Safety and Feasibility of Dopamine-Atropine Stress Echocardiography

Running head: Safety and Feasibility of Dopamine Stress Echo

Abhishek Khemka, MD, MBA^a; Roopa Rao, MD^a; Waqas Ghumman, MD^b; Jothiwaran

Mahenthiran, MD^c, Harvey Feigenbaum MD^a, Stephen G. Sawada, MD ^a

^a Krannert Institute of Cardiology, Indiana University School of Medicine, Indiana Health, Indianapolis, IN.

^b Florida Heart and Vascular, JFK Medical Center, Atlantis, FL

^c Division of Cardiology, Community Health Network, Indianapolis, IN

Correspondence to:

Abhishek Khemka MD

1800 North Capitol Avenue

Noyes Building, Suite E371

Indianapolis, IN 46202

akhemka@iu.edu

Phone: (317) 962-0535

Fax: (317) 962-0115

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Abstract

Background: Dobutamine-atropine stress echocardiography (DSE) has lower sensitivity in patients with advanced liver disease (ALD) due to vasodilation. **Hypothesis:** Dopamine-atropine stress echocardiography (DopSE) may be an alternative to DSE in ALD patients by improving the blood pressure response to stress. **Methods:** The safety and tolerability of DSE and DopSE were compared in 10 volunteers. The safety, adverse effects, and efficacy of DopSE were then assessed in 105 patients, 98 of whom had ALD. Dopamine was infused in stepwise fashion from 5µg/kg/min to a peak dose of 40µg/kg/min. Atropine was given before and in early stages of dopamine infusion up to cumulative dose of 1.5 mg. The hemodynamic responses of 98 ALD patients were compared with 102 patients with ALD who underwent standard DSE. **Results:** In normal volunteers, systolic BP increased more with DopSE compared to DSE (61 ± 19 mmHg vs 39 ± 15 mmHg, $p=0.008$). In 105 patients who underwent DopSE, none had adverse effects that required early stress termination. In the groups with ALD, the systolic BP increase (38 ± 28 mmHg vs 12 ± 27 mmHg, $p<0.001$) and peak rate pressure product (RPP) ($22,861 \pm 5,289$ vs $17,211 \pm 3,848$, $p = <0.001$) were both higher in those undergoing DopSE versus DSE. The sensitivity and specificity of DopSE were 45% and 88% respectively for coronary disease ($\geq 70\%$ stenosis) in 37 patients who had angiography. **Conclusions:** DopSE appears to be a safe stress modality and provides greater increases in RPP in patients with ALD compared to DSE.

Keywords:

Advanced liver disease, Dobutamine-atropine stress echocardiography, dopamine-atropine stress echocardiography, rate pressure product

Introduction

Dobutamine-atropine stress echocardiography (DSE) is a widely employed pharmacologic stress test. [1] Dobutamine stress increases myocardial oxygen demand in a similar but not identical fashion to exercise. Both modalities increase heart rate, but reductions in preload and afterload by dobutamine stress may result in lower rate pressure product (RPP) and reduced efficacy of DSE. [2] The beta-2 receptor stimulating effect of dobutamine may result in marked reductions of preload and systemic vascular resistance in certain populations, such as those with advanced liver disease (ALD) who are vasodilated at baseline. [3] Further reduction in preload and afterload can produce hypotension, inadequate stress, and marked reduction of test sensitivity. At our own institution, DSE was found to have a sensitivity of 24% for obstructive coronary disease in patients with ALD.[4] Dopamine may be a more effective stress agent than dobutamine because of alpha-adrenergic mediated vasoconstrictive effects that could result in higher RPP and wall stress. [5,6,7] In this study, we compared the safety and hemodynamic data in normal individuals who underwent both DSE and dopamine-atropine stress (DopSE). This was followed by assessing the feasibility, safety and efficacy of DopSE in patients referred for pharmacologic stress testing, the majority of whom had ALD.

