Editorial

Those who faced turbulence and launched the era of flow dynamic concepts for cardiac investigation

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Abstract

This paper puts emphasis on pioneers who developed cardiac flow dynamics concepts during the second half of the 20th century at a period where pressure measurements were the rule. Thinking flow instead of pressure dynamics corresponded to in-depth conceptual changes: whereas blood pressure generally has a single positive sign and a similar pattern at all points of a cardiac chamber or a vessel, flow fluctuates around the zero line and its pattern changes within a given cardiac chamber or vessel level. These specific changes and fluctuations were the exciting tools needed to renew our pathophysiological insights, just in time with the take off of Doppler ultrasound making noninvasive investigation of fluid dynamics easily available. Each decade was marked by a specific historical contribution to evolving concepts. Instead of a merely phenomenological approach to flow dynamics, pioneers assigned a value of paradigms to basic flow patterns. They generated a system of heuristical hypotheses which turned out to underlay a modernistic understanding of flow dynamics in normal and diseased hearts. So far, flow investigation had definitely gained acceptance completing pressure data at the middle of the 1980s, widely opening a breakthrough for future pathophysiological insights.

Keywords: Blood flow; Ultrasound

Once, Thales of Miletus arrived with a companion in front of a pyramid. “How could we know how high it is?” Rather than looking at the written answer handed to him by his companion, Thales said “There is a better way to know. When the shadow of a man will have reached his height, then we will have only to measure that of the pyramid to know its true height”. Thales, by associating the pyramid, a man, their respective shadows and the sun, provided a method which clearly passes the interest of the specific answer. This parable might apply to the breakthrough provided by the investigation of flow dynamics in cardiology in the last half of the 20th century. Most of these new insights were carried out by the growing Doppler ultrasound techniques: rather than the mere numerical values of new parameters, they provided an approach to a new conceptualisation of the cardiovascular system and improved our pathophysiological understanding.

The aim of this paper is to acknowledge, at the turning point of the millennium, the contribution of some pioneers, some of them forgotten, to changes into our cardiovascular concepts. These changes overrode the ‘pre-Doppler’ era and the growing edge of the Doppler era.

1. Conceptual mutation from the era of pressure measurements to that of flow dynamics; relationships between flow and pressure data

The relatively modern era of cardiology roughly took off in the 3rd to 5th decades of the 20th century. It became obvious that medicine needed objective data. Efforts were, at first, focused on pressure measurements and catheterisation, with or without contrast angiography. Patients generally suffered from valvular heart diseases. Making decision relied on catheterisation. Progresses in cardiac surgery,

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however, evidenced diagnostic limitations in many clinical situations and possible pitfalls due to pressure measurements alone while the increased rate of insertion of prosthetic valves reduced the feasibility of catheterisation. Problems arose in cases of prosthetic dysfunction and errors were frequent. Although the concept had been introduced by Kol in as early as 1936 [1], flow remained ignored because it required expensive and highly traumatic electromagnetic probes, surgically implanted around vessels.

A fundamental step was made by McDonald around the 1960s: he had computed blood flow in arteries from pressure data using Womersley calculations reported in the 1950s [2,3]. McDonald had shown that flow was not related to the absolute value of pressure but to the pressure gradient between two points. Briefly stated, pressure traces have the same sign during a phase and their patterns do not vary within a cavity. This is very different from what occurs with flow dynamics: two close points of a vessel wall are successively reached by a pulse pressure wave initiated by the source of pressure. Pressure becomes higher at the first point than at the farthest one, generating a pressure gradient between the points recorded as a positive vector of flow velocity since the fundamental law of fluid dynamics indicates that flow runs from higher to lower pressure areas. The reverse situation occurs when the farthest point is reached by the pulse pressure wave. The pressure gradient becomes negative and a negative vector of flow velocity is recorded, accounting for the possibility of a backflow in arteries. This explains the similarity between flow velocity and pressure derivative traces. Pressure and flow recordings are related both through the pressure derivative versus time (\(dP/dt\)) and through the local pressure gradient versus space (\(dz/dt\)), \(z\) being the distance between the close points aligned on the vessel wall. It is the pulsatile character of the pressure wave that entails the oscillatory pattern of flow velocity.

