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Feasibility evaluation of non-invasive cardiac function technology during echocardiography-based cardiac stress testing

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Abstract

Evaluation of cardiac function during periods of stress is of key importance for the perioperative setting. Non-invasive hemodynamic monitors provide markers of cardiac function. This pilot study sought to evaluate the ability of a non-invasive hemodynamic monitor to detect cardiac stress during formal stress echocardiography testing. The primary goal was to compare the change in hemodynamic values during the pre/during/post phases of stress echocardiography testing in patients who had results negative versus positive for myocardial ischemia. Adult patients scheduled for outpatient cardiac stress testing were screened. Only patients scheduled for stress-echocardiography testing were consented. Patients with history of arrhythmias were excluded. During the testing, patients wore a cuff-based hemodynamic sensor (Nexfin system, Edwards Lifesciences). Data from the hemodynamic sensor were compared to the findings of the stress study. A total of 37 patients were enrolled, with 31 patients included for analysis. Five patients had stress studies positive for coronary ischemia. Comparison of the hemodynamic variables between patients who had a positive stress study versus negative showed a significant reduction in the percentage change in dP/dt and stroke volume from baseline ($p < 0.05$). This pilot study indicates that patients who have abnormal stress echocardiograms also have significantly reduced values

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Conflict of interest Davinder Ramsingh, MD—Consultant and Funded Research from Edwards Lifesciences, Consultant for Fujifilm Sonosite, Funded research from General Electric on Point of Care Ultra-sound and Anesthesia Delivery Systems, Funded research from Merck Pharmaceuticals, Funded research from Pacira Pharmaceuticals, Funded research from Masimo Corporation. Maxime Cannesson, MD, PhD—Ownership interest in Sironis, a company developing closed-loop systems, Consultant and Funded Research from Edwards Lifesciences, Consultant for Masimo Corp, Funded Research from National Institutes of Health: Grant Nos. R01 GM117622 (“Machine Learning of Physiological Variables to Predict Diagnose and Treat Cardiorespiratory Instability”) and R01 NR013912 (“Predicting Patient Instability Noninvasively for Nursing Care-Two [PPINNC-2]”).

from a noninvasive hemodynamic monitor. Further evaluation of the clinical utility of this technology, to assist in the care of patients at risk for cardiac ischemia, should be carried out.

Keywords

Cardiac stress testing; Non-invasive hemodynamic monitoring; Preoperative cardiac function evaluation; Preoperative testing; Preoperative risk-stratification

1 Introduction

Perioperative cardiovascular events are responsible for a substantial proportion of the morbidity and mortality associated with non-cardiac surgery [1]. Recently, the American Heart Association (AHA), American College of Cardiology (ACC) and American Society of Anesthesiologists (ASA) guidelines made more specific recommendations about appropriate testing in the preoperative setting [2]. Support for these guidelines is based on previous research indicating the overuse of current costly preoperative cardiac stress testing [3, 4].

Despite these efforts, concern has still been raised about the gap between recent guidelines and current clinical care patterns [5]. Sigmund et al. demonstrated no reduction in routine pre-operative testing despite the updated ACC/AHA and ASA guidelines [6]. Review of Medicare claims data between 2006 and 2011 also found that among 300,000 eligible beneficiaries undergoing low-risk, non-cardiac surgery, approximately 50% received non-indicated preoperative stress testing [7]. Indeed, the cost associated with non-indicated preoperative stress testing is tremendous, with estimated annual Medicare spending ranging from $81 to $180 million [8].

This disconnect highlights the importance of developing strategies to improve adherence, but also suggests the need to evaluate other methods to assess cardiovascular risk at lower costs. Recently, non-invasive cardiac function technologies have been developed. These technologies have, in large part, been utilized in the perioperative setting to facilitate the hemodynamic (HD) management of patients undergoing surgery [9]. One such non-invasive technology, Nexfin (Edwards Lifesciences, Irvine CA), utilizes an inflatable cuff with a photoplethysmograph that is placed on the finger. The device utilizes the concept of volume clamp analysis to generate an arterial pressure waveform (continuous blood pressure) and provide markers of one’s hemodynamics: (1) stroke volume (SV), (2) cardiac output (CO), and (3) change in pressure over change in time (dP/dt). This system captures cardiovascular function data several times a second and alerts can be adjusted.