Methods

The Indiana University Institutional Review Board approved the study and informed consent was obtained from all subjects. In the initial phase, 10 healthy subjects underwent DopSE and DSE in randomized fashion to compare the hemodynamic responses between the two modalities. In the second phase, 105 subjects referred for pharmacologic stress testing for assessment of coronary disease and for risk stratification prior to non-cardiac surgery underwent DopSE. The choice to perform DopSE or DSE was determined by investigators, with DopSE the preferred choice in subjects who had hypotension at baseline or during a prior DSE exam. Consequently, of the 105 patients that had DopSE, 98 had ALD and were being evaluated for liver transplant.

Exclusion criteria for DopSE were: resting SBP > 170 mm Hg or diastolic pressure > 90 mm Hg at the time of testing, unstable coronary syndromes, peripheral vascular disease with symptoms at rest, or previous reaction to dopamine infusion. The hemodynamic response of the 98 subjects with ALD was compared with the hemodynamic response of 102 patients with ALD who had DSE. This comparison group was randomly selected from a population of 850 subjects with ALD who had DSE and received at least 40 $\mu\text{g/kg/min}$ of dobutamine. Patients undergoing DSE in whom the test was terminated for hypotension or another reason prior to achieving the 40 $\mu\text{g/kg/min}$ dose or heart rate $\geq$ 85% of the age predicted max were excluded from the comparison group.

All 10 volunteers had stress testing done with both DopSE and DSE within a one week period in a randomly selected order. An antecubital vein was utilized for infusion of dopamine. Dopamine stress was administered according to the protocol shown in Figure 1, using atropine before and during the early stages of dopamine infusion. The protocol was specifically designed to blunt vagally mediated suppression of the heart rate response to dopamine as a result of baroreceptor stimulation from increases in blood pressure. The maximum dose of atropine was 1.5 mg and the maximum dose of dopamine was 40 $\mu\text{g/kg/min}$. After acquisition of peak dose images, 2.5 to 5 mg of intravenous metoprolol was used to reverse the effects of stress. Intravenous phentolamine was available in case of skin infiltration. The standard dobutamine stress protocol was modified for testing in the 10 volunteers to mimic the dopamine infusion protocol. Pretreatment with atropine and early stage atropine administration was utilized with a peak dose of 40 $\mu\text{g/kg/min}$ of dobutamine and metoprolol was administered after peak dose imaging.

In patients referred for stress testing that underwent DopSE, beta-blockers were held 24 hours before testing. The protocol was similar to the one utilized for the normal volunteers except for pretreatment with 4 to 8 mg of intravenous ondansetron. This was due to higher

proportion of nausea for volunteers undergoing DopSE compared to DSE (90% vs 70%). An investigator supervised each DopSE.

In the comparison group of 102 patients who underwent DSE according to the standard protocol, a peak dose of 50 µg/kg/min of dobutamine was utilized with a maximum dose of 2.0 mg of atropine. The initial dose of atropine was typically given at a dobutamine dose of ≥ 20 µg/kg/min but four patients received atropine at lower dobutamine doses. Endpoints for both DopSE and DSE included attainment of $> 85\%$ age-predicted maximal heart rate, maximum catecholamine dose, SBP ≥ 250 mmHg, angina, ≥ 2 mm of ST segment depression, significant side effects or arrhythmias, as determined by the supervising physician.

Parasternal long and short-axis images (papillary muscle level) and apical 4 and 2-chamber images were obtained at baseline, and at the 10, 30, and 40 µg/kg/min dose stages of dopamine infusion and 6 minutes of recovery. In the normal volunteers, the imaging protocol during dobutamine infusion was identical to that used for the dopamine exams. In patients who underwent DopSE, the standard 2-3 minute intervals was used for titrating up the dose of stress agent and obtaining images. Regional wall motion was visually assessed by faculty experienced in the interpretation of stress echocardiograms. Exams were interpreted without knowledge of the results of nuclear imaging or coronary angiography. The development of a new wall motion abnormality or worsening of a baseline wall motion abnormality with stress in one or more segments was considered evidence of ischemia except for dyskinesis with stress in a segment with baseline akinesis. Delays in regional contraction (tardokinesis) or lack of hyperkinesis were not considered markers of ischemia in this study.

