke

Neki ehokardiografski parametri su utvrđeni kao važni za prognozu bolesti. Bolesnici sa PH koji razviju disfunkciju DK imaju lošu kvalitetu života i loš ishod. Bolesnici s kroničnim zatajivanjem srca i PH te smanjenom funkcijom RV su posebno povezani s lošim ishodom.

Varijable povezane s lošijom prognozom su perikardni izljev i sistolički pomak trikuspidnog prstena (TAPSE) manje od 1,5 cm. Smanjena TAPSE, kao marker za smanjenu logitudinalnu funkciju DK je povezan s većim rizikom od smrti ili hospitalizacije.

Za procjenu funkcije DK važno je nekoliko parametara: dimenzije i volumeni desne pretklijetke i klijetke, promjene funkcionalnog područja (FAC%), D-oblik lijeve klijetke, sistolički pomak trikuspidnog prstena (TAPSE), indeks miokardne performanse, veličina i kolapsibilnost donje šuplje vene, S brzina procijenjena tkivnim Dopplerom, i dodatne informacije dobivene naprednim ehokardiografskim tehnikama, kao što su deformacija, postotak deformacije, 3D-ehokardiografija[10-14] (**Slike 3-5**).

Mean PAP (mmHg) = 4 (V at the begining of the PR curve)^2 + RAP

DPAP (mmHg) = 4 (V at the end of the PR curve)^2 + RAP

In the ESC guidelines there are defined criteria for detecting the presence of PH based on TR peak velocity and Doppler calculated pulmonary artery pressure at rest1:

1. Echocardiographic diagnosis — PH unlikely (Class I, Level B)

TR velocity <2.8 m/sec, SPAP <36 mmHg and no additional echocardiopgraphic variables suggestive of PH

2. Echocardiographic diagnosis — PH possible (Class IIa, Level C)

TR velocity <2.8 m/sec, SPAP <36 mmHg, presence of additional echocardiopgraphic variables suggestive of PH

TR velocity <2.9-3.4 m/sec, SPAP <37-50 mmHg, with or without additional echocardiographic variables suggestive of PH

3. Echocardiographic diagnosis — PH likely (Class I, Level B)

TR velocity <3.4 m/sec, SPAP <50 mmHg, with or without additional echocardiopgraphic variables suggestive of PH

4. Exercise Doppler echocardiography is not recommended for screening of PH (Class III, Level C).

Estimation of PH based on Doppler echocardiography measurements is not suitable for screening of mild, asymptomatic PH. If the echocardiographic diagnosis of PH is possible, without symptoms and risk factors for pulmonary arterial hypertension, echocardiographic follow-up is recommended (Class I, Level C); however, if there is presence of symptoms and associated conditions or risk factors for pulmonary arterial hypertension, right heart catheterization may be considered (Class IIb, Level C)[1].

Echocardiography can be recommended as a screening tool for PH assessment due to lung diseases (Class I, Level C), discovering PH in symptomatic patients with liver diseases and/or in candidates for liver transplant (Class I, Level B), and for detection of PH in symptomatic patients with all other connective tissue diseases (Class I, Level C)[1].

Echocardiography is one of the methods for following up the success of the therapy. Estimation by TTE has to be done prior to therapy, 3-4 months after therapy initiation or changes and in case of clinical worsening.

The importance of the right ventricular function assessment

Some echocardiographic parameters have been established as important for prognosis of the disease. Patients with PH who develop right ventricular dysfunction have a poor quality of life and poor outcome. Patients with chronic heart failure co-existence of PH and impaired RV function are associated with particularly poor outcome, as well.

Parameters associated with worse prognosis are pericardial effusion and tricuspid annular plane systolic excursion (TAPSE) less than 1.5 cm. A reduced TAPSE, as a marker for reduced longitudinal RV function, is associated with a higher risk of death or hospitalization.

Several parameters are important for estimation of the right ventricular function: right atrial and ventricular dimensions and volumes, functional area changes (FAC%), D-shape of the LV, tricuspid annular plane systolic excursion (TAPSE), myocardial performance index, inferior vena cava size and

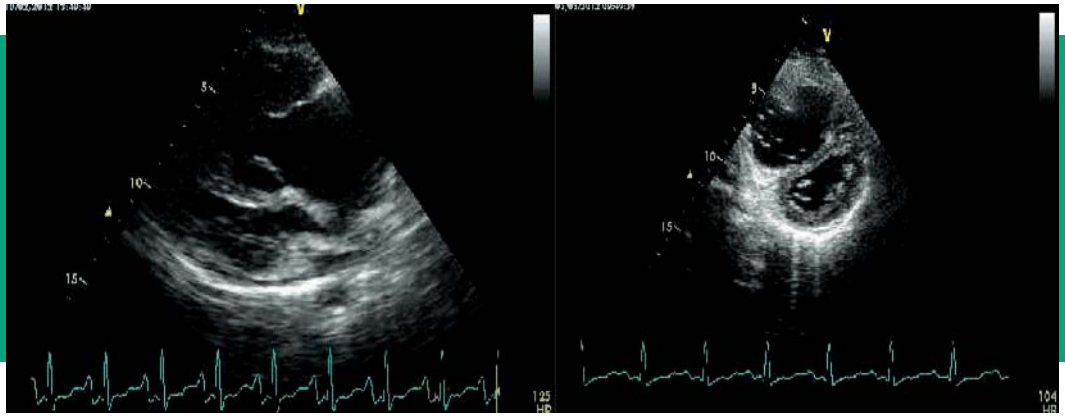

Figure 4. *Two dimensional parasternal long axis view on which is showen a small left ventricle, with a big right ventricle (left image), and D shape of the left ventricle because of the right ventricle overload on the short axis view (right image).*