A considerable amount of research into flow studies developed around the 1960s. Methods, mainly experimental, often relied on catheterisation and became less traumatic than surgical insertion of a sutured flow probe. Spencer and Denison made the first clinical applications of the pressure gradient technique through pulmonary and aortic pressure catheterisations in 1956 and could derive flow velocity ejectional traces of great vessels from their data [4]. Later on, Noble et al. and Schultz et al. studied flow velocity distribution in large vessels using hot thin film anemometers and thin film techniques, respectively in 1967 [5] and in 1969 [6]. Another trend of equipment consisted of an electromagnetic velocity catheter-tip by Mills in 1967 [7]. From 1956 to 1970, a series of studies, mainly on experiments or during surgery, were dedicated to vena cava flow investigation [8–11]. Flow profiles were studied by Taylor and Wade by means of an optical Janus needle with wide-angled lens [12]; when the direction of flow was not constant, it was possible to derive flow at any time within the cardiac cycle, by locating the needle in two positions at right angles. Flow paths could also be cinefilmed and correlated with timing of cusp motions. So far, models only involved a left ventricular cavity and a mitral valve [13]. Physicians needed information on the assessment of prosthetic hydraulic performances; thus, prostheses were studied through experiments involving electromagnetic probes inserted on both sides of the heart and by means of two dimensional visualisation of flow vortices [14]. Specific measurement of annular flow-rates, however, still required surgical insertion of an electromagnetic probe around the annulus on animals [15–18]. J.P. Shillingford was a conceptual pioneer. He organised a symposium entitled ‘The growing edge of the theory and measurement of blood flow’ at the Royal Society of Medicine in London, UK, on April 21 1969 (Fig. 1). Only a handful of about thirty scientists acquainted with the cutting edge of these cardiovascular advances attended the symposium! The fact that a noninvasive clinical method of flow velocity measurement, namely the Doppler directional velocimeter, was admitted for lecturing among presenters of invasive and mainly experimental procedures, was also ‘avant-garde’.

2. Launching the Doppler era; from ‘heart beat’ analysis to ‘flow’ concept

Early Doppler ultrasound developments, delayed more than one century after the publication of Christian Doppler’s so-called ‘principle’ in 1843 [19], were boosted by ultrasonic sophisticated developments during World War II. A tight cooperation between physicians, engineers and physicists succeeded to bridge the gap between invasive and noninvasive techniques in flow measurement and to yield the bases of the Doppler technique in less than 15 years.

In spite of the maturation of minds toward flow concepts, the first Doppler studies achieved with the early ultrasonic Doppler device [20], later known as an ‘ultrasonic Doppler cardiograph’, were not aimed on flow recordings, but solely dedicated to heart beat and valve motion velocity recordings. Thus, the first Doppler apparatus was designed to record their typically rough signal, under the direction of Nimura. 1956 was the birth of the Doppler technique with the report of Yoshida, Nimura and Satomura, on the examination of the heart with the ultrasonic Doppler method in Osaka, Japan. They used a 3-Mhz continuous wave Doppler transducer with a frequency spectrogram output signal (Fig. 2). Nimura initiated and directed cardiac applications. A series of princeps reports was dedicated to heart beat and valve motion velocity recordings [21–25]. Thus, the Japanese group, particularly Nimura, were true pioneers in equipment and in tissue Doppler [26–29]. High-pitched signals were also heard but they were discarded at this early phase.
Fig. 1. Content of the program of the symposium held at the Royal Society of Medicine, section of measurement in medicine on April 21, 1969, entitled 'The growing edge of the theory and measurement of blood flow', under the chairmanship of J.P. Shillingford. In 1969, the newness and promises of this topic were overlooked by most of the scientific community.

of the Doppler era, because of their uncertain origin. Kaneko, however, a Japanese neurologist, thought they could possibly be attributed to flow signals and asked Satomura to enhance these signals heard in the area of the extracranial carotid artery. Equipment was designed for this goal. Flow signal acquisition was facilitated by some alterations in gain and filtering. Frequencies under 120 Hz were cut-off to eliminate noise related to walls [30]. The report was promisingly entitled ‘Study of the flow patterns in peripheral arteries by ultrasonics’ [31]. Indeed, the so-called ‘flow patterns’ appeared more as the inscription of sound vibrations than as traces. Practical applications to carotid arteries on patients could start under the guidance of Kaneko and co-workers [32,33].

Some time elapsed between the birth of the Doppler equipment and its validation. The rationale for the development of Doppler flowmetry was reported in 1962 by Kato et al. showing a positive correlation between the magnitude of Doppler frequencies and the number of corpuscles on experiments [34]. Finally, Reneman et al. validated Doppler versus electromagnetic flowmeters [35]. Although the gap between Doppler ultrasound and flow-
metry was bridged, many users continued to only record the human or fetal heart beats and sounds with Doppler ultrasounds [36,37].