There were 37 patients that underwent coronary angiogram within 6 months of their DopSE. Patients were referred for angiography in cases of positive or equivocal stress test or with a negative stress test in the presence of one or more risk factors in a model that has demonstrated decreased post-liver transplant myocardial infarction and all-cause mortality.[8] Risk factors included age > 60 years, family history of coronary atherosclerosis, smoking history

(>10 pack-years or current smoker), history of diabetes or hypertension (HTN) requiring treatment, prior history of coronary atherosclerosis, and obesity (body mass index > 30 kg/m²). Coronary angiograms were visually assessed by an experienced interventional cardiologist. Significant coronary disease was defined as ≥70% stenosis of a major epicardial vessel except for the left main artery, where ≥50% was considered significant.

In the 10 normal volunteers the hemodynamic responses to dopamine and dobutamine stress were compared by paired T- test. A p value < 0.05 was considered significant. The hemodynamic variables of the 98 liver disease patients who underwent DopSE and the 102 subjects who had DSE were compared using single factor ANOVA and unpaired T-test. Categorical variables were compared using Fisher exact test or Chi-square.

Results

The 10 volunteers had a mean age 31 ± 2 years and there were 4 men. There were no significant differences between baseline heart rate, blood pressure and heart rate- systolic blood pressure product before or after testing with either agent (Table 1). Peak RPP exceeded 25,000 for both forms of stress. There was a significant difference in the rest to peak stress change in SBP between DopSE and DSE (increase of 61 ± 19 mmHg vs 39 ± 15 mmHg, $p=0.008$).

There were no serious adverse events with either stress test, as defined by arrhythmias, allergic reaction, IV infiltration, or skin necrosis. Nausea was the most common side effect with both stress agents (DopSE n=9 vs DSE n=7). Less common side effects included palpitations (DopSE n=3 vs DSE n=5) and headache (DopSE n=2 vs DSE n=2). None experienced chest pain.

Table 2 shows the characteristics of the 105 patients (mean age 53 ± 8 years, 65% male) who underwent DopSE. Ninety-eight (93%) had DopSE for risk assessment as part of evaluation for liver transplantation. Seventeen (16%) patients had a history of chest pain. The

mean duration of the entire study was 17.5 ± 3.8 minutes of which, the stress portion was 9.6 ± 2.3 minutes and recovery was 7.9 ± 2.2 minutes. The most common side effects during the studies were nausea ($n = 58$, 54%), palpitations ($n=33$, 31%), and chest pain ($n=10$, 9%). Fifteen (14%) patients subjectively reported moderate side effects and 5 (5%) patients reported severe side effects during max dose of dopamine. No studies were terminated prematurely due to side effects. No patients had sustained ventricular arrhythmias. Two (2%) patients had non-sustained ventricular tachycardia lasting up to 8 beats and in 5 (5%) studies, patients had non-sustained supraventricular tachycardia, all of which spontaneously resolved. Temporary atrial fibrillation occurred in one patient and spontaneously resolved. Confirmed IV infiltration occurred in one patient and another may have had IV infiltration. Both were given IV phentolamine and warm compresses with no incidences of skin necrosis. One patient reported unilateral facial swelling without rash or breathing difficulties that may have been due to an allergic reaction.

