Static filling pressure in patients during induced ventricular fibrillation

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Submitted 26 June 2003; accepted in final form 30 July 2003

Schipke, J. D., G. Heusch, A. P. Sanii, E. Gams, and J. Winter. Static filling pressure in patients during induced ventricular fibrillation. Am J Physiol Heart Circ Physiol 285: H2510–H2515, 2003. First published August 7, 2003; 10.1152/ajpheart.00604.2003.—The static pressure resulting after the cessation of flow is thought to reflect the filling of the cardiovascular system. In the past, static filling pressures or mean circulatory filling pressures have only been reported in experimental animals and in human corpses, respectively. We investigated arterial and central venous pressures in supine, anesthetized humans with longer fibrillation/defibrillation sequences (FDSs) during cardioverter/defibrillator implantation. In 82 patients, the average number of FDSs was 4 ± 2 (mean ± SD), and their duration was 13 ± 2 s. In a total of 323 FDSs, arterial blood pressure decreased with a time constant of 2.9 ± 1.0 s from 77.5 ± 34.4 to 24.2 ± 5.3 mmHg. Central venous pressure increased with a time constant of 3.6 ± 1.3 s from 7.5 ± 5.2 to 11.0 ± 5.4 mmHg (36 points, 141 FDS). The average arteriocentral venous blood pressure difference remained at 13.2 ± 6.2 mmHg. Although it slowly decreased, the pressure difference persisted even with FDSs lasting 20 s. Lack of true equilibrium pressure could possibly be due to a waterfall mechanism. However, waterfalls were identified neither between the left ventricle and large arteries nor at the level of the diaphragm in supine patients. We therefore suggest that static filling pressures/mean circulatory pressures can only be directly assessed if the time after termination of cardiac pumping is adequate, i.e., >20 s. For humans, such times are beyond ethical options.

mean circulatory (filling) pressure; vascular waterfall; implantable cardioverter/defibrillator; defibrillation threshold testing

After acute termination of cardiac pumping, arterial blood pressure drastically decreases, whereas venous pressure moderately increases. The pressures are expected to converge ultimately throughout the circulatory system. The resulting equilibrium pressure has been termed “statischer Füllungsdruck” (24), hydrostatic mean pressure (2), or static blood pressure (23).

Recently, another equilibrium pressure, namely, the mean systemic filling pressure (P_{ms}), was measured in 10 patients during implantation of cardioverters/defibrillators (10). In that study, which primarily addressed the effects of positive airway pressure on venous return, the arterial pressure at the time of P_{ms} measurement significantly exceeded P_{ms} demonstrating the absence of systemic pressure equilibration and the lack of a “true” P_{ms}.

If arterial and venous pressures do not converge during ventricular fibrillation (VF), then the observation time is too limited for equilibration, the vascular system is functionally discontinuous, or both. Such a persisting difference between arterial and venous blood pressure would be indicative of a Starling resistor mechanism or a vascular waterfall (1, 4, 6, 17, 22).

An implantable cardioverter/defibrillator (ICD) can detect VF and terminate it. For determining the optimal defibrillation threshold, VF is repetitively induced intraoperatively and terminated using direct current (DC) shocks of different energy (26). Thus, depending on the protocol employed, several fibrillation/defibrillation sequences are mandatory before final implantation of an ICD, thus providing an elegant model to study arterial and venous pressures during functional cardiac arrest in anesthetized patients (10).

METHODS

Patients. The age of the 82 patients (15 women; 18%) averaged 59 ± 10 yr (from 33 to 79 yr). For all interventions that were not a genuine component of the implantation of the ICD, written informed consent was obtained from all patients.

Of the 82 patients, 49 patients had mild heart failure [New York Heart Association (NYHA) class I or II] and 33 patients had more severe heart failure (NYHA class III or IV). Fifty-nine patients had coronary artery disease, 16 patients had dilated cardiomyopathy, 3 patients had hypertension, 2 patients had idiopathic VF, 1 patient had previously had endocarditis of the mitral valve, and 1 patient had myocarditis.