3. Onset of the ‘Doppler flow velocimetry’ era, an explosive ‘avatar’ of early ultrasonic approaches

Meanwhile, the various invasive procedures used to record flow velocity had alerted physicians to flow concept in the US. Convenient analog demodulated flow traces had been developed. In 1961, Franklin and co-workers seized the crucial interest of the ultrasonic continuous wave equipment for investigation of peripheral arteries [38,39]. They are pioneers for the first Doppler equipment available for peripheral flowmetry, i.e. the nondirectional Doppler device. They were followed by George and Pourcelet and co-workers in France in 1965 [40]. Light investigated the aortic arch for purposes of monitoring aortic velocities as a surrogate for cardiac output in emergency cases in 1969.
4. Advantages drawn from traces with an effective ‘zero’ line to initiate the era of physiological significance of arterial and venous ‘Doppler flow velocimetry’

In the mid-1960s, the introduction of directional Doppler recordings launched this era. Directionality enabled recognition of spectral velocity signs toward and away from the transducer with respect to a zero line. Studies emerged nearly simultaneously in three locations. In 1966, Kato and Izumi in Japan [47] and in November 1967, McLeod in the US [48], reported a directional continuous wave Doppler velocimeter prototype in engineering meetings. In France, Kalmanson et al. presented a new device designed by Toutain, on January 19 1968 at the French Society of Cardiology [49]. The equipment involved a phase detector. Kalmanson anticipated that the new flow data would underlie major pathophysiological messages and that, to gain acceptance, data needed a simple readout displayed as a single channel output for both velocity signs, successively displayed on each side of the zero line on a stripchart. The output waveform was transformed into a demodulated curve by an analogue converter. At the end of 1968, Kalmanson’s pioneer works had been issued, reporting all arterial and venous directional Doppler flow velocity patterns in controls and patients and singling out the fundamental features of flow velocity recordings [50–53]: namely, the pattern was oscillatory; there could be backflow in arteries; specific patterns were assigned according to each site of recording with minor possible variations. For several years, the fact that there could be backflow in arteries appeared particularly iconoclastic to many scientists familiar with pressure measurements but it finally got acceptance. As for venous return, Doppler data were consistent with those obtained by electromagnetic probes on experiments [54]. Accurate timing of changes in flow direction had been demonstrated in pipes, validating the use of a single channel for Doppler recordings [55] (Fig. 3). For a while, separate channels, one for positive, the other one for reverse flow, also recorded as a positive vector, could be shown (Fig. 4) [56,57]. Finally, recording on one single channel prevailed. Flow recordings were similar to those obtained nowadays. It is noteworthy that probe frequency allowed only peripheral traces to be transcutaneously recorded.

5. New systemisation of intracardiac flow dynamics drawn from changes in patterns: from a three-wave pattern (venous inlet) to a single wave pattern (arterial outlet)

In 1969, flow patterns had hardly, if at all, been studied in detail within the heart. Information existed about patterns in vena cava [8–11,54] and about aortic flow [4,44]. Non-directional Doppler catheterisation would soon be applied to right atrium [45] and to coronary arteries [46]. What could be guessed for intracardiac flow patterns was anticipated from pressure traces: when the
veins enter the right atrium, pressure trace fluctuates throughout the cardiac cycle and shows an abrupt descent when the tricuspid valve opens with flow taking place into the ventricle at the onset of diastole. Although smoothing of aortic pressure and decrease of the mean pressure level had occurred during the passage through the systemic microcirculation, pulsation was still high enough at the venous end of the capillary bed to generate flow towards and within the heart and there was still basically a steady driving force. In addition to the effects of the muscular pump and of respiration, pressure changes related to cardiac contraction were expected to add further oscillations [58].

During 1968, a new directional Doppler probe was devised and inserted at a catheter-tip to investigate heart cavities. A series of lens enabled to focus 2 or 3 mm ahead of the tip. Results obtained in dogs and in man in the heart cavities by venous route and in large vessels by retrograde catheterisation with this prototype were first published in 1969 [55].

Recording from the vena cava through the heart to the pulmonary artery on the right side evidenced a continuum of progressive changes in flow velocity patterns within the heart: in order to obtain a single systolic wave in the arterial system from a venous return trace involving three waves, two positive, S systolic and D diastolic, one negative A diastolic waves, flow within the heart must undergo progressive changes, each one being specific of a given site of recording and of a given timing of the cardiac cycle (Fig. 5).

