UCLA
UCLA Previously Published Works

Title

A Carotid Doppler Patch Accurately Tracks Stroke Volume Changes During a Preload-Modifying Maneuver in Healthy Volunteers.

Permalink

https://escholarship.org/uc/item/9m64q683

Journal

Critical Care Explorations, 2(1)

Authors

Kenny, Jon-Émile
Barjaktarevic, Igor
Eibl, Andrew
et al.

Publication Date

2020

DOI

10.1097/CCE.0000000000000072

Peer reviewed

OPEN

A Carotid Doppler Patch Accurately Tracks Stroke Volume Changes During a Preload-Modifying Maneuver in Healthy Volunteers

Jon-Émile S. Kenny, MD[1]; Igor Barjaktarevic, MD, PhD[2]; Andrew M. Eibl, BComm[1];
Matthew Parrotta, MSc[1]; Bradley F. Long, MD[1,3]; Joseph K. Eibl, PhD[1,3]; Frederic Michard, MD, PhD[4]

Objectives: Detecting instantaneous stroke volume change in response to altered cardiac preload is the physiologic foundation for determining preload responsiveness.

Design: Proof-of-concept physiology study.

Setting: Research simulation laboratory.

Subjects: Twelve healthy volunteers.

Interventions: A wireless continuous wave Doppler ultrasound patch was used to measure carotid velocity time integral and carotid corrected flow time during a squat maneuver. The Doppler patch measurements were compared with simultaneous stroke volume measurements obtained from a noninvasive cardiac output monitor.

Measurements and Main Results: From stand to squat, stroke volume increased by 24% while carotid velocity time integral and carotid corrected flow time increased by 32% and 9%, respectively. From squat to stand, stroke volume decreased by 13%, while carotid velocity time integral and carotid corrected flow time decreased by 24% and 10%, respectively. Both changes in carotid velocity time integral and corrected flow time were closely correlated with changes in stroke volume ($r^2 = 0.81$ and 0.62, respectively). The four-quadrant plot found a 100% concordance rate between changes in stroke volume and both changes in carotid velocity time integral and changes in corrected flow time. A change in carotid velocity time integral greater than 15% predicted a change in stroke volume greater than 10% with a sensitivity of 95% and a specificity of 92%. A change in carotid corrected flow time greater than 4% predicted a change in stroke volume greater than 10% with a sensitivity of 90% and a specificity of 92%.

Conclusions: In healthy volunteers, both carotid velocity time integral and carotid corrected flow time measured by a wireless Doppler patch were useful to track changes in stroke volume induced by a preload-modifying maneuver with high sensitivity and specificity.

Key Words: carotid ultrasound; corrected flow time; fluid responsiveness; stroke volume; velocity time interval

[1]Health Sciences North Research Institute, Sudbury ON, Canada.

[2]Division of Pulmonary and Critical Care, Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA.

[3]Northern Ontario School of Medicine, Sudbury ON, Canada.

[4]michardconsulting.com, Denens, Switzerland.

Tracking changes in stroke volume (SV) during a fluid challenge is the reference method to detect fluid responsiveness (1). Patients experiencing a significant (e.g., > 10%) rise in SV are considered fluid responders, whereas other patients are classified as nonresponders. Predicting fluid responsiveness is useful to identify patients who may benefit from fluid administration and, maybe more importantly, to prevent unjustified fluid administration in nonresponder patients (2). A recent meta-analysis suggests that predicting fluid responsiveness is useful to rationalize perioperative fluid management and to improve the postoperative outcome of surgical patients (3). Predicting fluid responsiveness is also one of the recommendations of the Surviving Sepsis guidelines when treating patients with suspected or confirmed sepsis (4).

