Left ventricular or Bi-ventricular assist device? How dobutamine stress echocardiography can untie the dilemma of right ventricular dysfunction.

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Short title: DSE to assess the RV function before LVAD implant

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Right ventricular failure (RVF) after left ventricular assist device implantation (LVAD) is associated with increased mortality, higher risk of bleeding, re-operation, renal insufficiency and longer hospitalization [1,2]. Prognosis of patients treated with biventricular assist devices (BiVAD) is worse than prognosis of those treated with LVAD [1,3]. Although markers and scores of risk to assess the RVF after LVAD implant can support the decision on the most suitable surgical approach, the final choice for individual patient can be challenging [4-6]. The present report represents a clinical case where the final decision has been guided by dobutamine stress echocardiography (DSE), a tool that is not usually reported in the stratification of RVF risk assessment [7].

A 33-year-old Caucasian man with a 3-year history of heart failure (HF) due to dilated cardiomyopathy was hospitalized due to worsening HF, with visceral congestion despite high dosage oral furosemide (250 mg bd) and periodic infusions of levosimendan [8]. The patient experienced 6 hospitalizations for worsening HF despite maximal medical therapy and a cardiac resynchronization therapy-defibrillator device in the last 3 years. The patient was listed for heart transplantation (HTx), but due to clinical conditions (symptoms and signs of congestion and hypoperfusion, "wet and cold" profile at admission, hepatorenal dysfunction, Interagency Registry for Mechanically Assisted Circulatory Support [INTERMACS] profile 4 plus "frequent flyer" modifier) and low estimated probability to get a heart within a short time due to size (110 kg x 190 cm) and uncommon blood group type (B), LVAD implant was considered.. Risk of early RVF emerged as a potential peri-operative risk, from that the dilemma to treat the patient with a LVAD versus a BiVAD or a total artificial heart. Echocardiography showed severe left ventricle (LV) enlargement (Figure 1A) and systolic dysfunction (LV ejection fraction [LVEF] 20%; Online Videos 1–2). A mild functional mitral regurgitation was observed, associated with slightly increased pulmonary artery pressure

(PAP), and moderate right ventricular (RV) dysfunction. Tricuspid annulus (TA) was dilated (46 mm, Figure 1B; TA diameter >43 mm is associated with increased mortality after LVAD [5]), although longitudinal peak strain of the RV (-14%) suggested a decreased risk of post-operative RVF (proposed cut-off of risk: value above -9.6% [9]). After proper decongestion with intravenous furosemide, the right heart catheterization (RHC, Table) showed a low output state with slightly increased PAP (36/24, mean 28 mmHg), pulmonary capillary wedge pressure (PCWP: 22 mmHg) and right atrium pressure (RAP: 12 mmHg). Pulmonary hypertension (PH) was reverted with low-dose sodium nitroprussiate (SNP 0.5 mg/kg/min): PAP of 39/15 and mean 25mmHg.

Scores to assess RV function based on hemodynamic parameters demonstrated conflicting results, in fact the RAP/PCWP ratio (0.54, after SNP 0.55) did not show a risk of RVF (>0.63 of RAP/PCWP ratio is associated with risk of RVF), whereas the RV stroke work index (RVSWI: 276 mmHg*mL/m^2; after SNP: 218 mmHg*mL/m^2) showed a risk of RVF after LVAD implantation [4]. The RVSWI, calculated as (mean PAP – RAP)*cardiac index CI/heart rate is associated with increased risk of RVF for values <300 mmHg*mL/m^2. After a 48-hour infusion of SNP (0.25 μg/kg/min) associated with usual patient's drug regimen echocardiographic and RHC parameters showed just a mild improvement, but still unable to give a help in planning the most suitable surgical option. Based on a previous study on a limited number of cases [7], we decided to assess the functional capacity of the RV by DSE (increasing dosage from 5 to 20 μg/Kg/min). In particular a significant increased of the TA plane systolic excursion (TAPSE: from 16 to 26 mm) and fractional area change (FAC: from 23 to 40%) was observed compared with baseline (Table, Online Videos 3-4), together with increase in pulmonary artery systolic pressure (39 to 59 mmHg). LVAD implant was planned, and intra-aortic balloon counterpulsation for 48 hours before surgery was performed. On day 1after surgery intra-aortic ballon pump was removed, on day 2 SNP was suspended, on day 3 inotropic support

was stopped. The patient was discharge after 3 weeks since the date of surgery. No signs of RVF occured. After 6 months since the LVAD implantation, the patient was asymptomatic without re-hospitalizations.