Anesthesia. The anesthetic regimen was standardized for all patients. As premedication, 5–10 mg of diazepam (Hoffmann-La Roche; Grenzach-Wyhlen, Germany) were ad-
ministered in the evening before and in the morning of the day of surgery. Thirty minutes before the induction of the anesthesia, 50 mg of pethidin ( Hoechst; Frankfurt/Main, Germany), 50 mg of promethazin ( Tropon; Cologne, Germany), and 2.5 mg of droperidol ( Janssen; Neuss, Germany) were injected.

After induction with 3–5 mg/kg iv thiopental sodium ( Byk Gulden Lomberg; Konstanz, Germany) and intubation using relaxation with 0.1 mg/kg iv vecuronium bromide ( Organon Teknika; Eppelheim, Germany), the anesthesia was maintained with 1.5% enflurane in oxygen. The ventilation was controlled by means of pulsoximetry and capnometry ( Capnomac Ultima; Datex Instrumentarium; Helsinki, Finland). The end-expiratory pressure was set to zero.

**Physiological monitoring.** Arterial blood pressure was measured via a cannula ( P23 XL transducer, ViggoSpectra; Oxnard, CA) in the right radial artery. The height of the right forearm was adjusted to the level of the superior vena cava with a lifting platform. The central venous pressure was measured through a cannula ( P23 XL transducer, ViggoSpectra; Oxnard, CA) in the right basilic vein, which was advanced into the superior vena cava. To measure left ventricular pressure, a micropipetted catheter was introduced through the femoral artery ( SPC 360, Millar Instruments; Houston, TX). The pressure transducers were calibrated using a calibration device ( linearity: 0.2%, Kal 84, Halstrup; Kirchzarten, Germany).

In five patients, the pressure in the inferior vena cava was measured with two transducers ( P23XL transducer, ViggoSpectra) located distally and proximally to the diaphragm to assess whether or not the diaphragm was the site of a vascular waterfall. The exact transducer positions were verified using fluoroscopy. All blood pressure transducers were calibrated to the zero point at the level of the right atrium.

ECG leads I, III, and V5 were recorded.

**General surgery.** In all patients, the multifunction electrode was introduced via the cephalic vein and advanced into the right atrium. The tip of the electrode was anchored in the apex of the right ventricle under fluoroscopic control. The distal defibrillation electrode was placed adjacent to the septum.

Subsequent to the termination of the test protocol, the electrode was anchored at the major pectoralis and deltoid muscles. The ICD and the peripheral part of the electrode with the connectors were brought into an intramuscular pouch in the left upper abdomen. After the electrode was connected to the ICD device, the integrity and functionality of the system including the recognition and termination of VF were checked telemetrically. An endocardial, tripolar multifunctional electrode system ( ENDOTAK C-model 0092, Cardiac Pacemakers; St. Paul, MN) was used in all patients.

**Induction and termination of VF.** In all patients, VF was induced with a fibrillator ( 50 Hz, 10 V, UNIFIB II, Unitek; Sittard, The Netherlands). The fibrillation current was delivered between the positive ( proximal) and the negative ( distal) defibrillation electrode.

The defibrillation threshold was set via an external cardioverter/defibrillator ( modified Ventak ECD 2815, Cardiac Pacemakers) that could deliver 16 preset energy levels ( 0.1–35.0 J). If a rescue shock of 40 J did not terminate VF, an external defibrillator ( DC defibrillator, Hellige; Freiburg, DE) with a maximal energy of 340 J was employed. After conclusion of the defibrillation threshold testing and implantation of the cardioverter/defibrillator, the functionality of the implanted device was tested by a final induction of VF and its subsequent termination by the ICD ( device test).

**Data collection and analysis.** To eliminate respiration-induced oscillations of intrathoracic pressures, artificial respiration was suspended immediately before and during VF. An eight-channel chart recorder was used to record the pressure and ECG signals ( Picker Schwarz PD 14, Madaus Schwarz; Munich, Germany). During periods of interest, the paper speed was set at 50 mm/s.