The hemodynamics of the 98 DopSE and 102 DSE studies with ALD were compared in Table 3. DopSE patients received an average dopamine dose of $36 (\pm 6) \mu\text{g/kg/min}$ with $1.2 (\pm 0.3)$ mg of atropine. DSE patients received an average dobutamine dose of $47 (\pm 7) \mu\text{g/kg/min}$ with $0.7 (\pm 0.5)$ mg of atropine. Systolic blood pressures increased significantly more for patients undergoing DopSE compared to DSE ($117 \pm 17\text{mmHg}$ to $156 \pm 29\text{mmHg}$ vs $116 \pm 19\text{mmHg}$ to $128 \pm 27\text{mmHg}$, $p = <0.001$). Five (5%) patients had a decrease in SBP from rest to peak stress during DopSE compared to 40 (39%) undergoing DSE ($p = <0.001$). Peak RPP was significantly higher in those who had DopSE ($22,861 \pm 5,289$ vs $17,211 \pm 3,848$, $p = <0.001$). RPP increased from rest to peak on average for DopSE by $14,458 \pm 5,592$ and for DSE by $8,372 \pm 4,204$, $p = <0.001$). Peak heart rate was also significantly higher in those undergoing DopSE ($146 \pm 18 \text{bts/min}$ vs $135 \pm 19 \text{bts/min}$, $p <0.001$). The lower peak heart rate in DSE subjects was unexpected and to address the possibility of bias in selection of the 102 patients in the DSE group, the peak heart of the DopSE group was also compared to the mean peak heart rate of a larger group of 687 DSE studies performed in 633 patients with ALD.

[4] In 76% of these exams the target heart rate was achieved. The peak heart rate with DopSE was again significantly higher than with DSE (146 ± 18 bts/min vs 138 ± 15 bts/min, $p < 0.001$).

Of 105 patients who underwent DopSE, 37 patients had coronary angiography within 6 months of their stress test. The prevalence of significant coronary disease ($\geq 70\%$ stenosis) was low at 30% (11/37 patients). The sensitivity and specificity of DopSE was 45% and 88% (Table 4). We have previously shown that DSE sensitivity in ALD patients is higher in those with LV cavity dimension > 4.8 cm. [4] In patients with diastolic cavity dimension ≤ 4.8 , DopSE sensitivity and specificity were 38% (3/8) and 87% (13/15). DopSE sensitivity was 67% (2/3) and specificity was 91% (10/11) in those with cavity dimension > 4.8 cm. Given the small sample sizes, the differences in sensitivity ($p=0.39$) and specificity ($p=0.74$) were not significant.

Discussion:

To our knowledge, this is the first study to investigate the safety and hemodynamic effects of dopamine and atropine stress in ALD patients and the second study to investigate the use of dopamine as a stress agent. Wisenberg et al found peak heart rate, SBP and RPP were comparable between dopamine-atropine stress and bicycle exercise suggesting the potential of dopamine stress to approximate the hemodynamic changes and degree of stress produced by exercise. [9] Our study was prompted after the realization that DSE yields a lower than desired sensitivity in patients with ALD.

In our study, normal volunteers had greater increases in SBP with DopSE compared with DSE. In 105 patients, DopSE was performed safely with no serious complications. Nausea was a common side effect, but pretreatment with ondansetron made this side effect tolerable. In patients with ALD, declines in SBP below baseline values were rare with DopSE and common with DSE. Patients undergoing DopSE achieved a significantly higher peak RPP (approaching 23,000) than those who underwent DSE. In a small subset of patients who had angiography

and a low prevalence of significant coronary disease, the sensitivity of DopSE was 45%.

Sensitivity was 67% in those with left ventricular diastolic dimension > 4.8 cm.

Adequacy of Catecholamine Stress: Rate Pressure Product versus Heart Rate

Multiple lines of evidence suggest that the adequacy of catecholamine stress is dependent on substantial increases in SBP and heart rate-blood pressure product rather than heart rate alone. [10] Use of heart rate alone as an indicator of myocardial oxygen consumption overlooks the importance of afterload and wall stress. In normal individuals assessed by positron emission tomography, dobutamine-induced increases in myocardial oxygen consumption were closely correlated to increases in RPP ($r = 0.94$). Myocardial oxygen consumption and blood flow were closely coupled ($r = 0.91$), and changes in flow correlated more closely with changes in SBP ($r = 0.86$) and RPP ($r = 0.77$) rather than changes in heart rate ($r = 0.59$). [11] In a study of patients with known coronary disease undergoing both exercise echo and DSE, the sensitivity of exercise echo was 73% versus 62% for DSE ($p = 0.14$), and the extent of stress-induced wall motion abnormalities was greater with exercise versus dobutamine stress ($p < 0.0001$). The peak heart rate was higher with DSE versus exercise echo (153 bts/min vs 143 bts/min, $p < 0.001$), but RPP was higher with exercise echo versus DSE (24,600 vs 19,400, $p < 0.0001$). [2] Garot et al demonstrated that the severity of coronary stenosis correlates better with ischemic threshold based on RPP rather than heart rate ($r = -0.72$ vs $r = -0.52$). They also showed that a third of patients with 70-80% diameter stenosis require a RPP > 18,000 to demonstrate ischemia and nearly all patients with $\geq 50\%$ stenosis who achieved RPP > 25,000 manifested ischemic wall motion abnormalities. [12]