Several preload-modifying maneuvers have been proposed to predict fluid responsiveness before fluid administration. The passive leg raising (PLR) maneuver mobilizes one part of the blood volume from the legs to the abdomen and the right side of the heart, mimicking the hemodynamic effects of a fluid challenge (5). Assessing SV changes during a PLR maneuver is useful to predict fluid responsiveness without the need to give a single drop of fluid (6). Other methods such as the quantification of changes in SV during a lung recruitment maneuver or during an end-expiratory occlusion test have been proposed as well to predict fluid responsiveness (7, 8). These methods have their own advantages and
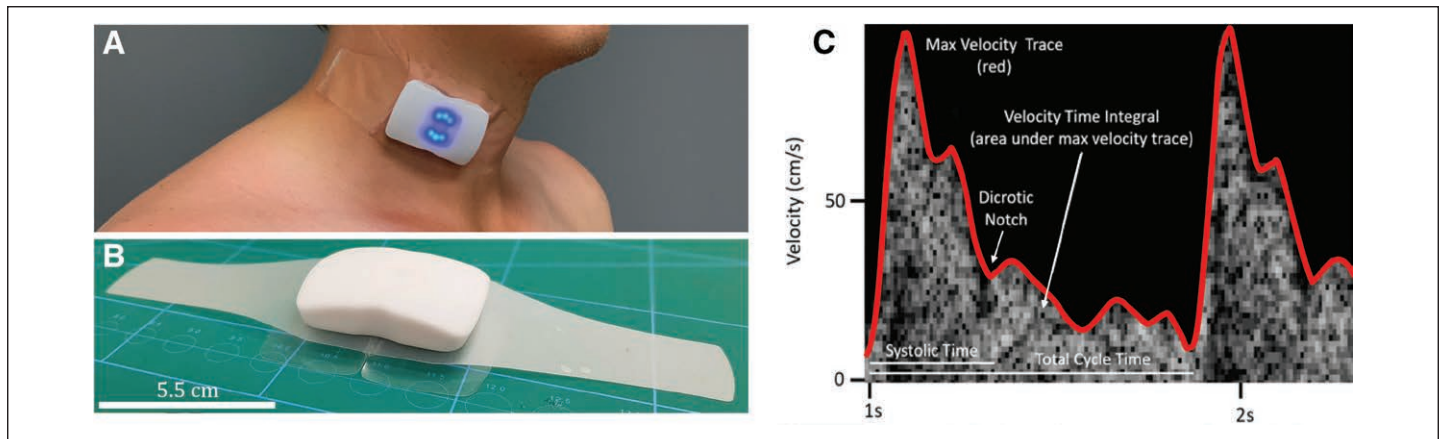
Figure 1. Overview of device. **A**, Novel hands-free Doppler patch placed over common carotid artery of a healthy volunteer and used to collect carotid velocity time integral and corrected flow time. **B**, To scale image of the Doppler patch. **C**, Spectrogram and metrics obtained from Doppler patch.

limitations, but all have in common the need for continuous SV monitoring. Unfortunately, many patients are not equipped with a cardiac output monitoring system. This is particularly true in the emergency department and in the operating room. Even in the ICU, a minority of patients are monitored with cardiac output measurement systems, which are usually cumbersome, invasive, and expensive.

During preload-modifying maneuvers, echocardiography-Doppler is an alternative to cardiac output monitoring systems for quantifying changes in SV, or its main surrogate, the velocity time integral (VTI) of aortic blood velocity (9, 10). However, using echocardiography-Doppler requires a specific training, is time consuming and operator dependent. Sometimes, ultrasound measurements are simply not doable when clear images of the left ventricular outflow tract are impossible to obtain. Therefore, there is a need for a simple and easy way to track changes in SV during preload-modifying maneuvers.

An adhesive Doppler patch was recently developed for the continuous monitoring of carotid blood velocity. When positioned on the neck, it enables a real time quantification of the carotid VTI and corrected flow time (FTc) (**Fig. 1**). It is light and wireless and could represent an appealing solution for tracking changes in SV during preload-modifying maneuvers. Therefore, in healthy volunteers, we investigated whether it could be used to track changes in SV during a squat maneuver, that is known to induce a rise in cardiac preload and SV (11–13). We hypothesized that the rise in SV during squat and the drop in SV when standing back could be detected by the wearable Doppler patch.

MATERIALS AND METHODS

Clinical Setting

We recruited 12 healthy adult volunteers with no known cardiovascular history and on no regular cardiovascular medications. The study was conducted in the Simulation Laboratory at Health Sciences North (Sudbury, ON. Canada). Written informed consent was obtained for all subjects, and the study was approved by the Research Ethic Board of Health Sciences North.

The Squat Maneuver

The entire protocol was 3 minutes in duration (i.e., 180 s); the protocol began with 60 seconds of quiet standing followed by 60 seconds of passive squat and a subsequent 60 seconds return-to-stand (**Fig. 2**). Each subject performed the protocol twice separated by at least 3 minutes of rest. Blood pressure, heart rate (HR), and symptoms of orthostasis were monitored throughout.