Before the induction of fibrillation, peak arterial pressure, LV peak pressure, and LV end-diastolic pressure of three consecutive beats were averaged. After the onset of fibrillation, the pressure values were assessed in 1-s intervals until termination of VF. If termination of VF was unsuccessful, additional values were assessed until successful termination. In contrast, sequences with spontaneous termination of VF were excluded from the analysis.

All arterial and venous pressure values during each individual fibrillation were used to derive an exponential function. Linear and quadratic functions were also tested but yielded less tight correlations and were therefore disregarded. For all 323 fibrillation/defibrillation sequences ( FDSs), the following exponential equation was employed to describe the arterial pressure ( P\text{art} ) decay during VF

\[
P_{\text{art}}(t) = A \cdot \exp(-t/\tau_{\text{art}}) + B
\]

where A is a factor to determine the starting pressure ( in mmHg) at time ( t) = 0 s, \( \tau_{\text{art}} \) is the constant of arterial pressure decay ( in s), and B is the nonzero asymptote ( in mmHg).

In 36 of 82 patients, the following exponential equation for the venous pressure ( P\text{ven} ) increase during VF was determined for 141 FDSs

\[
P_{\text{ven}}(t) = C \cdot \exp(-t/\tau_{\text{ven}}) + D
\]

where C is a factor to determine the starting pressure ( in mmHg) at ( t) = 0 s, \( \tau_{\text{ven}} \) is the constant of venous pressure increase ( in s), and D is the nonzero asymptote ( in mmHg).

To assess whether characteristics of the arterial pressure decay might time dependently change with larger FDS duration, the exponential equation was repetitively employed with an increasing time frame; i.e., exponential equations for the same patients ( n = 13) were derived for the data between the onset of fibrillation and 7 s and then in 1-s steps up to 23 s.

Standard statistical software was used to calculate the correlations ( SPSS; Chicago, IL). Correlations with a P value < 0.05 were regarded to indicate statistically significant differences. Data are presented as means ± SD.

**RESULTS**

In 82 patients, a total of 323 FDSs was analyzed; i.e., an exponential function was calculated for each individual FDS. In these patients, the arterial blood pressure decreased markedly from 77.5 ± 34.4 to 24.2 ± 5.3 mmHg ( means ± SD for 323 FDSs) with an average time constant of 2.9 ± 1.0 s. The coefficient of correlation ( R) for the 323 FDSs equaled 0.92 ± 0.05. The central venous pressure increased on average from 7.5 ± 5.2 to 11.0 ± 5.4 mmHg in 36 patients and 141 FDSs with a time constant of 3.6 ± 1.3 s. R, at 0.80 ± 0.11, was somewhat lower compared with the arterial value.

During VF of 13 ± 2 s, both pressures did not reach an equilibrium pressure ( Fig. 1). In all patients and during all FDSs, a positive pressure difference re-
mained between the arterial and venous pressure, averaging 13.2 mmHg. A representative registration is displayed in Fig. 2.

In a subgroup of patients (n = 14), both LV pressure and arterial pressure at 20 s of fibrillation were further decreased by 2.1 and 2.5 mmHg, respectively. In turn, the venous pressure was slowly further increased by 1.1 mmHg. In consequence, the arteriovenous pressure difference was decreased to 9.6 mmHg in this group.

In another subgroup of patients (n = 13), the arterial pressure decay was calculated for intervals with an increasing duration of FDS, beginning with an interval between the onset of fibrillation and 7 s and up to 23 s (Fig. 3). With increasing durations of fibrillation, R remained almost unchanged (7 s: 0.99 vs. 23 s: 0.98). However, the time constant at 7 s (−1.54 s) was significantly larger than at 23 s (−2.93 s). In consequence, the arterial pressure in this subgroup of patients continued to decrease from 34.8 mmHg (7 s) to 22.7 mmHg (23 s).

