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Smart Flow for the evaluation of the hemodialysis arteriovenous fistula

Marco Colucci[1]*, Massimo Torreggiani[1]*, Irene Bernardi[1], Simone Stangalino[1], Davide Catucci[1], Vittoria Esposito[1], Giuseppe Sileno[1] and Ciro Esposito[1,2]

Abstract

Background: Smart Flow is an innovative tool available on the Carestream Touch Prime Ultrasound machines, which provides automated blood flow measurement and shows the vectors that form the blood flow in the vessel. We compared the use of Smart Flow with traditional Duplex Doppler Ultrasound to evaluate blood flow of arteriovenous fistulas in prevalent hemodialysis patients.
Methods: A total of 31 chronic patients on hemodialysis were enrolled. Blood flow was measured on the brachial artery with Smart Flow and duplex Doppler ultrasound. In a subset of 26 patients, a video of the juxta-anastomotic efferent vein was recorded and analyzed to calculate an index of flow turbulence.
Results: We enrolled 21 males and 10 females aged 68.52 ± 11.64 years at the time of evaluation with an average arteriovenous fistulas vintage of 50.23 ± 47.42 months and followed them up for 18.03 ± 5.18 months. Smart Flow and Duplex Doppler Ultrasound blood flow measurements positively correlated ($p < 0.0001$) in the same patient but Smart Flow gave higher blood flow values (995.0 vs 730.3 mL/min, $p < 0.0001$), and the Duplex Doppler Ultrasound blood flow standard deviation was similar to Smart Flow (125.4 vs 114.4 mL/min, $p < 0.0001$). The time needed to evaluate arteriovenous fistulas with Smart Flow was significantly shorter than Duplex Doppler Ultrasound (67.58 ± 19.89 vs 146.3 ± 26.35 s, $p < 0.0001$). No correlation was found between blood flow turbulence and the subsequent access failure.
Conclusion: Smart Flow is reliable, reproducible, and faster than traditional duplex ultrasound. However, the additional information given by the Smart Flow technique does not seem to add any further benefits in terms of prediction of the access failure.

Keywords
Chronic kidney disease, end-stage renal disease, dialysis, vascular access, arteriovenous fistula

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Introduction

The prevalence of end-stage renal disease is increasing worldwide, with extracorporeal hemodialysis being the most widely used renal replacement therapy.[1] Functional vascular access is needed to connect the patient to the artificial kidney. Native arteriovenous fistula (AVF) is the gold standard vascular access for hemodialysis according to the US and European guidelines,[2,3] because fistulas grant higher blood flow rates and reduced incidence of thrombotic and infectious complications compared to arteriovenous grafts and central venous catheters. In recent years, a great effort has been made in encouraging the placement of an AVF as the first option vascular access.[4,5] However, the rate of AVF failure is still high,[6] mainly due to the development of stenosis and thrombosis, with increased morbidity, mortality, and an elevated economic burden because of the need of hospitalization and invasive procedures to restore the patency of the access.[7] It is thus crucial to establish a surveillance protocol to early identify

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[1]Unit of Nephrology and Dialysis, ICS Maugeri s.p.a. SB, Pavia, Italy
[2]University of Pavia, Pavia, Italy

*These authors contributed equally to this work.

Corresponding author:
Massimo Torreggiani, Unit of Nephrology and Dialysis, ICS Maugeri s.p.a. SB, Via Maugeri 4, Pavia 27100, Italy.
Email: maxtorreggiani@hotmail.com

AVFs at risk of complication, in order to timely act to preserve the patency and functionality of the vascular access.

In AVFs, stenosis can be localized at the arterial side, at the anastomosis, or at the venous side. The development of stenosis is a complex process, involving the whole vascular wall, with adventitial fibrosis,[8] smooth muscle cell proliferation and neointimal hyperplasia (NIH).[9] Local hemodynamic forces have been implicated as triggering factors; in particular, it is well known that turbulent flow, with low and oscillating wall shear stress, can induce endothelial dysfunction and NIH.[10] In AVFs, the blood flows roughly from a thick, muscular walled artery into a thin-walled vein, often with a narrow anastomosis angle, causing the transition from an ordered laminar flow to a chaotic, turbulent pattern, as shown by numerous in vivo and computational fluid dynamics studies.[11–13]