Stroke Volume Measurements

All subjects were monitored with a noninvasive, U.S. Food and Drug Administration-approved, pulse contour method (Clearsight; Edwards Lifesciences, Irvine, CA) enabling measurements of SV every 20 seconds. Briefly, this cardiac output monitoring system uses the "volume clamp" method for transducing the digital artery
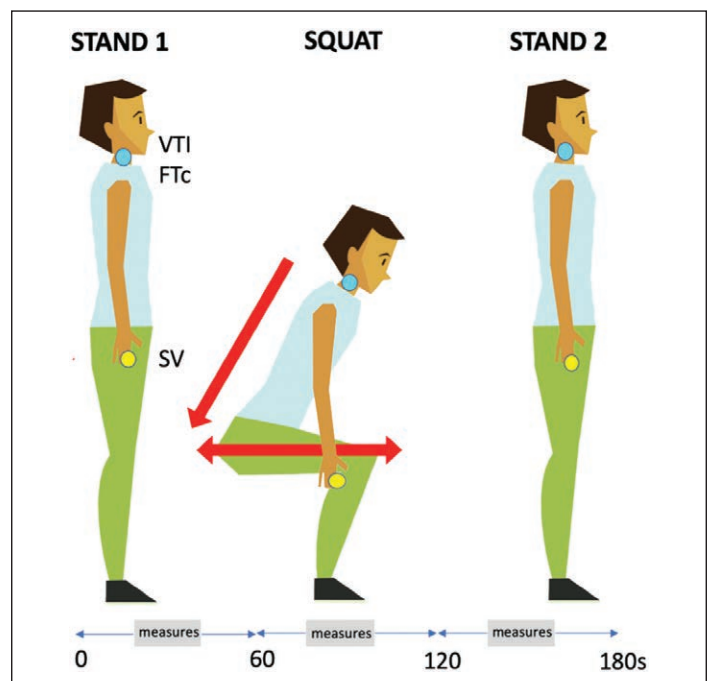

Figure 2. Illustration of stand-squat-stand preload-modifying maneuver. FTc = corrected flow time, SV = stroke volume, VTI = velocity time integral.

waveform. The digital artery waveform is transformed into a brachial artery waveform and then analyzed using pulse contour analysis to derive SV (14, 15).

Carotid VTI and Carotid FTc Measurements

The carotid ultrasound patch (Flosonics Medical, Sudbury, ON, Canada) was placed by palpation over the carotid artery below the angle of the jaw in an effort to ensure Doppler sampling below the bifurcation (Fig. 1). Once an adequate spectrogram signal was visualized in an open-access audio-recording program (Audacity; https://audacityteam.org) the protocol was initiated. The maximum velocity of the Doppler waveform was automatically traced using an algorithm based on the approach described by Steinman et al (16). The waveform analysis was done off-line on a personal computer. The automated maximum velocity estimation for each timepoint in the waveform was used to calculate the VTI as the area under the curve. The duration of systole (i.e., from systolic velocity upstroke to the dicrotic notch, in ms) was recorded from the Doppler signal and corrected for HR using Wodey's formula (17) to obtain the carotid corrected flowtime (FTc). In the equation below, FTc and systolic flowtime are in milliseconds (ms), HR is in cycles per minute and 1.29 is a correction factor with the units of ms × (min/cycle).

$$FTc = \text{systolic flow time} + \left(1.29 \times \left[HR - 60\right]\right)$$

Figure 1C describes the carotid metrics derived from the continuous wave Doppler patch.

Data Analysis

Because the cardiac output monitor provides SV averaged over 20 seconds time intervals, we averaged VTI and FTc measurements over the same time period to ensure the synchronization of measurements. The following time intervals were considered for analysis: 20 to 40 seconds for baseline measurements in the stand position, 80 to 100 seconds for measurements done during squat and 140 to 160 seconds for measurements done after return to the stand position (Fig. 2). Changes in carotid VTI, carotid FTc, and SV measurements were compared using a two-tailed Student t test. The ability of VTI and FTc measurements to track changes in SV values during the squat maneuver was investigated. To do so, we computed four-quadrant plots and performed a concordance analysis, as previously described (18). The four-quadrant plot shows the relationship between changes in VTI or changes in FTc (y-axis) and changes in SV (x-axis) in a scatter plot. We defined a 10% change exclusion zone at the center of the plot to exclude changes in SV which are not clinically relevant. Based on the data points outside the exclusion zone, we calculated the concordance rate as the proportion (percentage) of concordant data pairs to all data pairs. Finally, we quantified the sensitivity and specificity of changes in VTI and changes in FTc to detect significant changes in SV (> 10%).