Pharmacological adrenergic stimulation with esclating doses is utilized to elicit contractile response in chronically hypokinetic myocardium due to various cardiac conditions, in order to predict regional and/or global improvement in myocardial function after pharmacological or interventional/surgical treatment (e.g. revascularization). The LV is the main focus of attention rather than the RV. The use of DSE for evaluating the RV functional reserve in LVAD candidates and recipients has been proposed in a short paper [7], but other echocardiographic and hemodynamic parameters appear to be considered, alone or combined into multiparametric scores [4,6]. However, individual parameters and scores may provide contradictory results,, while DSE allow visual assessment of global changes in RV function beyond calculation of specific parameteric scores.

Nevertheless, in patients who are chronically dependent from inotropic therapy, especially if high-dose or with multiple drugs (INTERMACS profile 3 or less), DSE is probably neither feasible nor appropriate in most cases. In patients with INTERMACS profile 4 the risk-benefit ratio of mechanical circulatory support may be unclear, especially when the patient is a suitable HTx candidate in particular when an short time on waiting list is expected. Current outcomes of continuous-flow LVAD but not those of BiVAD, appear to be superior to those of waiting heart transplantation in urgency condition, thus the prediction of the need for RV assist support is critical when deciding LVAD implantation in a candidate for HTx.

In conclusion, this emblematic case further support the DSE to guide the decision on LVAD versus BiVAD in selected patients with moderate RV dysfunction. DSE can support a personalized choice beyond scores, based on the individual response of the RV to dobutamine. In particular the improvement of the RV parameters of contractility associated with a

significant increase of PAP could be an accurate marker to re-stratify patients at moderate-to-high risk of post-operative RVF, although perspective studies are needed to support these preliminary findings.

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The Authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

DISCLOSURES

None

References

1. Feldman D, Pamboukian SV, Teuteberg JJ, Birks E, Lietz K, et al. (2013) The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. J Heart Lung Transplant 32: 157-187.
2. Miller LW, Guglin M (2013) Patient selection for ventricular assist devices: a moving target. J Am Coll Cardiol 61: 1209-1221.
3. Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson LW, et al. (2014) Sixth INTERMACS annual report: A 10,000-patient database. J Heart Lung Transplant 33: 555-564.
4. Kormos RL, Teuteberg JJ, Pagani FD, Russell SD, John R, et al. (2010) Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: incidence, risk factors, and effect on outcomes. J Thorac Cardiovasc Surg 139: 1316-1324.

5. Kukucka M, Stepanenko A, Potapov E, Krabatsch T, Kuppe H, et al. (2012) Impact of tricuspid valve annulus dilation on mid-term survival after implantation of a left ventricular assist device. J Heart Lung Transplant 31: 967-971.

6. Dandel M, Potapov E, Krabatsch T, Stepanenko A, Low A, et al. (2013) Load dependency of right ventricular performance is a major factor to be considered in decision making before ventricular assist device implantation. Circulation 128: S14-23.

7. Deswarte G, Kirsch M, Lesault PF, Trochu JN, Damy T (2010) Right ventricular reserve and outcome after continuous-flow left ventricular assist device implantation. J Heart Lung Transplant 29: 1196-1198.