Multiple studies have demonstrated a good correlation between cardiac output assessment of this technology for non-critically ill patients as compared to: pulmonary artery catheter [10], arterial waveform analysis [11], and echocardiography [12] technologies. Additionally, this technology has also demonstrated strong trending capabilities of flow parameters to invasive thermodilution technologies, with one study demonstrating a concordance of 100% in CO changes greater than 5% [13]. However, the utilization of these technologies to detect acute cardiac stress has not been studied. This pilot study was designed to evaluate if the parameters provided by the Nexfin system are significantly reduced in patients who have

stress echocardiography testing that is positive for ischemia vs those who are negative. The overall goal was to evaluate the utility of non-invasive HD monitoring technologies to detect changes in cardiac function secondary to acute cardiac ischemic events.

2 Materials and methods

The methods are presented following the standards for the reporting of diagnostic (STARD) checklist methodology.

2.1 Participants

The study was performed at the University of California, Irvine after Institutional Review Board (2014–1651) approval. The study enrollment period was from April 2015 to February 2016. Written informed consent and HIPAA release were obtained for all subjects prior to their participation in the study. All patients scheduled for stress echocardiography were included in the screenings. Thirty-seven subjects were recruited based on inclusion criteria of: at least 18 years of age, undergoing echocardiography-based stress testing, willingness to participate, and willingness to keep the finger on which the device was placed straight during the entire study. The last criterion is of unique importance, as the Nexfin Device requires adequate flow to the digit to obtain accurate HD data. Exclusion criteria included: age less than 18 years, pregnancy, history of cardiac arrhythmias, and known history of peripheral artery disease. The latter exclusion criterion is secondary to the impact peripheral artery disease may have on volume clamp analysis technologies.

2.2 Study protocol

Patients were approached for study participation after procedural consent for the cardiac stress echocardiography study. After written consent was obtained, the patient had the fingercuff based device placed on the middle finger between the proximal and distal interphalangeal joint opposite of the blood pressure cuff (Fig. 1). The appropriate-sized finger cuff was determined as per the suggested guidelines from the manufacturer. A tongue depressor with Velcro straps was placed loosely on the finger with the cuff to remind the patient to keep their finger straight throughout data capture. The device (Nexfin, Software version: 1.9.0.1001) was initiated and verification of an arterial w6aveform was performed before data collection. Data was recorded for the entirety of the study procedure, including pre-stress, stress, and post-stress periods. Patients were informed that the device could be removed at any time if they felt discomfort. Patient’s exercised on a treadmill according to the Bruce protocol [14]. A member of the research team remained with the patient for the entirety of the study to monitor appropriate data capture. Studies in which the patients were not able to keep their finger straight, failing appropriate data capture for 40 s, were flagged for removal from data analysis. As this study was a departmental supported pilot project, subject enrollment was limited to an enrollment period of 11 months.

2.3 Data acquisition

Patient demographics (age, height, weight, gender) and vital signs were recorded during the initiation of the study. The Nexfin device recorded HD data several times a second throughout the study. Research personnel were present to record exact times in which the

patient was in the pre-stress phase, when the stress intensity increased, when the stress ended, any other events that may alter the device's ability to capture HD data, along with heart rate and blood pressure. To establish homogeneity in our data analysis between studies of varying lengths of time, data was averaged to each second and analysis was performed for a forty second period during each of the three study phases (pre-stress, stress, and post-stress) for a total collection time of 120 s (data points) per study. Data was collected for each phase in the following manner: the highest centered value during the pre-stress portion, the lowest centered value during the stress portion, and highest centered value during recovery portion (20 points above and below each of the centered values). All data regarding results of the stress study were recorded from the official stress study report in the subject's electronic medical record.

2.4 Statistical analysis

The primary outcome was a detection of a difference in HD data, from the pre-stress to stress periods, between patients with positive stress studies and those who had negative studies. This was assessed by examining the percent change of the following HD variables: dP/dT and SV. Secondary outcome markers included comparisons of the aforementioned variables from the pre-stress to post-stress periods. We conducted a test for variability (Levene's test) and normality (Shapiro–Wilk test) to verify that the two group comparisons should be performed with a nonparametric unpaired analysis (Mann–Whitney). As the study was a pilot project, no sample size calculation was performed. Study size was determined by the number of patients able to be consented during the 11-month enrollment period.