RESULTS

Twelve healthy volunteers were recruited to complete the squat maneuver. Eleven of the 12 volunteers were included in the study results. In one volunteer, we did not obtain reliable measures of SV

TABLE 1. Characteristics of Healthy Volunteers ($n = 11$)

Average age, yr, median (IQR)	32.1 (23–38)
Percent female, %	45
Average body mass index, median (IQR)	23.4 (19–32.4)
Mean heart rate and range, beats/min, median (IQR)	81 (59–98)
Systolic blood pressure and range, mm Hg, median (IQR)	117 (92–135)
Diastolic blood pressure and range, mm Hg, median (IQR)	69 (60–78)

IQR = interquartile range.

with the cardiac output monitor (autocalibration failure). Baseline characteristics of the 11 healthy subjects studied are described in **Table 1**. Each subject performed the protocol twice.

Hemodynamic Effects of the Squat Maneuver

From stand to squat, there was a significant increase in SV (+24%; $p = 0.0003$), in carotid VTI (+32%; $p = 0.001$), and in carotid FTc (+8.5%; $p = 0.002$). From squat back to stand, there was a significant decrease in SV (–12.9%; $p = 0.0296$), in carotid VTI (–24%; $p = 0.0013$), and in carotid FTc (–10%; $p = 0.0005$). **Figure 3** demonstrates the individual and averaged changes in SV, carotid VTI, and FTc.

Evaluating Agreement Between Changes in SV, Carotid VTI, and Carotid FTc

Figure 4, *A* and *B* shows the four-quadrant plot comparing changes in SV and changes in carotid VTI and FTc; the concordance rate was 100% for both carotid metrics. **Figure 4**, *C* and *D* shows the change in VTI and in FTc dichotomized by the presence or absence of a 10% change in SV. A 15% change in carotid VTI revealed a sensitivity of 95% and specificity of 92% for detecting a 10% change in SV. A 4% change in carotid FTc revealed a sensitivity of 90% and specificity of 92% for detecting a 10% change in SV.

DISCUSSION

Our study done in healthy volunteers shows that both changes in carotid VTI and in carotid FTc measured by a wireless Doppler patch are useful to track changes in SV induced by a preload-modifying maneuver.