Doppler ultrasonography is one of the first-line tools for AVFs surveillance, allowing morphological examination of the vessels, recognition of disturbed flow, and flow measurement through spectral Doppler analysis. In particular, blood flow measurement is considered the preferred technique, according to the Kidney Disease Outcomes Quality Initiative (KDOQI) Guidelines, to identify AVFs at risk of failure that need second-line diagnostic procedures.[2] Blood flow measurement is usually performed at the brachial artery, regardless of the proximal or distal type of AVF, due to anatomical reason and better reproducibility.[14] However, blood flow measurement requires technical skills in order to appropriately adjust ultrasound beam steering, sample volume size, gain, pulse repetition frequency (PRF), angle of insonation (θ) and measure the vessel diameter. Moreover, the dependency from the insonation angle allows the collection of reliable data only when θ is less than 60°, which can be difficult to achieve, in case of unfavorable vessel course or complex anatomy, with the need to identify a favorable position. These difficulties and intrinsic pitfalls can make the blood flow assessment time-consuming, with discomfort for both the patient and the physician.

Vector flow imaging (VFI) is a relatively novel and still unexploited method, which is based on different technologies,[15–17] allowing the collection of speed and direction data of all the blood cells moving in the sampled volume, regardless of the insonation angle. Smart Flow (SF) is a VFI tool, available on the Carestream Touch Prime Ultrasound System, based upon transverse oscillation principle. Briefly, independent firings insonate a tissue region in multiple directions; the echoes received by the transducer are coherently summed together taking into account the difference in round trip travel time from the transducer to the tissue and back, for each firing. All these information are then integrated by the graphical processing unit (GPU) of the ultrasound machine.[18] Thanks to the oscillating component of the ultrasound beam and the simultaneous processing of the echoes, SF can calculate not only the axial component of the velocity, but also the transverse component, eliminating thus the insonation angle dependency and allowing a reliable graphical representation of complex blood flow patterns,[19] otherwise not possible with standard color Doppler ultrasound, making it particularly suitable for the examination of AVFs.[11] Smart Flow Assist software can also adjust all the parameters (beam steering, PRF, sample size, gate control, etc.), perform the Doppler spectrum analysis, and measure the vessel diameter in an automated fashion,[18] returning a real-time blood flow measurement. The aim of this study was to compare the performance of SF with standard Doppler ultrasonography for AVFs blood flow measurement and early identification of AVFs at high risk of complication.

Methods

We conducted a prospective study, between 27 March 2017 and 31 December 2018 on 31 patients on chronic hemodialysis with a functioning AVF. All patients, between March and April 2017, underwent the evaluation of the AVF by ultrasound scan: blood flow was measured on the brachial artery, as an average of three measurements, with both SF and Duplex Doppler Ultrasound (DDU), by a single trained operator, sequentially, with no delay between the assessments. Measurements were performed with the Carestream Touch Prime Ultrasound machine (Carestream Health Inc., Rochester, NY, USA) for both techniques. Time needed to achieve three valid measurements of blood flow was recorded for each technique. For each patient, the following data were additionally recorded for every measurement performed: peak systolic velocity, end-diastolic velocity, pulsatility index, resistive index, acceleration time, deceleration time, and the vessel area. Blood flow was measured at the level of the brachial artery while the turbulence was determined in the efferent vein within 5 cm from the anastomosis. Blood flow was calculated automatically by the machine for the SmartFlow technique and using the mean time-averaged velocity during the DDU assessment according to the following formula: mean time-averaged velocity × cross-sectional area. In a subset of 26 patients, a video of the juxta-anastomotic efferent vein, spanning three complete cardiac cycles, was recorded during the SmartFlow examination and each photogram analyzed with the MATLAB software (The MathWorks Inc., Natick, MA, USA), according to a color map, to determine the direction of the flow and calculate the mean standard deviation of the flow angles (MSTDA) as an index of flow turbulence as previously described.[20] Figure 1 shows a representative image of the blood flow inside the fistula with different colors defining the direction of the flow itself. A representative video of three complete cardiac cycles used to calculate the turbulence inside the access is available in the Supplemental material.