3 Results

3.1 Demographics

Of the 37 enrolled patients, 31 subjects were used for analysis. Patient demographics are listed Table 1. Six subjects were excluded either due to the subject's inability to keep their finger straight during the study period causing inaccurate data capture (n = 4) or due to a cancelled stress test post-consent (n = 2). No patient reported discomfort from wearing the device at any point. All subjects were referred for the evaluation of chest pain and had reported normal LV ejection fraction at the baseline phase of the study. Hemodynamic summary values for the pre-stress, stress, and post-stress phases are included in Table 1.

3.2 Outcome comparison

The subjects who had positive stress test had a significantly reduced percent change in both dP/dt ($p < 0.05$) and stroke volume ($p < 0.05$) from the pre-stress to stress phases when compared to the subjects with negative stress tests (Table 2). A density map of the percent change in dP/dt parameter from the pre-stress to stress time periods for both the positive and negative stress-study subjects is shown in Fig. 2. No statistically significant differences were observed between the percent change in HD values from the pre-stress to post-stress periods between groups.

4 Discussion

The use of cardiac stress testing outside of recommended guidelines is a common occurrence. Prior studies have demonstrated limited impact of professional guidelines on physician behavior [15–17]. Along with this is the evidence indicating that physicians are more likely to follow guidelines that add, rather than eliminate, a test or procedure [17, 18]. As referenced above, this non-indicated testing results in a tremendous cost to healthcare [8].

Current cardiovascular function testing requires a high level of resources including specialized personnel and expensive diagnostic equipment. In addition, testing can often only be performed in a designated location, all of which may delay ones treatment. Given these points, one can see the utility in evaluating the ability of technology to facilitate the assessment of a patient's acute cardiac function status in a manner that does not require advanced diagnostic training or significant health system resources. It is important to note that this project was not designed to suggest or evaluate the utility of HD monitoring technology to replace appropriate cardiac stress examinations. Rather, this project was designed as a pilot study to support further evaluation of the utility of this technology in patients who are currently receiving preoperative cardiac stress testing outside what is recommended by the AHA/ASA guidelines. To the authors' knowledge, this study is the first that has demonstrated the ability of non-invasive HD monitoring to trend with cardiac stress studies. Hopefully, this project suggests the further evaluation of non-invasive HD technologies in patient care environments that historically have not had access to these devices.

As the majority of HD monitors have some connection with the pulmonary artery catheter (PAC), either via industry and/or validation, these technologies have in most part been implemented in patient care settings in the which the PAC historically has been used (operating room and intensive care units). However, with the latest versions of these technologies now becoming completely non-invasive, the exploration of providing flow-guided parameters in new clinical settings is warranted.

This study has several limitations. It was designed as a pilot observational study to evaluate differences in HD information from the non-invasive device in patients with positive versus negative stress echocardiograms. Limitations of this study include the small study population and the sole use of Nexfin as the continuous noninvasive monitor without the use of other available devices. In addition, the number of abnormal cardiac stress echocardiograms available for correlation was limited. More positive stress tests would allow for better evaluation of the device's ability to detect such events and greater statistical power. Additionally, while all patients received stress testing for the evaluation of chest pain, there past medical history were not captured. Finally, this study did not attempt to validate the Nexfin measurements of CO, dP/dt, and other HD variables, though it has been validated by others [10–12].

5 Conclusions

This pilot study demonstrated significant differences in the HD changes detected with a non-invasive device between patients who were positive to those who were negative for ischemia during stress-echocardiography testing. Further evaluation of the clinical utility of non-invasive HD monitoring to assist care of patients at risk for cardiovascular injury should be evaluated.