From a physiologic standpoint, carotid blood flow depends on global blood flow (i.e., on cardiac output) but also on the distribution of global flow through the different regional circulations. It depends as well on cerebral autoregulation, a mechanism ensuring that cerebral blood flow does not increase if the brain metabolic demand does not change. As a result, several studies have shown that carotid blood flow cannot be used to estimate SV or cardiac output in steady state conditions (19–21). In contrast, acute and transient changes in SV, as those induced by a preload-modifying maneuver, have been shown to induce proportional changes in the common carotid artery Doppler signal (17, 22–26). In 34 critically
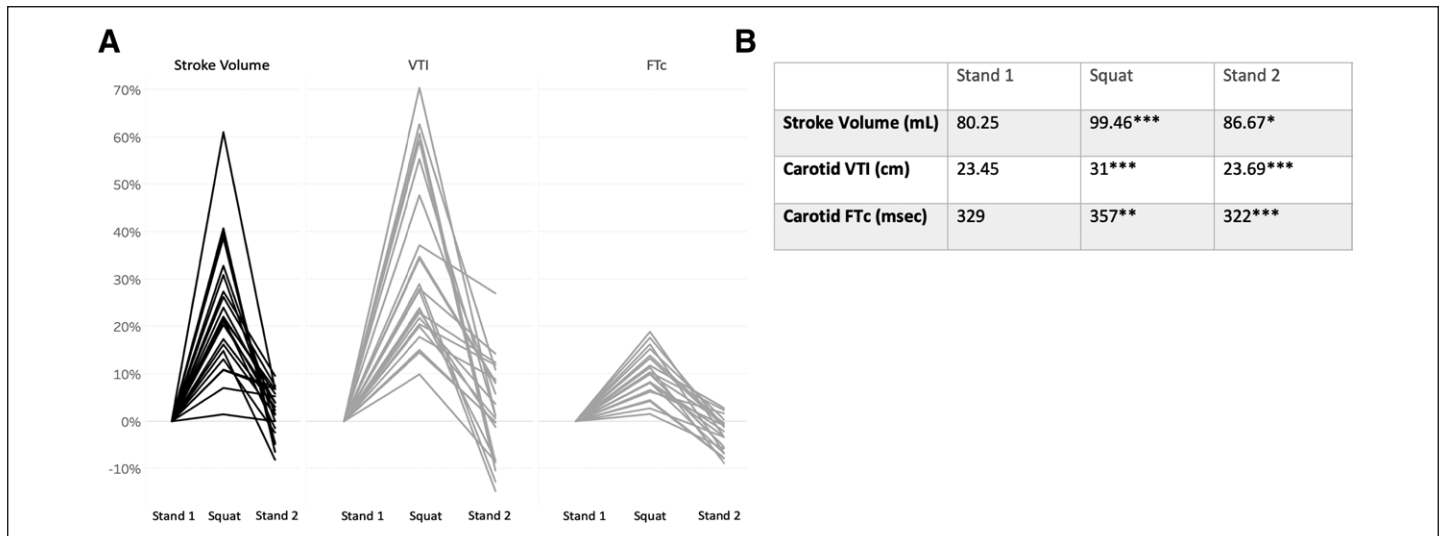
Figure 3. Results of preload-modifying maneuver. **A**, Individual percent changes in stroke volume, carotid velocity time integral (VTI), and carotid corrected flow time (FTc) during the squat maneuver ($n = 22$); (**B**) averaged absolute values for changes in stroke volume, VTI, and FTc during the squat maneuver (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

ill patients, Marik et al (25) observed a strong correlation ($r^2 = 0.59$) between the percent change in SV assessed using a bioreactance technique and the concomitant percent change in carotid blood flow during a PLR maneuver. In 22 medical ICU patients, Jalil et al (26) compared changes in carotid FTc and changes in SV assessed with an invasive pulse contour method during a PLR maneuver, and reported a fair agreement between the two methods. Barjaktarevic et al (17) quantified the carotid FTc in 77 patients with undifferentiated shock before and after a PLR maneuver. They showed that changes in carotid FTc during the PLR maneuver were predictive of changes in SV measured with bioreactance.

As far as we know, this is the first study to simultaneously measure the sensitivity and specificity of carotid VTI and carotid FTc for predicting clinically significant changes in SV. Our findings suggest that tracking changes in VTI may be more clinically relevant. Indeed, the magnitude of changes in FTc was much smaller than the magnitude of changes in VTI and was therefore more prone to measurement errors. In addition, changes in VTI were more closely correlated with changes in SV than changes in FTc (Fig. 4). These findings make sense from a physiologic standpoint since VTI is directly related to blood flow (blood flow = VTI × carotid area × HR), whereas FTc is only indirectly related to SV (the ejection time depends on the ejected volume, or SV, but also on contractility and afterload). On the other hand, the concordance rate was 100% (Fig. 4) and the sensitivity and specificity to detect a significant change in SV was greater than 90% both with VTI and FTc. Therefore, we believe that our small sample size does not allow us to draw definitive conclusions and that larger studies done in real clinical conditions are needed to assess the respective value of carotid VTI and carotid FTc to track changes in SV during a preload-modifying maneuver.

Our study is also the first evaluation of a wireless adhesive Doppler patch. Importantly, carotid measurements were easy to obtain in all subjects. Cardiac output monitors are today reserved to a limited number of patients, mainly from the ICU. In addition, most of these monitoring systems are bulky, expensive, and invasive. Echocardiography-Doppler is an invaluable technique to assess cardiac function and predict fluid responsiveness (27, 28). However, it is operator dependent and requires specific skills. Pocket echo devices and probes, increasingly used in the ICU and beyond, do not have continuous Doppler capabilities and therefore cannot be used to quantify VTI. Therefore, the use of a wireless wearable Doppler sensor has potential to facilitate the routine detection of fluid responsiveness before administering fluid boluses.