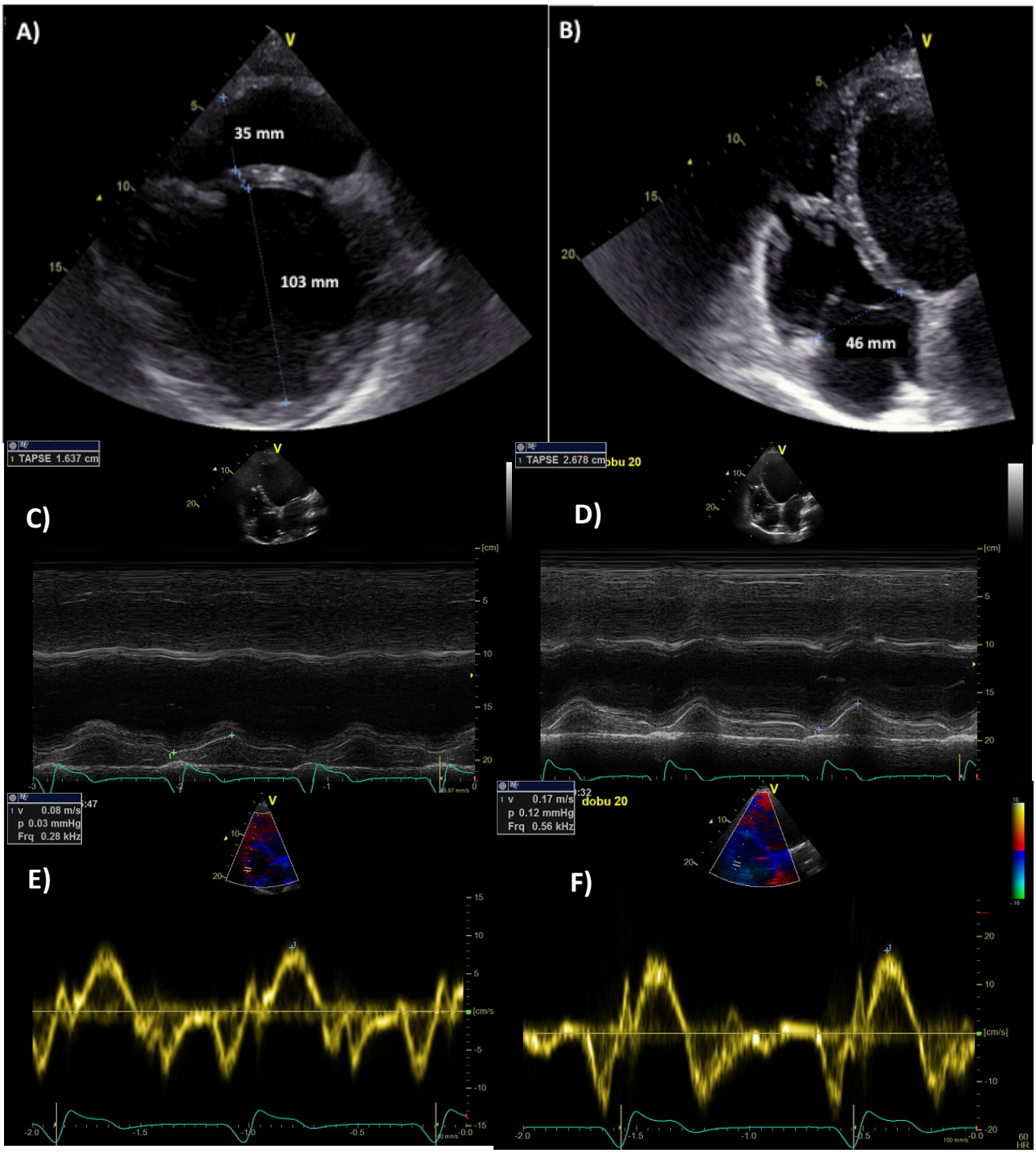
8. Nieminen MS, Altenberger J, Ben-Gal T, Bohmer A, Comin-Colet J, et al. (2014) Repetitive use of levosimendan for treatment of chronic advanced heart failure: Clinical evidence, practical considerations, and perspectives: An expert panel consensus. Int J Cardiol 174: 360-367.

9. Grant AD, Smedira NG, Starling RC, Marwick TH (2012) Independent and incremental role of quantitative right ventricular evaluation for the prediction of right ventricular failure after left ventricular assist device implantation. J Am Coll Cardiol 60: 521-528.

Figure Legend

Figure 1. Basal echocardiographic parameters of the right ventricle (RV) and assessment of the functional capacity of the RV by dobutamine stress echocardiography (increasing dosage from 5 to 20 μ g/Kg/min). A) Severe left ventricular enlargement and ratio between left and right ventricle diameter. B) Tricuspid annulus dilation (46 mm). C) and D) Tricuspid annular plane systolic excursion at baseline (16 mm) and peak dosage of dobutamine, respectively (26 mm). E)

and F) S wave on Tissue Doppler Imaging at baseline and peak dosage of dobutamine, respectively (from 0.08 to 0.17 m/s)


A)
35 mm
103 mm
B)
46 mm
C)
TAPSE 1.637 cm
D)
TAPSE 2.678 cm
dobu 20
E)
v 0.08 m/s
p 0.03 mmHg
Frq 0.28 kHz
F)
v 0.17 m/s
p 0.12 mmHg
Frq 0.56 kHz
dobu 20