Along with cavity dimension and wall thickness, systolic pressure is an important but often ignored component of ventricular wall stress that contributes to myocardial oxygen consumption. Wall stress and myocardial oxygen consumption are lower than desired in subjects with small cavity size, and there may be declines in blood pressure and vascular resistance with stress, which routinely occur in ALD patients undergoing DSE. This can lead to

more limited ischemia and more difficulty in detection of limited or subtle wall motion abnormalities in hyperkinetic, small ventricles.

In our study, the higher peak SBP and RPP and the greater increase in SBP and RPP with DopSE versus DSE can be attributed to the vasoconstrictive properties of dopamine versus the vasodilatory effects of dobutamine. Patients with ALD have systemic vasodilatation and decreased effective circulatory volume. The beta-2 stimulating effects of dobutamine administration produce further reductions of preload and afterload that frequently result in falls in blood pressure with DSE. In our study, 39% of ALD patients had declines in systolic blood pressure with DSE versus 5% with DopSE. Declines in SBP can result in inadequate stress both from early termination of stress and inadequate RPP. The peak RPP reported in studies utilizing DSE in patients with ALD have ranged from 11,397 to 18,602 which is inadequate to induce ischemia in some patients with obstructive coronary artery disease. [4,13]. DopSE might also provide higher degrees of stress than DSE in patients without ALD. In a recently published study, the peak RPP was 18,216 in 4,494 patients who underwent DSE before non-cardiac surgery. Less than 2% of their population had ALD. [14]

Catecholamine Stress for Detection of Coronary Disease in Advanced Liver Disease

Guidelines from the American Association for the Study of Liver Diseases and the American Society of Transplantation still recommend the use of stress echocardiography as an initial screening test in patients with cardiac risk factors. DSE is suggested over coronary angiography due to concerns of bleeding and contrast nephropathy in cirrhotics with tenuous renal function. [15] DSE is frequently performed instead of exercise echocardiography given the limited ability for ALD patients to perform adequate exercise. In the US, the number of patients waiting for a liver transplant has been increasing. [16] In patients with ALD, the reported sensitivity of DSE for obstructive coronary disease has ranged as low as 13%. [17] A meta-analysis including 110 patients from four studies who had both DSE and angiography reported a sensitivity of 32% in those who achieved 85% of the age predicted maximal heart rate with

stress. [18] The sensitivity of DSE was 24% in a study of 633 patients evaluated in our laboratory. The peak RPP of this population was 18,087 and 76% of patients achieved their target heart rate. Achievement of the target heart rate was not found to be predictive of a positive DSE in those with coronary disease. [4] In the current study, the sensitivity of DopSE for coronary disease was 45% which remains lower than desired but is nearly twice the sensitivity of DSE. In our study, the prevalence of coronary disease was low which reflects the fact that there was not a bias towards referral to angiography of only those patients with abnormal stress tests. Mayo clinic investigators reported that the sensitivity of exercise echocardiography was 32% in women and 42% in men after adjustment for test verification bias in the setting of an artificially high prevalence of coronary disease. [19] In our laboratory, the sensitivity of DSE in ALD patients was higher in those with baseline left ventricular diastolic dimension > 4.8 cm compared to those with diastolic dimension ≤ 4.8 cm (38% vs 13%, $p = 0.01$). The sensitivity of DopSE may also be influenced by cavity dimension. In our study, sensitivity was 67% in those with diastolic dimension > 4.8 cm and 38% in those with dimensions ≤ 4.8 cm.

