Journal of Cardiothoracic and Vascular Anesthesia 35 (2021) 1509−1515

Contents lists available at ScienceDirect

Journal of Cardiothoracic and Vascular Anesthesia

journal homepage: www.jcvaonline.com

Emerging Technology Review

Functional Hemodynamic Monitoring With a Wireless Ultrasound Patch

Jon-Émile S. Kenny, MD[1]

Health Sciences North Research Institute, Sudbury, Ontario, Canada

In this Emerging Technology Review, a novel, wireless, wearable Doppler ultrasound patch is described as a tool for resuscitation. The device is designed, foremost, as a functional hemodynamic monitor—a simple, fast, and consistent method for measuring hemodynamic change with preload variation. More generally, functional hemodynamic monitoring is a paradigm that helps predict stroke volume response to additional intravenous volume. Because Doppler ultrasound of the left ventricular outflow tract noninvasively measures stroke volume in realtime, it increasingly is deployed for this purpose. Nevertheless, Doppler ultrasound in this manner is cumbersome, especially when repeat assessments are needed. Accordingly, peripheral arteries have been studied and various measures from the common carotid artery Doppler signal act as windows to the left ventricle. Yet, handheld Doppler ultrasound of a peripheral artery is susceptible to human measurement error and statistical limitations from inadequate beat sample size. Therefore, a wearable Doppler ultrasound capable of continuous assessment minimizes measurement inconsistencies and smooths inherent physiologic variation by sampling many more cardiac cycles. Reaffirming clinical studies, the ultrasound patch tracks immediate SV change with excellent accuracy in healthy volunteers when cardiac preload is altered by various maneuvers. The wearable ultrasound also follows jugular venous Doppler, which qualitatively trends right atrial pressure. With further clinical research and the application of artificial intelligence, the monitoring modalities with this new technology are manifold.

Key Words: carotid Doppler; volume responsiveness; functional hemodynamic monitoring; corrected flow time; velocity time integral; wearable technology

MEASURING the cardiovascular response after a defined preload perturbation undergirds the paradigm known as "functional hemodynamic monitoring" (FHM).[1-4] Perhaps the most widely taught functional hemodynamic measure is orthostatic vital signs—whereby heart rate and blood pressure are measured before and after a patient stands. Importantly, it is neither absolute heart rate nor blood pressure that is the key measure, but rather its change in response to gravitationally diminished cardiac preload. Thus, reaction to standing reveals something clinically meaningful about cardiovascular status.[2]

FHM is used similarly in the operating room and the intensive care unit (ICU).[5-7] However, instead of standing upright, preload may be reduced cyclically by mechanical ventilation; this underpins stroke volume, pulse pressure, and peak velocity variation, as well as the tidal volume challenge.[1,2,8,9] Additionally, preload may be reduced transiently by end-inspiratory occlusion[10] or augmented by the passive leg raise (PLR),[4,11,12] end-expiratory occlusion test, or mini-fluid challenge.[3,8,13-16] Although each of these preload stresses carries its own indications and contraindications,[2,17] the physiologic reasoning flows from that previously described—nudging the heart and measuring its reaction to glean additional hemodynamic information.

Though the measured output during FHM is typically stroke volume (SV), or its surrogate, the ultimate yield for the clinician is the slope of the Frank-Starling curve (Fig 1, A). In other words, when preload is modified, a large or small SV response intimates a steep or flattened Frank-Starling curve, respectively.[11,12] Consequently, whether in the context of ICU resuscitation or goal-directed intravenous fluid therapy as a part of enhanced surgical recovery, FHM affords extra hemodynamic data—how SV will respond to additional preload. There is ample evidence demonstrating that FHM is superior to static

[1]*Address correspondence to* Jon-Emile S. Kenny, MD, Health Sciences North Research Institute, 56 Walford Rd, Sudbury, ON, Canada, P3E 2H2.