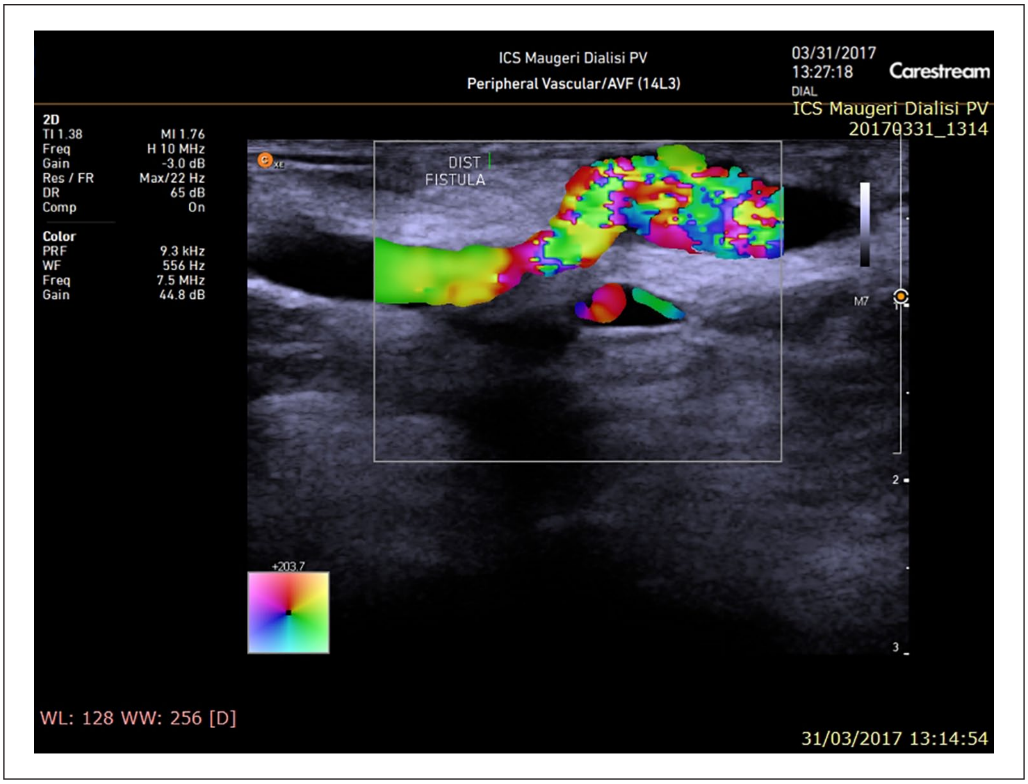

Figure 1. Representative picture of the Smart Flow image in the outflowing vein of a fistula: colors reflect the direction of the turbulent blood flow inside the vessel.

Table 1. Characteristics of our patients.

Number	31
Sex (M/F)	21/10
Age (years)	68.52 ± 11.64
Dialysis vintage (months)	55.26 ± 57.35
Arteriovenous fistula vintage (months)	50.23 ± 47.42
Follow-up (months)	18.03 ± 5.18
Type of vascular access (distal/proximal)	23/8
Type of anastomosis (ES/SS)	24/7

ES: end-to-side; SS: side-to-side.

Patients were then followed up until the end of December 2018 to record fistula failures or the need to perform invasive procedures in order to achieve the secondary patency of the access. Hemodialysis data of the session preceding, concomitant, and following the ultrasound examination, such as arterial and venous pressures and Qb, were also recorded. We also analyzed the average Kt/V of the whole observation period.

Data are shown as mean ± standard deviation. All statistical analyses were performed using the Prism 6.00 software (GraphPad Software, La Jolla, CA, USA). Correlations were made using the two-tailed Pearson's test with a confidence interval equal to 95%. A p-value of less than 0.05 was considered statistically significant.

Results

We enrolled 31 patients in this study, 21 males and 10 females. Table 1 shows the baseline characteristics of our cohort. At the time of evaluation, mean age was 68.52 ± 11.64 years and the average duration of the AVF was 50.23 ± 47.42 months. Patients were followed-up for an average of 18.03 ± 5.18 months. All distal fistulas were radio-cephalic ones with end-to-side anastomosis while among the proximal ones the majority was a radio-median anastomosis with a side-to-side connection and only one was an end-to-side brachio-perforating anastomosis. SF and DDU blood flow measurements positively correlated ($p < 0.0001$) in the same patient (Figure 2) but SF gave higher blood flow values (955.0 vs 730.3 mL/min, $p < 0.0001$, Figure 3). Figure 2(b) shows the Bland–Altman plot of the difference between the blood flow measured with SF and DDU (bias 224.7). We analyzed the standard deviation of three different blood flow measurements with each technique and we found that DDU standard deviation was similar to SF (125.4 vs 114.4 mL/min, p = NS). Furthermore, the time needed to evaluate an AVF with SF was much shorter than with DDU (67.58 ± 19.89 vs 146.3 ± 26.35 s, $p < 0.0001$, Figure 4). The mean MSTDA was 80.59 ± 12.20 while the maximum and the minimum were 91.90 ± 10.92 and 69.55 ± 13.94, respectively. Also, the MSTDA did not correlate with any of the