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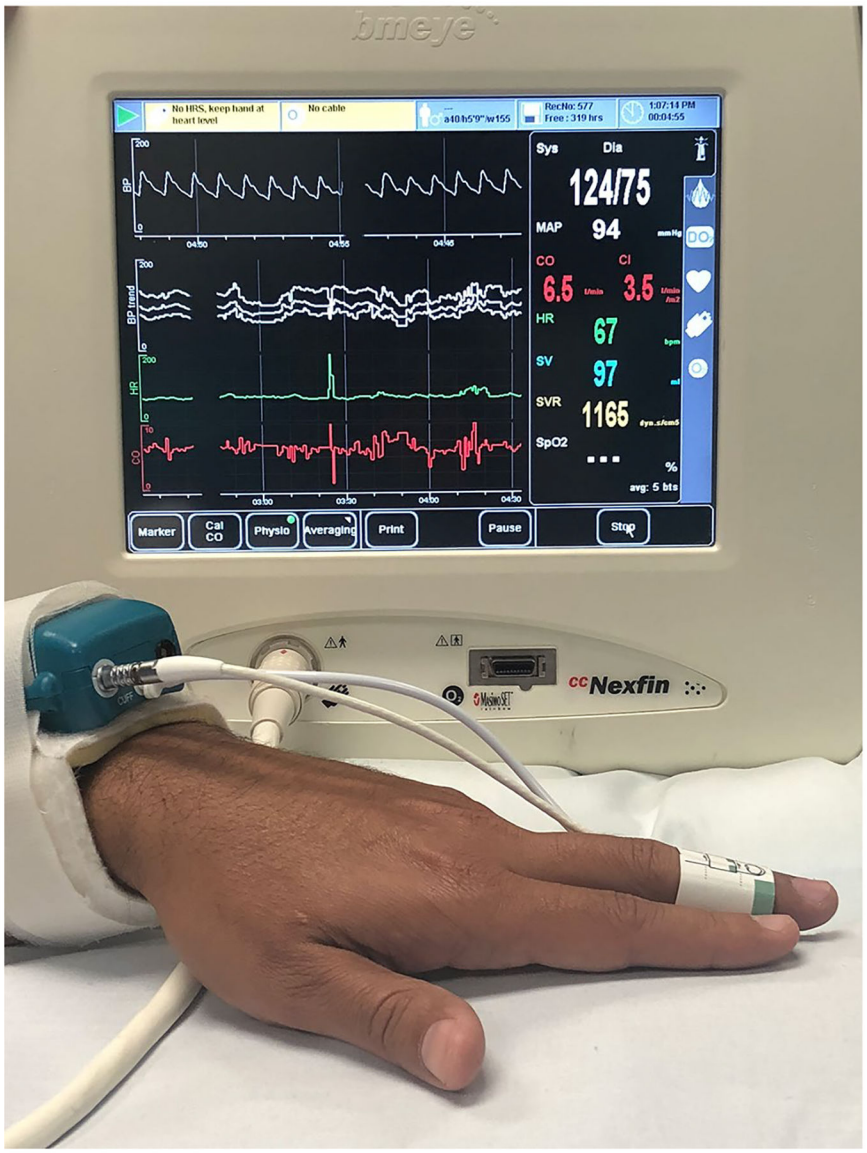

Fig. 1.

Non-invasive hemodynamic monitoring device (Nexfin, Edwards Lifesciences, Irvine, California). White curve = blood pressure trend, green curve = heart rate trend, red curve = cardiac output trend