E-mail address: jon-emile@heart-lung.org

https://doi.org/10.1053/j.jvca.2021.01.040

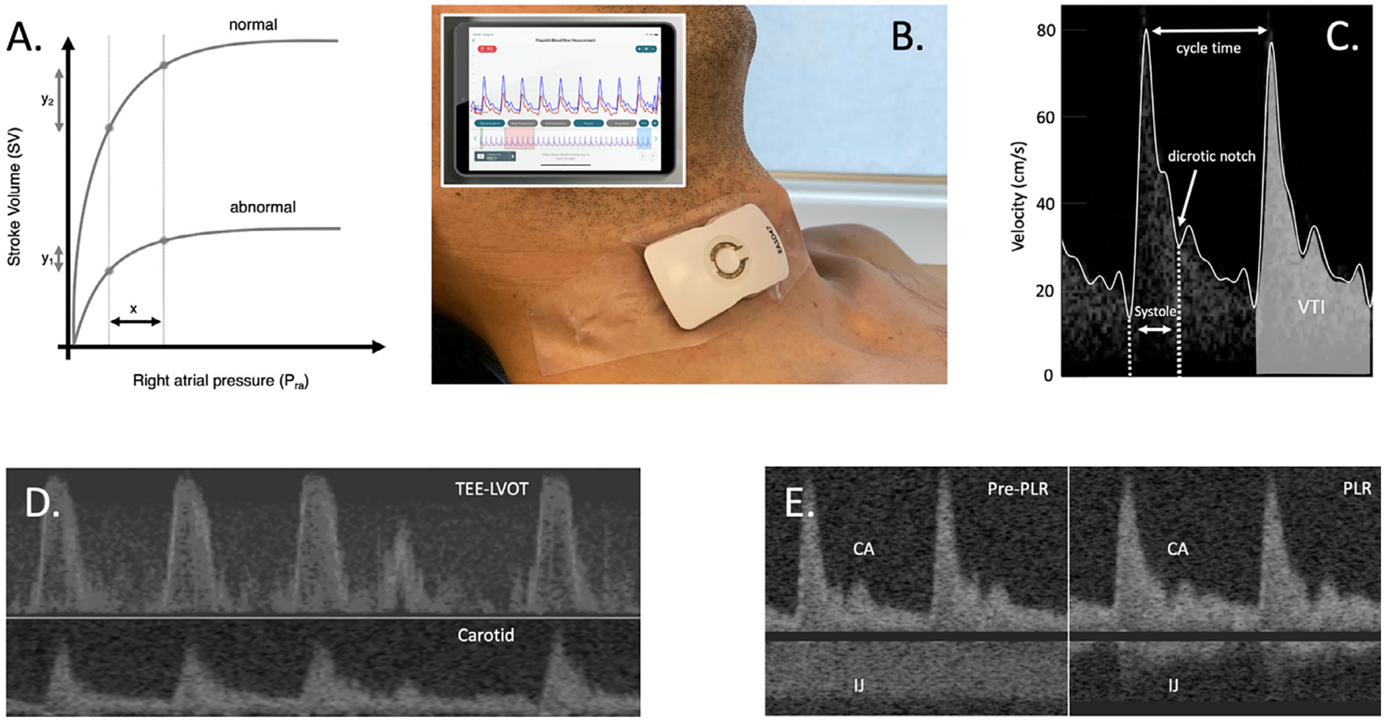

Fig 1. Overview of functional hemodynamic monitoring and the wireless Doppler ultrasound patch. (A) Illustrates the basic Frank-Starling mechanism between normal and abnormal (volume unresponsive) states. For a change in preload (x), there are different SV responses (y1 *v* y2). (B) Shows the ultrasound patch worn by a healthy volunteer and the inset reveals the user interface on an iOS device. (C) Illustrates generic carotid Doppler waveforms with systole (from which FTc is derived) and the velocity time integral (VTI) marked. (D) Shows five cardiac cycles synchronously measured via transesophageal echocardiography (TEE) insonation of the left ventricular outflow tract (LVOT) and the ultrasound patch (carotid). (E) Shows simultaneously measured internal jugular (IJ) and carotid artery (CA) before and during a passive leg raise (PLR). During PLR, the IJ velocities decrease and become pulsatile, consistent with increasing right atrial pressure.