6. From phenomenology to heuristics

Beyond a mere description, pioneers assigned a physiological significance to flow velocity patterns. Through heuristical hypotheses, their specific features, including the tricuspid annular flow pattern recorded for the first time in man, were systematised. Not a single detail lacked: the small negative deflexion during the isometric contraction (ic) no flow velocity during systole, a small deflexion during the isovolumic relaxation ending with the atrioventricular opening which started ventricular filling. Both filling waves were described, the early filling which was labelled D like diastole, later renamed E by similarity to early-diastolic valve echocardiographic labelling and the late filling wave A. This was achieved for the left side by a new orientable catheter-tip which enabled the recording of the mitral annular trace through transseptal catheterisation in 1970 [59–61]. The trace was similar to that recorded at the tricuspid annulus in 1969. Electromagnetic flow probes validated these patterns at the annuli on experiments [15–
Fig. 5. Schematic drawing of the continuum of changes in flow patterns from the venous inlet to the outlet arterial chamber. After having assigned a physiological significance to these three archetypes, pioneers started the systemization and modelling of their pathophysiological patterns (after Kalmanson et al. [55,60] explanations in text).

18]. Physiological significance of flow velocity patterns gave rise to new system dynamics concepts from 1969 to 1972. For instance, the finding of two possible outcomes for the atrial A wave depending on the site of recording, suggested the hypothesis that, beyond a certain atrial plane, which could be labelled the ‘watershed plane’, the atrial contraction drives blood ahead toward the annulus, and above this plane, it pushes it back toward venous return. This suggested that the venous return extended to this plane in a wider concept of a lump return system. Conversely, the diastolic double-wave pattern transformed abruptly into a high systolic–low diastolic pattern at the junction between inflow and outflow tracts. Furthermore, preferential flow paths were singled out within the ventricles. Importantly, capability of any organic or functional alteration of atrial relaxation, downward displacement of the annular closed floor, ventricular relaxation or filling and atrial contraction to induce anomalies on-site and in venous return patterns, was demonstrated [62–64].

7. Modern ‘diagnostic’ era of Doppler with one-dimensional echo imaging and range-gated Doppler

Unless a catheter-tip was used, the frequency of the probe confined continuous wave Doppler applications to superficial vessels. Some physicists found an elegant solution to sampling within the heart by designing a range-gated pulsed Doppler, namely Wells in the UK [65], Peronneau et al. in France in 1969 [66], and in 1970, Baker in the US [67] and Ohtsuki and Okujima in Japan [68]; there were two piezo-electric crystals, one emitter and one receiver. The range-gating system made it possible to pick-up any sample of blood, generally tear-drop shaped known as the ‘Doppler gate’ along the axis of the beam. Optimal spatial resolution allowed unequivocal recognition of the sampling site and noninvasive access to velocity profiles and velocity distribution across a vessel diameter, previously available only from invasive equipment. Besides the investigation of the left posterior wall [69] and of small vessels [70], evaluation of graft patency after coronary by-pass was proposed by Gould et al. in 1972 [71]. A separate one-dimensional echocardiogram imaging checked the location of the graft and was followed by a Doppler flow velocity recording at its approximate depth.

A true breakthrough occurred when simultaneous imaging and Doppler recordings were developed and proposed by Johnson and Baker in 1975 [72]. The range-gated pulsed Doppler was combined with one-dimensional echocardiographic imaging. The authors recorded the disturbances generated by heart lesions using a time-interval histogram and a zero-crossing detector. This application was a kind of intracardiac stethoscope, yielding the ‘diagnostic era’. Thus, it was possible to relate the spectral disturbances to specific valvular or heart cavities, as shown by Stevenson et al. for ventricular septal defects [73]. A demodulated analog trace was also added to reproduce the flow velocity traces previously recorded by catheterisation. This method was applied to valvular and congenital lesions from 1975 to 1980 [74–78] (Fig. 6 bottom left). Regrettably, the occurrence of ‘aliasing’, due to the inability of pulsed Doppler to record velocities exceeding the physic ‘Nyquist’ limit, prevented calibration of velocities. Conversely, ‘aliasing’ was a reliable marker of increased velocities usually related to lesions. Although far from perfect, pulsed Doppler turned out to be a reliable diagnostic tool on the basis of a recognition pattern. It compared favourably with diagnostic capabilities of one-dimensional echocardiography. In addition, pulsed Doppler step-by-step sampling in the left atrium in case of mitral stenosis yielded unexpected information on the progressive flow acceleration proximal to a narrowed orifice, consistent with the flow net theory in fluid dynamics, ten years ahead from its demonstration by colour Doppler. Anomalies of flow
velocity traces led to devise indices for grading severity of the lesions (Fig. 6, bottom left). Extension of disturbances in the cardiac chambers was also proposed for grading [79]. The success rate was limited by frequent changes in the direction of the valvular jet out of the scanning line [80].