Limitations and Conclusions

This study had several limitations. The DopSE and DSE cohorts were not matched in terms of peak catecholamine or atropine doses. Recently, DSE sensitivity in ALD patients has been shown to be higher when delays in contraction (tardokinesis) or lack of hyperkinesis are considered abnormal responses. [20] In the current study, these findings were not considered as abnormal. The small number of patients who had obstructive coronary disease in our study limits conclusions about the true sensitivity of DopSE.

DopSE appears to be a safe and generally well-tolerated stress modality. Compared with dobutamine-atropine, dopamine-atropine infusion produces a higher degree of stress as judged by RPP in patients with advanced liver disease. DopSE may have enhanced sensitivity compared to DSE for the detection of coronary disease in patients with ALD but further studies are needed.

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Author Contributions:

Dr Khemka was involved in data collection, data analysis/interpretation, statistics, drafting and revising the article, approving the article.

Dr Rao was involved in data collection, data analysis, revising and approving the article.

Dr. Ghumman was involved in data collection, data analysis, revising and approving the article.

Dr. Mahenthiran was involved in concept/design, data collection, revising and approving the article.

Dr. Feigenbaum was involved in concept/design, revising the article and final approval.

Dr. Sawada was involved in concept/design, data collection, data analysis/interpretation, statistics, drafting and revising the article, and final approval.

Data Availability Statement:

The data that support the findings of this study are available from the corresponding author, AK, upon reasonable request.

References

[1] Sawada SG, Segar DS, Ryan T, et al. Echocardiographic Detection of Coronary Artery Disease During Dobutamine Infusion. *Circulation* 1991; 83: 1605-1614.

<https://doi.org/10.1161/01.CIR.83.5.1605>

[2] Rallidis L, Cokkinos P, Tousoulis D, et al. Comparison of Dobutamine and Treadmill Exercise Echocardiography in Inducing Ischemia in Patients with Coronary Artery Disease. *J Am Coll Cardiol* 1997; 30: 1660-1668. [https://doi.org/10.1016/S0735-1097\(97\)00376-8](https://doi.org/10.1016/S0735-1097(97)00376-8)

- [3] Tanimoto M, Pai RG, Jintapakorn W, et al. Mechanisms of Hypotension During Dobutamine Stress Echocardiography in Patients with Coronary Artery Disease. *Am J Cardiol* 1995; 76: 26-30. [https://doi.org/10.1016/S0002-9149\(99\)80795-4](https://doi.org/10.1016/S0002-9149(99)80795-4)
- [4] Doytchinova AT, Feigenbaum TD, Pondicherry-Harish RC, et al. Diagnostic Performance of Dobutamine Stress Echocardiography in End-Stage Liver Disease. *J Am Coll Cardiol Img.* 2019; 12:2115-22
- [5] Jewitt D, Mitchell A, Birkhead J, et al. Clinical cardiovascular pharmacology of dobutamine. *Lancet.* 1974; 2: 363-367. [https://doi.org/10.1016/S0140-6736\(74\)91754-1](https://doi.org/10.1016/S0140-6736(74)91754-1)
- [6] Liang CS, Hood WB. Dobutamine infusion in conscious dogs with and without autonomic nervous system inhibition: Effects of systemic hemodynamics, regional blood flows and cardiac metabolism. *J Pharmacol Exp Ther.* 1979; 211: 698-705.
- [7] McGillem MJ, Deboe SF, Friedman HZ, et al. The effects of Dopamine and Dobutamine on Regional Function in the Presence of Rigid Coronary Stenoses and Subcritical Impairments of Reactive Hyperemia. *Am Heart J* 1988; 115: 970-977. [https://doi.org/10.1016/0002-8703\(88\)90065-8](https://doi.org/10.1016/0002-8703(88)90065-8)
- [8] Maddur H, Bourdillon PD, Liangpunsakul S, et al. Role of cardiac catheterization and percutaneous coronary intervention in the preoperative assessment and management of patients before orthotopic liver transplantation. *Liver Transplantation.* 2014; 20: 664-672. <https://doi.org/10.1002/lt.23873>
- [9] Wisenberg G, Zawadowski AG, Gebhardt VA, et al. Dopamine: Its potential for inducing ischemic left ventricular dysfunction. *J Am Coll Cardiol.* 1985; 6: 84-92. [https://doi.org/10.1016/S0735-1097\(85\)80257-6](https://doi.org/10.1016/S0735-1097(85)80257-6)
- [10] Sawada SG. A reappraisal of dobutamine echocardiography for risk stratification before noncardiac surgery. *J Am Soc Echocardiogr.* 2020; <https://doi.org/10.1016/j.echo.2020.01.017>
- [11] Krivokapich J, Huang SC, Schelbert HR. Assessment of the effects of Dobutamine on Myocardial Blood Flow and Oxidative Metabolism in Normal Human Subjects Using Nitrogen-13