indices (eg, absolute SV, cardiac output, central venous pressure, blood pressure) for predicting response to further intravenous volume. Although conflicting data exist,[5,7,18,19] goal-directed fluid therapy for enhanced surgical recovery may be beneficial by reducing postoperative complications and length of stay. As well, this paradigm decreases unnecessary and, potentially harmful, intravenous fluids in the ICU.[5,20-22]

Doppler Ultrasound as a Functional Hemodynamic Measure

There are numerous monitoring utensils for FHM. Ultimately, each of them directly measures SV, or a surrogate, because it is the change in blood volume leaving the heart that is the dependent variable of the traditional Frank-Starling curve (Fig 1, A). Evaluating the various technologies is beyond the scope of this Emerging Technology Review. Instead, emphasis is placed on Doppler ultrasound, as it is noninvasive and increasingly adopted by intensivists and anesthesiologists.[23] A cursory overview of Doppler measures and their use in FHM is offered as background for the ultrasound patch described thereafter (Fig 1, B and C).

When ultrasound of known frequency reflects off of moving red blood cells, the change in the returned frequency imputes blood velocity by the Doppler equation. As the area under the velocity-time curve yields distance, blood velocity in centimeters per second (cm/s) is integrated to give the velocity time integral (ie, VTI, distance in centimeters) that the blood travels over a single beat. Then, distance multiplied by vessel area (assumed to be circular, πr^2) confers the cylindrical volume defined by the moving blood in cm^3. For example, if blood is insonated at the left ventricular outflow tract (LVOT), then the aforementioned calculation yields stroke volume in cm^3 or milliliters (mL). Then, assuming constant LVOT area, SV change depends only on the measured blood velocity.[24]

The aforementioned principles have been adopted in the ICU and operating room to help gauge the slope of the Frank-Starling curve.[7,25] For example, change in the LVOT VTI measured by transthoracic echocardiography (TTE) in response to a PLR accurately detects patients who respond to further preload.[12] As well, TTE used in conjunction with an end-inspiratory, end-expiratory occlusion test (EEOT), does the same.[10] The EEOT is a defined respiratory maneuver applied by a ventilator, physiologically akin to Valsalva and release.[16]

A similar approach has been extrapolated to Doppler of the descending aorta. Esophageal Doppler as a functional hemodynamic measure was pioneered by anesthesiologists[26] and expanded into the ICU.[27] Again, whether in response to a PLR,[27] EEOT,[15] or peak systolic velocity variation during controlled, mechanical ventilation,[28] the principles described for the aortic outflow tract also apply to the descending aorta. Notably, because the descending aorta is elastic, measuring its diameter and velocity change in response to a hemodynamic intervention is important.[29] However, a recent investigation using esophageal Doppler during an EEOT revealed excellent diagnostic attributes without measuring aortic diameter.[15]

In addition to VTI, another commonly reported ultrasound measure is the corrected systolic flow time (FTc).[30] The duration of systole measured from the Doppler trace corresponds to the time that the aortic valve is open and ejecting blood. The length of systole is mediated by multiple variables, especially heart rate,[31] afterload,[32,33] and SV. Nevertheless, when afterload is kept constant and the raw systolic time is mathematically corrected for heart rate to obtain the FTc (eg, by Wodey's equation[34]), then there is a good correlation between FTc and SV.[35-38]