Our study has several limitations. First, we studied a limited number of healthy volunteers. Our findings need to be reproduced in a larger number of subjects and in real clinical conditions. Second, the volume clamp technique used to measure SV has limitations that include peripheral vasoconstriction and continuous infusion of vasopressors (14, 29). Importantly, none of our volunteers had peripheral vasoconstriction (e.g., a Raynaud syndrome), and of course, none of them were receiving vasopressors. In this favorable context, the volume clamp method has been shown to provide reliable estimations of changes in blood pressure and flow (14, 15, 30, 31). This method had the major advantage to be noninvasive and nonoperator dependent. Third, we did not perform fluid challenges. Future studies are therefore needed to investigate the ability of the new Doppler patch to predict fluid responsiveness before fluid administration. Fourth, we did not account for differences between the internal and external carotid arteries. The internal carotid artery has a lower resistance in its downstream arterial bed and, consequently, has higher diastolic velocities than the relatively high resistance external carotid artery (32). The common carotid artery, which we measured, is a hybrid between the aforementioned. An increase in blood flow to the internal carotid artery is normally met with auto-regulatory changes that increase downstream resistance and, accordingly, decrease diastolic velocity; the degree to which this is transmitted to the common carotid artery is an avenue of future study in both healthy volunteers and the critically ill. Finally, we did not measure total carotid artery flow but rather VTI. We believe that this is an adequate surrogate for flow in
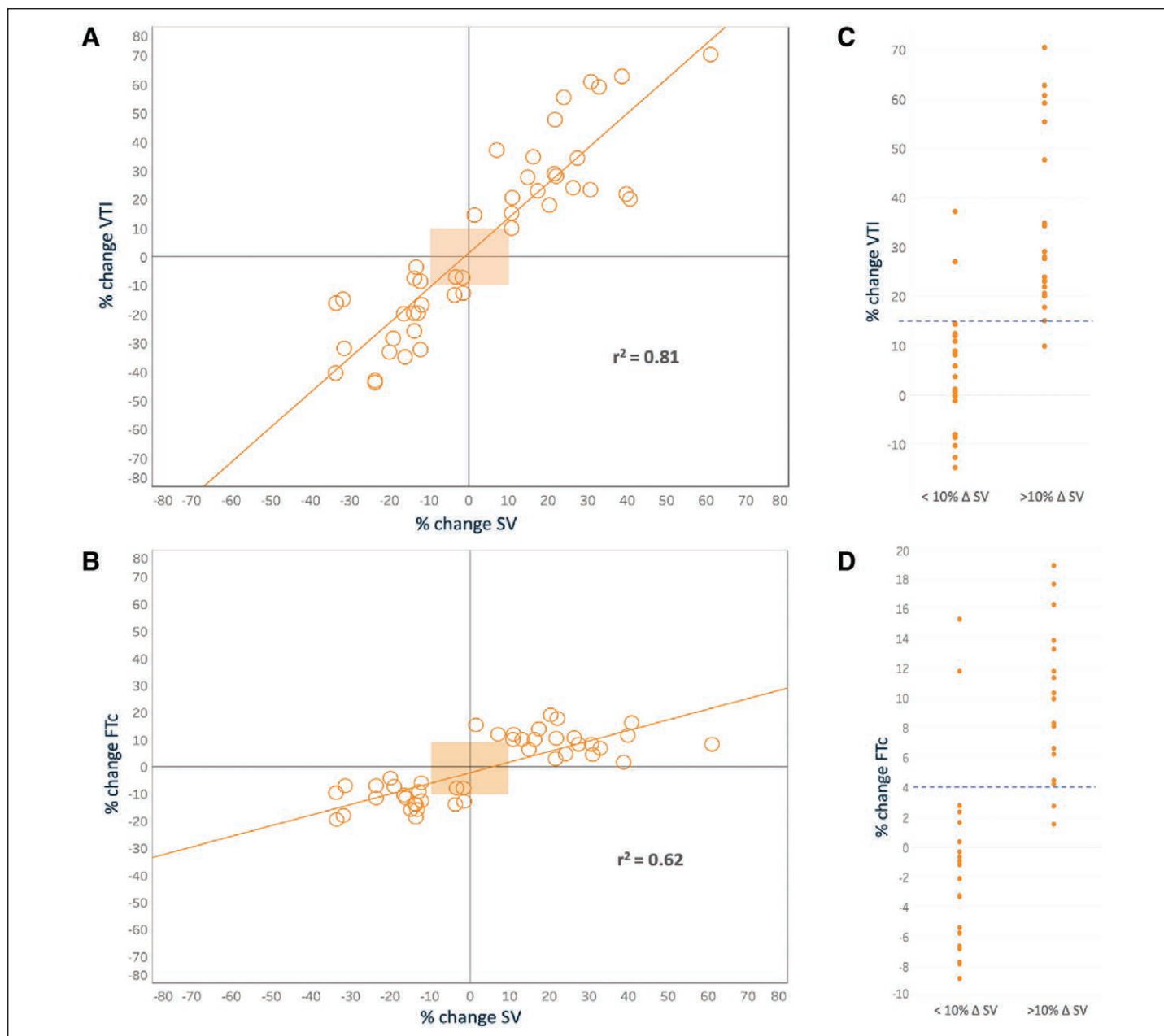
Figure 4. Comparative statistics for stroke volume and carotid Doppler metrics. **A** and **B**, Four-quadrant plots comparing percent change in stroke volume on *x*-axis to percent change in carotid velocity time integral (VTI) and carotid corrected flow time (FTc) on *y*-axis, respectively. **C** and **D**, Optimal thresholds for changes in carotid VTI and changes in carotid FTc, respectively, to detect a change in stroke volume greater than 10% (delta stroke volume [SV]).