8. ‘Grading’ and ‘pathophysiological’ eras through two-dimensional flow mapping

After the diagnostic preliminary phasis, surgeons boosted Doppler users to grade valvular lesions. This was made possible by a new breakthrough: combination of pulsed Doppler with two-dimensional echocardiography. The first pioneer paper was published in 1977 by Matsuo et al. [81] followed by Griffith et al. in the US [82]. Even more exciting than the improved grading it provided, this era yielded new pathophysiological insights. The new technology enabled to follow the trajectory of the jet in a two-dimensional plane, such as for mitral valve prolapse [83,84]. Indices for a semiquantitative grading gained acceptance and were first reported by Miyatake and Kalmanson’s groups between 1980 and 1984 [85,86]. Three-dimensional indices were devised for valvular regurgitations by combination of two orthogonal planes [87,88]. A new quantitative procedure was also proposed by measuring the jet area, later called the vena contracta at the site of the valvular regurgitant or stenosed lesions in the short axis view from 1983 [89] (Fig. 6, right). Noninvasive quantification of flow-rate became possible and several two-dimensional innovative methods were proposed and validated [90,91]. Two other progresses took also place in the early 1980s: colour Doppler was first
designed by Brandestini, who studied congenital defects with Stevenson [92], and by Bommer and Miller [93] and Namekawa et al. [94]; the time interval histogram was replaced by the more reliable fast Fourier transform signal processing.

9. ‘Quantitative’ era with continuous wave Doppler

Except for planimetry of regurgitant and stenosed flow areas [95,96], other grading indices were semiquantitative and a lot of parameters of crucial usefulness were lacking with pulsed Doppler, such as the measurement of pressure gradients and that of functional valve areas, because of the Nyquist limit. This was a fundamental reason to return to continuous wave Doppler, the more so as progresses in transducers had made available lower frequency probes allowing sampling deep in the heart. Spatial resolution was still lacking but with a minimal physiological knowledge and training, it was easy to distinguish a regurgitant from a stenosed jet by their timing. A pioneer in this field was Jarle Holen, Norway. He applied the Bernoulli equation to the calculation of the pressure drop in mitral stenoses and prostheses as early as 1976 [97]. He validated the calculations derived from ultrasound versus simultaneous invasive pressure measurements. He understood that pressure drop depending on cardiac output, valve area calculation was the needed parameter and reported this calculation combining the ultrasound technique with an invasive measurement of flow-rate [98]. True quantitative Doppler methods could start. From 1978 to 1985, Bjorn Angelsen and Liv Hatle proposed to simplify the Bernoulli equation as $4V^2$ and popularized this Doppler procedure [99–101]. The formula is routinely used in all laboratories and its efficiency has been validated in most clinical situations. Finally, Skaerpe et al. proposed to calculate valve areas using the continuity equation from 1985 [102]. Valvular heart diseases are less frequent but the formula found a series of applications providing a true noninvasive hemodynamic evaluation in nonvalvular cardiology, diastology and emergency situations.

10. Present status and future trends

The year 1984 marks the entrance to present time because colour flow Doppler evidenced the adequacy of flow concepts with pathophysiology. Consequently, explosive trends of research could occur. These were generated by new transoesophageal and intravascular approaches, new tools like contrast agents, technological improvements such as multidimensional and harmonic imagings and re-emergent tissue Doppler processing. Importantly, Doppler modalities are complementary: For instance, we may cross-check the assessment of a valvular lesion at three levels, downstream the lesion with measurement of pressure drop, at the vena contracta by planimetry of the jet area, and in the upstream chamber, by calculating the proximal isovelocity surface area derived from cardiac output calculations.

Future directions will depend on a pluridisciplinary cooperation. Studies should not dissociate intra-cardiac and -vascular flow dynamics from their surrounding tissues. Much remains to do for higher accuracy, resolution, insensitiveness to noise of signal processing, better 3D outline of jets relying on new fuzzy reasoning algorithms, relaxation technology, clinically relevant investigation of new diagnostic targets such as, for instance, the whole spectrum of coronary artery disease. Finally, flow investigation might be optimised by other physical sources.

11. Conclusions

This historical review recalled the impact of audacious pioneers who cleared the way in an unbroken field of cardiology during the last half of the past century. At the turning of the new millennium, princeps descriptions of flow events and innovative paradigms from which deviated patterns could be declined according to pathology, trace the way toward a promising continuum, whatever the available technology might be.

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