Carotid Doppler as a Functional Hemodynamic Measure

As blood pressure measured in the brachial artery infers central arterial pressure, blood flow in a peripheral artery informs on its central origin. Because the common carotid is easier to insonate at the bedside than the LVOT, the carotid may be used as a superficial window to the left ventricle. For example, Roehrig et al. observed significant correlation between common carotid blood flow and cardiac output after PLR in postoperative cardiac surgery patients.[39] Further, change in carotid blood flow[40] and FTc both demonstrated good accuracy as functional hemodynamic measures in critically ill patients,[30,41] though evidence for FTc is more supportive as detailed in this recent systematic review.[42]

FTc also detects clinically significant gastrointestinal hemorrhage[43] and hypotension after induction.[44] Further, FTc anticipates SV changes during blood donation and in response to a PLR following blood donation.[45,46] Similar findings are noted in healthy individuals who fast.[47] Of interest, patients receiving dialysis reduce FTc with volume removal, but augment FTc change with PLR after dialysis.[48,49] This implies that the slope of the Frank-Starling curve steepens with successful dialysis (Fig 1, A).

When the cardiovascular stress is cyclical intrathoracic pressure change induced by passive, mechanical ventilation, common carotid artery peak systolic velocity variation is also an accurate functional hemodynamic measure.[39,44,50-53] Importantly, however, when respiration is controlled (even partially) by the patient, peak velocity variation—such as pulse-pressure and stroke-volume variation—usually underperforms as a functional measure. Nevertheless, one group found that carotid artery peak velocity variation worked well in spontaneously breathing preoperative neurosurgery patients,[51] and another group could not replicate this finding in critically ill patients.[54]

Conflicting Data and Sources of Error

Yet, not all investigations have confirmed the common carotid artery as a successful site to infer SV change. Girotto et al. found that carotid blood flow was sensitive but not specific for detecting significant change in cardiac index (CI),[55] and Abbasi et al. found that novice sonographers were unable to use either carotid blood flow or FTc as adequate CI surrogates.[56] As elaborated next, this inconsistency may reflect investigational variability rather than an inherent paradigm flaw.

First, as previously described, flow calculation depends on the cross-sectional area of the common carotid artery. Because radius measurement error is amplified to the second power, flow calculation in this manner is problematic, especially for smaller arteries. More concretely, in a 6-mm carotid artery, a 1-mm measurement error becomes a 30% flow error.[57]

Second, velocity measurement has its own subtle, yet significant sources of error, especially in the carotid artery. Carotid artery velocity measurement requires the user to select the insonation angle relative to the centerline of blood flow; typically, this is 60°. Yet, because the Doppler equation is cosine-dependent, relatively large insonation angles magnify measurement error. If the user misjudges the insonation angle by 5°, it engenders a 15% velocity error.[58] Furthermore, blood velocity profile across the carotid artery is different from the LVOT or descending aorta. The former is typically "blunted parabolic," in which a velocity gradient exists from the fastest-moving, center line, red blood cells outward toward slower moving blood along the vessel walls. Thus, sampling the same population of red cells in the carotid is more challenging than a larger vessel in which all red cells are moving at essentially the same velocity (ie, plug flow).[59] Finally, superficial vessels, such as the carotid, are more susceptible to geometric spectral broadening (GSB).[60] To the extent that the clinician differentially compresses neck soft tissue between measurements, altered aperture-to-depth ratio may introduce additional velocity error by GSB.[61]

Third, intrinsic Doppler variation introduced by normal physiology adds uncertainty if too few cardiac cycles are sampled. That is, as blood flow varies throughout the respiratory cycle, detecting change before and after an intervention with statistical confidence requires an adequate beat sample size. Although three cardiac cycles from the LVOT are recommended,[62] this has not been described for the common carotid artery, and some investigations assessed only a single cardiac cycle. The number of cycles sampled depends—statistically—on the change threshold to detect and the intrinsic variation of the measured metric.[63] As subsequently discussed, a relatively small threshold with large variation can require dozens of quantified beats before and after an intervention—challenging with handheld Doppler.