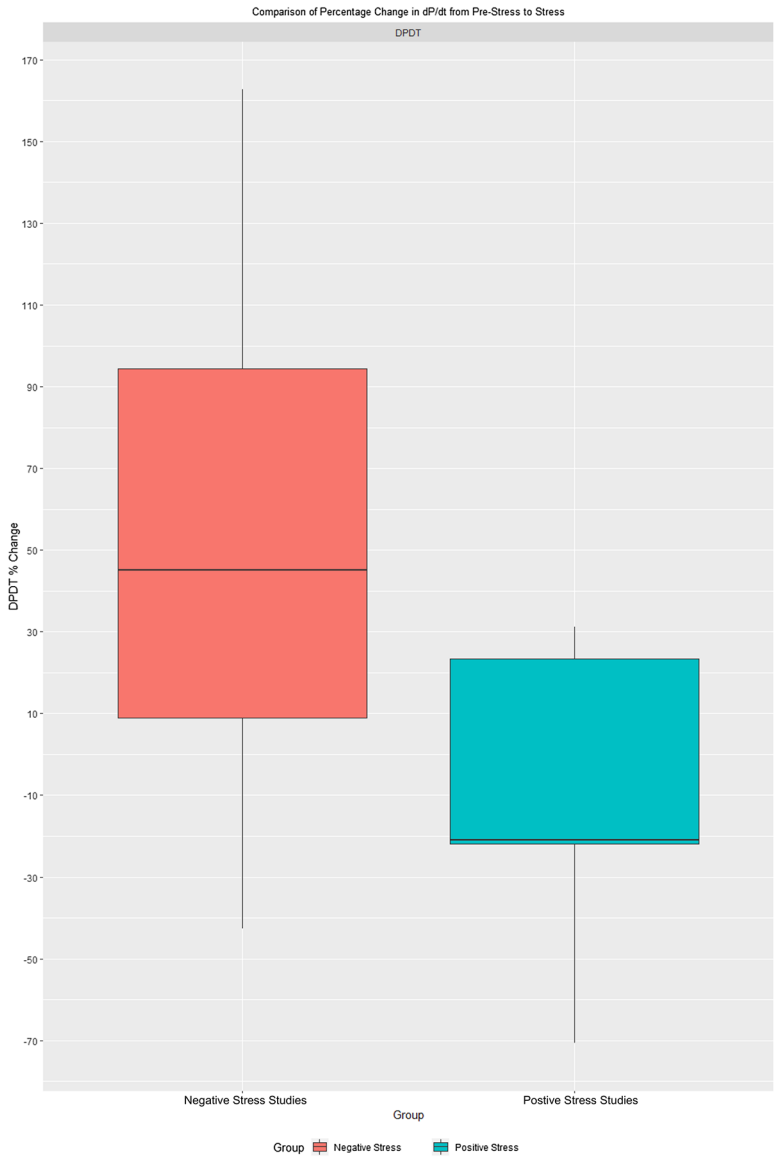

Fig. 2.

Density map of percent change in dP/dt from pre-stress to stress

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Table 1

Demographics and hemodynamic variables during study intervals

	Negative stress test	**Positive stress test**
N (subjects)	26 (81%)	5 (19%)
Age (years) [median (IQR)]	57 (16)	63 (13)
Male:female	14:12	4:1
Height (cm) [median (IQR)]	168 (18)	172 (10)
Weight (kg) [median (IQR)]	78 (23)	80 (37)
Total observations	3198 (123 total obs. per subject)	615 (123 total obs. per subject)
Pre-stress	1066 (41 obs. per subject)	205 (41 obs. per subject)
Stress	1066 (41 obs. per subject)	205 (41 obs. per subject)
Post-stress	1066 (41 obs. per subject)	205 (41 obs. per subject)
Duration in minutes [median (IQR)]		
Total	90 (23)	81 (25)
Pre-stress	39 (10)	32 (9)
Stress	22 (9)	20 (14)
Post-stress	25 (5)	23 (9)

Hemodynamic variables [median (IQR)]	**Pre-stress**	**Stress**	**Post-stress**
Negative stress test subjects			
dP/dt	763 (459)	1038 (764)	941 (664)
SV	80 (32)	71 (45)	76 (35)
HR	63 (26)	114 (40)	106 (27)
SBP	133 (32)	144 (57)	138 (39)
DBP	76 (22)	85 (34)	82 (22)
MAP	99 (26)	111 (43)	106 (27)
Postive stress test subjects			
dP/dt	1122 (1192)	386 (1148)	1055 (955)
SV	88 (16)	78 (38)	87 (40)
HR	76 (19)	120 (59)	103 (35)
SBP	125 (44)	98 (49)	126 (29)
DBP	65 (19)	62 (27)	67 (19)

Hemodynamic variables [median (IQR)]	Pre-stress	Stress	Post-stress
MAP	85 (27)	76 (35)	39 (20)

SVR systemic vascular × resistance (mmHg min/mL), *dP/dt* systolic index of contractility (mmHg/s), *SV* stroke volume (mL), *HR* heart rate (beats per minute), *SBP* systolic blood pressure (mmHg), *DBP* diastolic blood pressure (mmHg), *MAP* mean arterial blood pressure (mmHg)

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Table 2

Hemodynamic comparisons: pre-stress to stress periods (A) and pre-stress to post-stress periods (B)

	Negative stress echo	Positive stress echo	95% CI estimate (lower, upper)	*p* value
(A) Outcomes: (primary) (pre-stress to stress % change)				
dP/dt [median (IQR)]	45.13 (85.42)	−20.86 (45.40)	56.07 (0.072, 117.31)	0.0476
SV [median (IQR)]	−0.78 (18.85)	−18.56 (25.21)	15.52 (0.85, 33.20)	0.0476
(B) Outcomes: (secondary) (pre-stress to post-stress % change)				
dP/dt [median (IQR)]	38.75 (92.84)	18.24 (75.27)	13.40 (−30.54, 67.19)	0.548
SV [median (IQR)]	−4.28 (17.19)	0.94 (23.67)	−10.059 (−31.04, 14.99)	0.159

dP/dt systolic index of contractility (mmHg/s), *SV* stroke volume (mL)