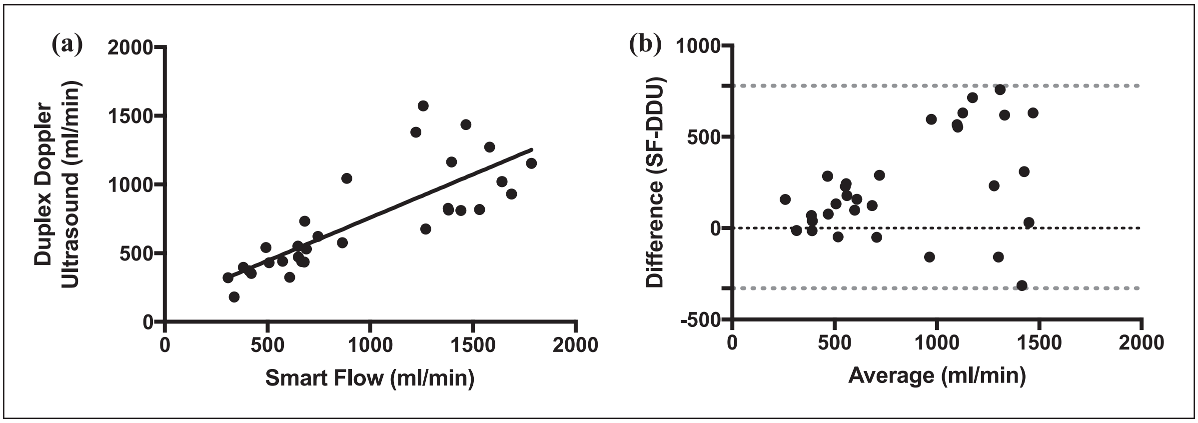

Figure 2. (a) Correlation between Duplex Doppler Ultrasound and Smart Flow blood flow measurements ($r = 0.86$; $p < 0.0001$). (b) Bland–Altman plot of the blood flow measurement with Smart Flow or DDU.

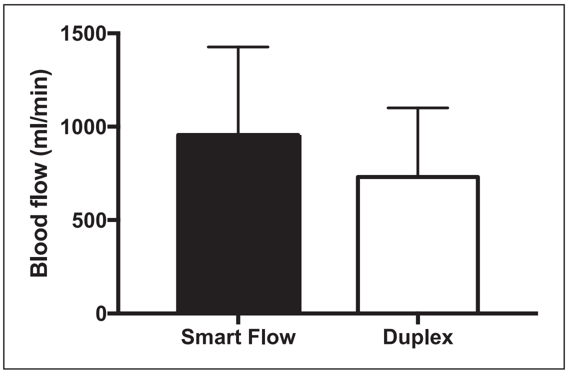

Figure 3. Absolute value of blood flow measurement with Duplex Doppler Ultrasound and Smart Flow ($p < 0.0001$).

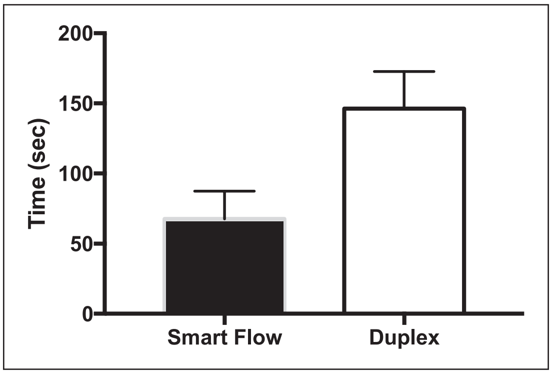

Figure 4. Time to assess blood flow by Duplex Doppler Ultrasound or Smart Flow ($p < 0.0001$).

other parameters recorded during the study. During the observation period, five patients experienced a malfunctioning of the access: four patients presented a stenosis and one patient had a thrombosis of the efferent vein. However, we found no correlation between the degree of blood flow turbulence in the fistula at the time of examination and the subsequent access failure.