Ammonia and Carbon-11 Acetate. *Am J Cardiol.* 1993; 71: 1351-56.

[https://doi.org/10.1016/0002-9149\(93\)90554-P](https://doi.org/10.1016/0002-9149(93)90554-P)

[12] Garot J, Hoffer EP, Monin JL, et al. Stratification of single-vessel coronary stenosis by ischemic threshold at the onset of wall motion abnormality during continuous monitoring of left ventricular function by semisupine exercise echocardiography. *J Am Societ Echocardiography.* 2001; 14: 798-805. <https://doi.org/10.1067/mje.2001.111936>

[13] Umphrey LG, Hurst RT, Eleid MF, et al. Preoperative dobutamine stress echocardiographic findings and subsequent short-term adverse cardiac events after orthotopic liver transplantation. *Liver Transpl.* 2008; 14: 886-892. <https://doi.org/10.1002/lt.21495>

[14] Cullen MW, McCully RB, Widmer RJ, et al. Preoperative dobutamine stress echocardiography and clinical factors for assessment of cardiac risk after noncardiac surgery. *J Am Societ Echocardiography.* 2020; 33: 423-432.

[15] Martin P, DiMartini A, Feng S, et al. Evaluation for Liver Transplantation in Adults: 2013 Practice Guidelines by the American Association for the Study of Liver diseases and the American Society of Transplantation. *Hepatology.* 2014; 59: 1144-1165.

[16] Fayek SA, Quintini C, Chavin KD, et al. The Current State of Liver Transplantation in the United States. *Am J Transplantation.* 2016; 16. <https://doi.org/10.1111/ajt.14017>

[17] Ehtisham J, Altieri M, Salame E, et al. Coronary Artery Disease in Orthotopic Liver Transplantation: Pretransplant Assessment and Management. *Liver Transpl.* 2010; 16: 550-557. <https://doi.org/10.1002/lt.22035>

[18] Nguyen P, Plotkin J, Fishbein TM, et al. Dobutamine Stress Echocardiography in Patients undergoing orthotopic liver transplantation: a pooled analysis of accuracy, perioperative and long term cardiovascular prognosis. *Int J Cardiovasc Imaging.* 2013; 29: 1741-1748. <https://doi.org/10.1007/s10554-013-0275-x>

[19] Roger VL, Pellikka PA, Bell MR, et al. Sex and Test Verification Bias: Impact on the Diagnostic Value of Exercise Echocardiography. *Circulation.* 1997; 95: 405-410.

[20] Pellikka PA, Arruda-Olson A, Chaudhry FA, et al. Guidelines for Performance, Interpretation, and Application of Stress Echocardiography in Ischemic Heart Disease: From the American Society of Echocardiography. J Am Societ Echocardiography. 2020; 33: 1-41.

Table I. Hemodynamic data of healthy volunteers undergoing dobutamine-atropine stress echocardiography and dopamine-atropine stress echocardiography. HR = Heart rate, BP = Blood pressure, RPP = Rate Pressure Product.