Fourth, and in a related vein, comparing a limited snapshot of cardiac cycles to the output algorithm of a noninvasive SV monitor may be problematic. Many SV monitors average data over dozens of seconds to smooth the aforementioned variability. Yet, this introduces timelag between physiology and response such that real-time Doppler beats might be misjudged as discordant from a gold standard when, in actuality, the incongruity is a temporal mirage.[64]

Finally, changes in vascular resistance downstream to the common carotid artery may mediate the relationship between stroke volume and carotid flow. The situation is complicated because the internal carotid artery has a lower intrinsic resistance than the external carotid and their inherent capacities for autoregulation are different.[65] Despite this, stroke volume and blood flow in the internal carotid artery correlate well with provocative maneuvers.[66-68] Furthermore, some have demonstrated good relationship between cardiac output and carotid blood flow over extended periods of time,[69] though other groups have not.[70] Given the clinical observations supporting carotid Doppler as a functional hemodynamic window and the healthy subject data presented below, autoregulation appears to mediate common carotid flow over many minutes to hours. Ostensibly, this presents a transient temporal window to assess the immediate functional state of the heart, especially given that the peak effect of the PLR typically is observed within 60 seconds[11] and that a rapid fluid bolus can augment SV within ten seconds.[71]

Wearable Doppler Ultrasound

To address some of these limitations, a wireless, wearable Doppler ultrasound patch that is easily applied over the common carotid artery has been developed (Fig 1, B and C).[64,72-76] The device (Flosonics Medical, Sudbury, Ontario, Canada) is cleared by both Health Canada and the US Food and Drug Administration. It uses two continuous-wave, 4-MHz ultrasound beams to transmit and receive; the transducers are housed on a wedge that generates a constant angle of insonation of approximately 60°. Adhesive straps affix the device to the neck, setting the insonation angle relative to the carotid artery. Each transducer creates a uniform, wide aperture, roughly three-to-four times the width of a typical carotid artery, affording fast and reliable signal acquisition and uniform insonation. The ultrasound patch is lightweight and transmits data via Bluetooth to an application compatible with any iOS device.

The user interface displays the real-time velocity trace or the spectrogram, as desired by the clinician. Below the velocity trace is a beat-to-beat trending function for which Doppler metrics are compared by the user sliding windows before and after intervention (Fig 1, B).

Carotid Arterial Doppler

This Doppler ultrasound system addresses a number of the aforementioned sources of human error. Because the device itself is lightweight and adhered with a fixed angle, sources of handheld sampling error are mitigated. In addition, continuous-wave ultrasound better achieves uniform insonation (UI) of all velocity samples across the carotid lumen. UI is when the entire volume of blood is exposed to a uniform ultrasound beam and when the angle between the beam and flow is constant across the entire volume. When realized, UI ensures that the mean Doppler frequency corresponds to the mean flow velocity in the vessel.[59] UI is particularly important in a vessel such as the carotid in which there is larger distribution of red cell velocities and, accordingly, when mean flow velocity is lower than the max, center-line velocity. In contradistinction, conventional pulsed-wave bedside ultrasound systems have a narrow beam with a highly localized sample volume. A narrow sample window is less problematic when calculating flow in the LVOT or descending aorta because the velocity profile is "plug"; that is, the mean and max velocities are nearly equivalent. Importantly, even when the window of a pulsed-wave Doppler is increased to include the entire diameter of a vessel, UI is not achieved.[77]