Discussion

Guidelines for the care of hemodialysis vascular access recommend the regular evaluation of the AVF by physical examination and DDU.[2] DDU is considered a valid method to assess AVF blood flow and ranks first among other methods because of its supposed ease of use and wide availability. However, DDU is highly dependent on operator's expertise because insonation angle, pulse repetition frequency, and wall-filter frequency are crucial for a reliable measurement of the blood flow inside the vessel and the high fistula flow increases the difficulty in reaching optimal readings.[21] Even if the learning curve of DDU seems to be quite steep, vascular Doppler evaluation suffers from the longest time for the operator to become independent and reliable.[22] Despite the recommendations of the guidelines, diagnostic ultrasound seems to be still neglected by nephrology training programs according to the literature.[23] Thus, the KDOQI 2006 vascular access guidelines advocated for new diagnostic tools that could be less dependent on the operator and could be performed rapidly at the patient's bedside. In this light, the Carestream apparatus is a valid option that allows performing regular DDU and introduces the long known technology of vector Doppler[24] in the same machine.[18] Previously, it has been demonstrated that VFI is a valid method to determine blood flow in hemodialysis AVFs compared to the ultrasound dilution technique.[25] However, Hansen and coworkers calculated the blood flow in a second time after the evaluation of the AVF and so we can assume that the time spent to have a final result would have been at least comparable, if not longer, than the time needed to assess the dilution. SF technology, instead, allows real-time automated data processing, providing an easy-to-use tool, which can be realistically used at patient's bedside and exploited for clinical decision-making. The ease of use reflects in the reduced time to perform an examination and the reproducibility of the results. In our study, we demonstrated that SF is much faster than DDU. Moreover, using the standard deviation of the blood flow measurements as an index of concordance of the measurements among themselves, we found that SF is similar to DDU in giving reproducible results. Another advantage of the SF system is that measurements can be performed in real time without the need to freeze the image or calculate the blood speed analyzing the Doppler spectrum. Fiorina et al.[11] have already analyzed the vectors obtained with the vector flow ultrasound imaging technology in hemodialysis AVFs. In their elegant work, they proposed the mean number of vectors (arrows) directed against the vessel wall, shown by the instrument, as a surrogate marker of the impact of the turbulence on the vessel wall. In our opinion, the visual elaboration of the data shown by the instrument in the form of arrows is not a reliable index of flow turbulence: the vectors shown are a finite number, derive from a gross approximation, and do not cover the entire surface of the vessel wall. Instead, they depend on the settings applied to the software: on our machine, for instance, it is possible to decide the magnification and the size of the vectors shown on the screen so the absolute number of arrows might not reflect the turbulence inside the vessel. To overcome this limitation, we used a mathematical formula that allowed us to analyze the whole spectrum of colors shown inside the vessel. First of all, the color occupies the entire vessel lumen, thus reflecting the blood flow in every part of it, from the center to the periphery. Second, there is a continuous change in colors during the cardiac cycle reflecting the complex direction of all blood flow vectors. Moreover, our estimate was a mean of all the photograms of a complete cardiac cycle as an average of three cycles. This calculation should give an index of turbulence reliable enough to be considered for clinical decision-making. Of course, we had to analyze the images after the examination but this innovation could be easily integrated into the machine to allow real-time measurement of the turbulence at the patient's bedside. The novelty of this approach is evident and, to our knowledge, this is the first time a study gives a quantification of the blood flow turbulence inside a hemodialysis AVF with a non-invasive method. Deviation from a laminar flow inside a vessel has been associated with endothelial proliferation, intima thickening, and vessel remodeling in normal vessels and hemodialysis AVFs.[26,27] The most recent research has focused on mathematical models and computer simulations, theoretical approaches confirmed or not by expensive or not widely diffused examinations such as magnetic resonance angiography.[28–30] Our innovative study poses the basis for future research. We are well aware that our small sample and relatively short follow-up could be the reason for the small number of access failures observed in this study but we believe that further research might benefit from our preliminary report, because our results could indicate normal values of turbulence for well-functioning fistulas within a year and a half. It is also fair to mention that in terms of a routine assessment of the hemodialysis fistula, the SF technique does not add any further information compared to DDU even if the speed of examination could promote a more regular evaluation of the accesses throughout the dialytic life of end-stage renal disease patients. The main limitations of this study were the small sample size and the short follow-up that did not allow us to detect the correlation of SF flow measurements with vascular access complications.

However, in conclusion, even if SF gave higher results than DDU and did not prove superior in predicting long-term access failure compared to DDU, the SF technology implemented with our analysis could open a new era of hemodialysis fistula evaluation and give deeper real-time and real-life insights into the mechanisms that lead to vascular remodeling in conditions of non-laminar blood flow.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical statement

The study was carried out in accordance with the Declaration of Helsinki. Every patient at the beginning of the dialysis treatment signed a consent for the use of clinical data for research purposes. Since all the procedures of this study were part of the routine clinical practice, specific informed consent was waived.

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ORCID iD

Massimo Torreggiani https://orcid.org/0000-0002-5561-948X

Supplemental material

Supplemental material for this article is available online.

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