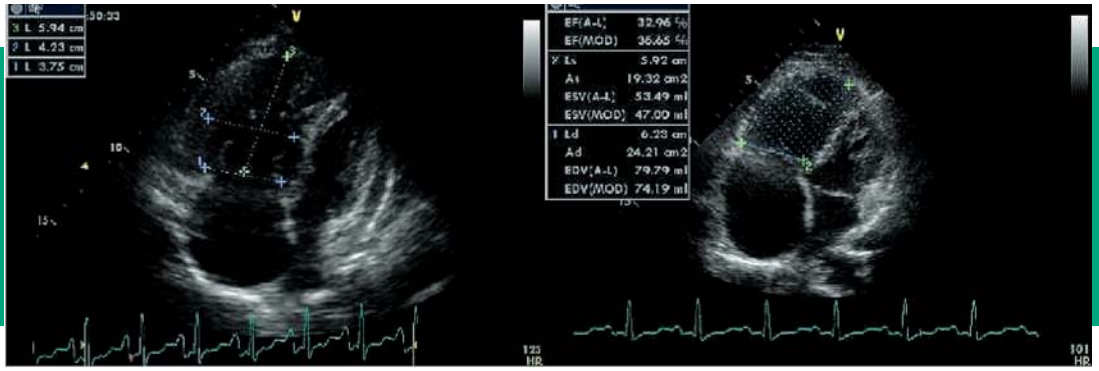

Figure 5. *Two dimensional four chamber view: increased dimension of the right ventricle (left image) and estimation of the right ventricle function with functional area changes method. There is a slightly decreased right ventricular systolic function despite of the enlarged right ventricle.*

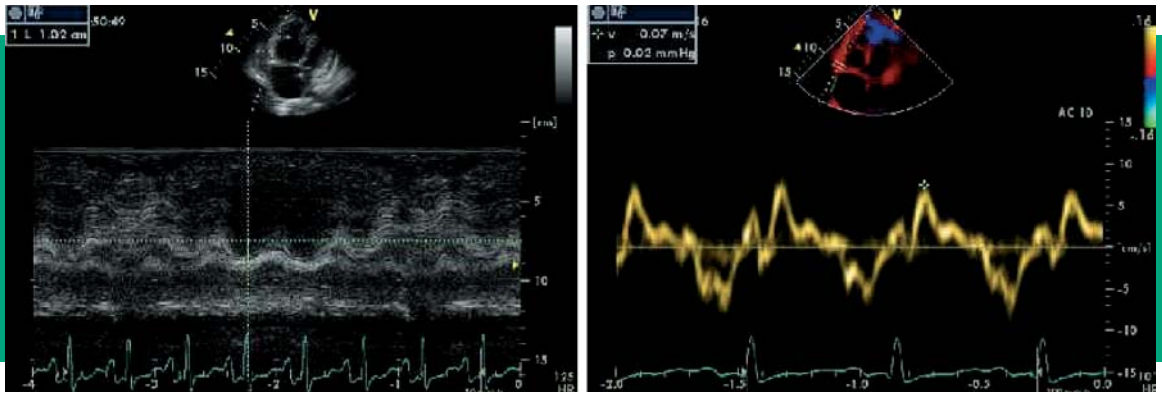

Figure 6. *Estimation of tricuspid annular plane systolic excursion by M-mode which show reduced value as a marker of reduced longitudinal function of the right ventricle (left image). Reduced systolic velocity on the Tissue Doppler Imaging (right image) less than 0.1m/s or 10cm/s, as a marker of reduced systolic right ventricular function.*

Zaključak

Ehokardiografija je neinvazivan, jednostavan alat koji može pomoći u otkrivanju PH kod bolesnika, utjecaja PH na funkciju DK, procjeniti ozbiljnost PH, otkrivanju mnogih stanja koja mogu biti uzrokovati PH, praćenju bolesnika tijekom bolesti te nakon nekih postupaka i terapije te davanju prognostičkih podataka o tim bolesnicima.

Ehokardiografske varijable mogu pomoći u prognostičkoj stratifikaciji rizika bolesnika s plućnom hipertenzijom.

Conclusion

Echocardiography is a noninvasive, easy tool which can help to discover PH in patients and the PH influence on the RV function, estimate the PH severity, discover many conditions which can be responsible causes for PH, follow up

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patients during the disease and after some procedures and therapy, and give prognostic information of these patients.

Echocardiographic parameters can help for prognostic risk stratification of pulmonary hypertension patients.

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