Table I			
	Dobutamine	Dopamine	P-Values
Healthy Volunteers	10	10	
Resting HR (beats/min)	72 ($\pm$ 10)	68 ($\pm$ 10)	0.429
Resting Systolic BP (mmHg)	115 ($\pm$ 12)	107 ($\pm$ 9)	0.123
Resting Diastolic BP (mmHg)	69 ($\pm$ 10)	69 ($\pm$ 8)	1.000
Resting RPP	8,224 ($\pm$ 1,690)	7,221 ($\pm$ 968)	0.121
Peak HR (beats/min)	164 ($\pm$ 5)	159 ($\pm$ 16)	0.407
% Reached 85% MPHR	70%	60%	0.660
Peak Systolic BP (mmHg)	154 ($\pm$ 24)	168 ($\pm$ 20)	0.162
Peak Diastolic BP (mmHg)	72 ($\pm$ 16)	83 ($\pm$ 20)	0.176
Peak RPP	25,181 ($\pm$ 4,424)	26,635 ($\pm$ 3,449)	0.423

Table II. Demographics of Patients undergoing Dopamine-atropine Stress Echocardiography.

Table II	
Dopamine	
Total number of patients	105
Male	68 (65%)
Average Age	53.0 ($\pm$ 8.1)
Body Mass Index	27.9 ($\pm$ 6.4)
Hypertension	30 (29%)
Diabetes Mellitus	19 (18%)
Dyslipidemia	15 (14%)
Current Smoker	32 (30%)
Family history of Coronary Atherosclerosis	35 (33%)
Known history of Coronary Atherosclerosis	12 (11%)
Preoperative candidate for liver transplant	98 (93%)

Table III. Hemodynamic data for patients with advanced liver disease undergoing dopamine-atropine stress echocardiography versus dobutamine-atropine stress echocardiography. HR = Heart rate, BP = Blood pressure, RPP = Rate Pressure Product

Table III			
	Dobutamine (N = 102)	Dopamine (N = 98)	P-value
Average Age	52.3	50.5	0.15
Male	64 (65%)	58 (57%)	0.22
Rest HR (beats/min)	75.9 ($\pm$ 15.1)	72.4 ($\pm$ 12.4)	0.07
Rest Systolic BP (mmHg)	116.0 ($\pm$ 18.5)	116.8 ($\pm$ 17.2)	0.74
Rest Diastolic BP (mmHg)	65.8 ($\pm$ 12.3)	67.3 ($\pm$ 10.7)	0.37
Rest RPP	8,839 ($\pm$ 2,455)	8,403.5 ($\pm$ 2,196)	0.19
Peak HR (beats/min)	135.4 ($\pm$ 18.5)	146.0 ($\pm$ 17.8)	<0.001
Peak Systolic BP (mmHg)	127.9 ($\pm$ 27.3)	155.6 ($\pm$ 28.5)	<0.001
Peak Diastolic BP (mmHg)	59.7 ($\pm$ 14.8)	81.5 ($\pm$ 16.2)	<0.001
Peak RPP	17,211 ($\pm$ 3,848)	22,861 ($\pm$ 5,289)	<0.001
Change in HR from rest to peak	59.6 ($\pm$ 19.9)	74.4 ($\pm$ 19.4)	<0.001
Change in Systolic BP from rest to peak	12.0 ($\pm$ 26.8)	38.4 ($\pm$ 27.8)	<0.001

Table IV. Dopamine Stress Echo as compared to coronary angiogram. CAD = Coronary artery disease, DopSE = Dopamine-atropine stress echocardiography

Table IV					
	Significant CAD on angiogram	Insignificant CAD on angiogram	Total		
Ischemic DopSE	5	3	8	Sensitivity	45%
Normal DopSe	6	23	29	Specificity	88%
				Positive Predictive Value	63%
Total	11	26	37	Negative Predictive Value	79%

Figure Legend:

Figure I. Dopamine Stress Protocol.