this study because the cross-sectional diameter of the carotid artery is known to change minimally in healthy volunteers within the normal range of mean arterial pressures (33). Change in carotid artery cross-sectional area is likely more important at lower mean arterial pressures, as observed in septic shock patients by Marik et al (25).

In conclusion, we describe the use of a novel hands-free continuous wave ultrasound patch placed over the common carotid artery to track changes in SV during a preload-modifying maneuver. Both changes in carotid VTI and in carotid FTc were useful to track changes in SV and detect potential fluid responders. Further evaluations are now needed in surgical or critically ill patients and during fluid challenges.

REFERENCES

1. Michard F, Teboul JL: Predicting fluid responsiveness in ICU patients: A critical analysis of the evidence. *Chest* 2002; 121:2000–2008
2. Michard F: Toward precision hemodynamic management. *Crit Care Med* 2017; 45:1421–1423

3. Benes J, Giglio M, Brienza N, et al: The effects of goal-directed fluid therapy based on dynamic parameters on post-surgical outcome: A meta-analysis of randomized controlled trials. *Crit Care* 2014; 18:584

4. Levy MM, Evans LE, Rhodes A: The surviving sepsis campaign bundle: 2018 update. *Intensive Care Med* 2018; 44:925–928

5. Monnet X, Teboul JL: Passive leg raising. *Intensive Care Med* 2008; 34:659–663

6. Cherpanath TG, Hirsch A, Geerts BF, et al: Predicting fluid responsiveness by passive leg raising: A systematic review and meta-analysis of 23 clinical trials. *Crit Care Med* 2016; 44:981–991

7. Biais M, Lanchon R, Sesay M, et al: Changes in stroke volume induced by lung recruitment maneuver predict fluid responsiveness in mechanically ventilated patients in the operating room. *Anesthesiology* 2017; 126:260–267

8. Silva S, Jozwiak M, Teboul JL, et al: End-expiratory occlusion test predicts preload responsiveness independently of positive end-expiratory pressure during acute respiratory distress syndrome. *Crit Care Med* 2013; 41:1692–1701

9. Feissel M, Michard F, Mangin I, et al: Respiratory changes in aortic blood velocity as an indicator of fluid responsiveness in ventilated patients with septic shock. *Chest* 2001; 119:867–873

10. Georges D, de Courson H, Lanchon R, et al: End-expiratory occlusion maneuver to predict fluid responsiveness in the intensive care unit: An echocardiographic study. *Crit Care* 2018; 22:32

11. O'donnell TV, McIlroy MB: The circulatory effects of squatting. *Am Heart J* 1962; 64:347–356

12. Lewis BS, Lewis N, Gotsman MS: Effect of standing and squatting on echocardiographic left ventricular function. *Eur J Cardiol* 1980; 11:405–412

13. Hanson P, Slane PR, Rueckert PA, et al: Squatting revisited: Comparison of haemodynamic responses in normal individuals and heart transplantation recipients. *Heart* 1995; 74:154–158