Because the wearable Doppler functions as a hemodynamic monitor, the effects of inherent, physiologic variability are accounted for and comparison over time with other noninvasive SV monitors is more equitable. For example, in resting, standing, healthy volunteers, the carotid artery FTc coefficient of variation (ie, the standard deviation divided by the mean) of more than 3,300 cardiac cycles was observed to be, on average, 6%. Thus, quiet respiration alone introduces clinically significant variation such that detecting a 3% to 4% FTc threshold[72,74] demands sampling dozens of beats before and after an intervention, for statistical confidence.[73] In addition, in a healthy volunteer, performing simultaneous descending aortic Doppler VTI while wearing the carotid artery ultrasound patch in addition to volume clamp and bioreactance SV monitors, there was clinically significant temporal discordance between the devices and Doppler ultrasound.[64] Thus, changing physiology is not represented simultaneously by measurement modality. Nevertheless, SV changes induced by squatting, passive leg raising, and simulated end-expiratory inspiratory occlusion maneuvers are captured reliably by the wearable carotid ultrasound patch in healthy subjects.[75] Additionally, novel metrics from the wearable ultrasound, such as the Doppler shock index (DSI, heart rate divided by common carotid VTI), might detect falling SV with greater diagnostic accuracy as compared with traditional vital signs.[74]

Although the data accumulated with the ultrasound patch were in healthy volunteers, it agreed with data previously described in various patient populations. For example, the FTc threshold that the ultrasound patch identified as best detecting 10% SV change was similar to that observed in undifferentiated shock.[30,73] Of note, the wearable ultrasound does not specifically measure carotid diameter. Nevertheless, artificial intelligence currently is deployed to identify unique signatures from the entire Doppler spectrogram for computing vascular area change. Furthermore, real-time trending of the carotid Doppler Resistance Index (RI) is planned to give clinicians a window into downstream, autoregulatory effects. Finally, investigation of the wearable ultrasound has expanded beyond healthy subjects to surgical patients, with transesophageal echocardiography (TEE) LVOT-VTI as a gold standard (Fig 1, D).

Internal Jugular Doppler

Of emerging interest, the wearable ultrasound patch simultaneously monitors internal jugular Doppler. As venous Doppler velocimetry qualitatively tracks right atrial pressure in the internal jugular,[78] superior vena cava,[79-81] hepatic and portal veins,[79,82] common femoral vein,[83] and intra-renal veins,[84] simultaneous assessment of arterial and venous Doppler adds hemodynamic sophistication. For example, during a passive leg raise (PLR), the wearable ultrasound patch synchronously relays arterial and venous indices consistent with increasing SV and right atrial pressure, respectively (Fig 1, E). In effect, this is real-time illustration of the Frank-Starling mechanism. Notably, such monitoring may be of benefit in less acute settings and in outpatients as well; for example, in dialysis units and congestive heart failure patients. Investigation is ongoing.

Conclusions

The goal of FHM is to predict SV response to additional preload; the initial rationale was optimizing oxygen delivery to tissues, though its ethos is evolving toward preventing physiologically unhelpful and, arguably, harmful intravenous fluids. Rather than absolute values of stroke volume, blood pressure, or filling pressure, FHM is predicated on detecting cardiovascular response following a defined preload stress. Because Doppler ultrasound of the LVOT yields rapid, real-time SV measures, it is a trusted FHM modality, but it is cumbersome to perform repeatedly at the bedside. Accordingly, Doppler ultrasound has moved distally from the mouth of the left ventricle to the descending aorta and peripheral arteries as reliable, easier-to-obtain SV surrogates. Nevertheless, human factors, inherent physiologic variation, and gold-standard algorithm features introduce pitfalls when deploying and investigating brief, Doppler "snap-shots" as functional hemodynamic assessments. A wearable, wireless, continuous-wave Doppler ultrasound that displays and trends real-time Doppler measures, such as VTI, FTc, and peak velocity, addresses many of the aforementioned caveats and affords the clinician a simple and reliable method for inferring the slope of the Frank-Starling curve. With artificial intelligence, Doppler resistance indices, and simultaneous jugular velocimetry, the ultrasound patch will report additional data on cardiovascular status—ostensibly increasing its value beyond the walls of the ICU and operating room.

Conflict of Interest

The author is co-founder and chief medical officer of Flosonics Medical, a start-up building the wearable ultrasound.

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