14. Ameloot K, Palmers PJ, Malbrain ML: The accuracy of noninvasive cardiac output and pressure measurements with finger cuff: A concise review. *Curr Opin Crit Care* 2015; 21:232–239

15. Bubenek-Turconi SI, Craciun M, Miclea I, et al: Noninvasive continuous cardiac output by the nexfin before and after preload-modifying maneuvers: A comparison with intermittent thermodilution cardiac output. *Anesth Analg* 2013; 117:366–372

16. Steinman A, Tavakkoli J, Myers J, et al: A new approach for determining maximum frequency in clinical Doppler ultrasound spectral estimates. Proceedings of the 22nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society (Cat No 00CH37143), Chicago, IL, 2000. IEEE, 2000, pp 2640–2643

17. Barjaktarevic I, Toppen WE, Hu S, et al: Ultrasound assessment of the change in carotid corrected flow time in fluid responsiveness in undifferentiated shock. *Crit Care Med* 2018; 46:e1040–e1046

18. Saugel B, Grothe O, Wagner JY: Tracking changes in cardiac output: Statistical considerations on the 4-quadrant plot and the polar plot methodology. *Anesth Analg* 2015; 121:514–524

19. Weber U, Glassford NJ, Eastwood GM, et al: A pilot assessment of carotid and brachial artery blood flow estimation using ultrasound Doppler in cardiac surgery patients. *J Cardiothorac Vasc Anesth* 2016; 30:141–148

20. Weber U, Glassford NJ, Eastwood GM, et al: A pilot study of the relationship between Doppler-estimated carotid and brachial artery flow and cardiac index. *Anaesthesia* 2015; 70:1140–1147

21. Eicke BM, von Schlichting J, Mohr-Ahaly S, et al: Lack of association between carotid artery volume blood flow and cardiac output. *J Ultrasound Med* 2001; 20:1293–1298; quiz 1300

22. Sidor M, Premachandra L, Hanna B, et al: Carotid flow as a surrogate for cardiac output measurement in hemodynamically stable participants. *J Intensive Care Med* 2018 Jan 1:885066618775694. [Epub ahead of print]

23. Ma IWY, Caplin JD, Azad A, et al: Correlation of carotid blood flow and corrected carotid flow time with invasive cardiac output measurements. *Crit Ultrasound J* 2017; 9:10

24. Ibarra-Estrada MÁ, López-Pulgarín JA, Mijangos-Méndez JC, et al: Respiratory variation in carotid peak systolic velocity predicts volume responsiveness in mechanically ventilated patients with septic shock: A prospective cohort study. *Crit Ultrasound J* 2015; 7:12

25. Marik PE, Levitov A, Young A, et al: The use of bioreactance and carotid Doppler to determine volume responsiveness and blood flow redistribution following passive leg raising in hemodynamically unstable patients. *Chest* 2013; 143:364–370

26. Jalil B, Thompson P, Cavallazzi R, et al: Comparing changes in carotid flow time and stroke volume induced by passive leg raising. *Am J Med Sci* 2018; 355:168–173

27. Lamia B, Ochagavia A, Monnet X, et al: Echocardiographic prediction of volume responsiveness in critically ill patients with spontaneously breathing activity. *Intensive Care Med* 2007; 33:1125–1132

28. Jozwiak M, Depret F, Teboul JL, et al: Predicting fluid responsiveness in critically ill patients by using combined end-expiratory and end-inspiratory occlusions with echocardiography. *Crit Care Med* 2017; 45:e1131–e1138

29. Thiele RH, Bartels K, Gan TJ: Cardiac output monitoring: A contemporary assessment and review. *Crit Care Med* 2015; 43:177–185

30. Hofhuizen C, Lansdorp B, van der Hoeven JG, et al: Validation of noninvasive pulse contour cardiac output using finger arterial pressure in cardiac surgery patients requiring fluid therapy. *J Crit Care* 2014; 29:161–165

31. Chen G, Meng L, Alexander B, Tran NP, et al: Comparison of noninvasive cardiac output measurements using the nexfin monitoring device and the esophageal Doppler. *J Clin Anesth* 2012; 24:275–283

32. McNaughton DA, Abu-Yousef MM: Doppler US of the liver made simple. *Radiographics* 2011; 31:161–188

33. Hansen F, Mangell P, Sonesson B, et al: Diameter and compliance in the human common carotid artery–variations with age and sex. *Ultrasound Med Biol* 1995; 21:1–9