Peak systolic LV pressure (119 ± 19 mmHg) before VF was comparable with systolic arterial pressure (122 ± 18 mmHg, n = 33). LV pressure at 13 s of fibrillation was decreased to 21.6 ± 5.1 mmHg, i.e., it was close to the arterial pressure of 24.2 ± 5.3 mmHg.
As expected, the arterial pressure signal (radial artery) was, depending on the heart rate, delayed by on average 97 ± 22 ms.

Pressures distal and proximal to the diaphragm were 8.0 and 7.2 mmHg, respectively, before the onset of VF (n = 5). During VF, these values increased to 11.5 and 10.5 mmHg, respectively. Thus the original pressure difference of ~1 mmHg remained unchanged during VF.

**DISCUSSION**

In the present study, a positive pressure difference persisted in all patients at the end of VF, averaging 13.2 ± 6.2 mmHg. This was probably due to inadequate time for the arterial pressure and venous pressure to equilibrate, i.e., to achieve a true static filling pressure or \( P_{ms} \) within the time frame of up to 20 s.

**Rapid pressure changes.** When we fitted our data of arterial pressure decay and venous pressure increase to different equations, an exponential curve fitting gave the best results. A process that changes exponentially over time approaches a constant value after five times the time constant. The pressure then would have fallen to the \( 1/e^5 \) level, i.e., to <1% of the initial pressure. With a time constant of the arterial pressure decay of 2.9 s, no remarkable changes can be expected after ~14.5 s. Likewise, the venous pressure with a time constant of 3.6 s should exhibit no more increases after 18.0 s. Thus our 13-s duration of VF was neither much too short for the arterial pressure to decrease nor too short for the central venous pressure to increase, at least for an initial phase with rapid and homogeneous pressure changes. In contrast, the 7.5-s duration of VF in the study of Jellinek and co-workers (10) on 10 patients appears to be relatively short to assess the initial pressure changes. Accordingly, the arterial pressure was higher (30.2 vs. 23.4 mmHg) and the \( P_{ms} \) was lower (10.2 vs 11.0 mmHg) in that study (10).

**Slower pressure changes.** Exponential pressure changes imply asymptotes, i.e., constant pressures after a while. However, the pressures assessed in 14 patients at 20 s of VF (Fig. 3) demonstrate that the arteriovenous pressure difference slowly further decreases. Guyton (7) proposed that arterial and venous pressure will almost reach equilibrium pressure 30–50 s after the heart stops beating. For ethical reasons, such an extended duration of VF in humans is intolerable. Even in experimental animals, the time to equilibrium presents a problem. Because of this, an equilibrium pressure (mean circulatory filling pressure) was artificially achieved immediately after circulatory arrest by rapidly pumping blood from the arterial to venous system (7, 16, 19).

**Vascular waterfalls.** Wenkebach’s dam-and-stream analogy (25), the Starling resistor (12), and the waterfall concept (17) describe essentially the same phenomenon: the flow velocity of water in a river proximal and distal to a waterfall does not depend on the height of the waterfall. Vascular waterfalls are known to exist in the microcirculation (9, 21) in many peripheral beds and were first described as critical closing behavior (3). Such a waterfall mechanism could be responsible for the initially rapid and the subsequently slower pressure changes.

Whereas a simple exponential decay with a given time constant derives from a compliant reservoir draining through a fixed resistance, the waterfall behavior causes resistance to rise as arterial pressure approaches the waterfall pressure. Consequently, the time constant increases with falling arterial pressure, as we indeed observed, because many of the parallel vascular beds drop out, and blood must flow into the veins through the few circuits that are still patent.

In anesthetized dogs in the (unphysiological) supine position, a waterfall exists between the visceral and intrathoracic venous system: the transdiaphragmatic pressure gradient was 3.3 mmHg (11). Possibly, the diaphragm could also present a vascular waterfall in our anesthetized, supine patients. The diaphragm pressure difference of 0.8 and 1.0 mmHg before and after VF in our five patients does not significantly contribute to the average pressure difference of 13.2 mmHg. Similarly, a pressure difference of only 0.1 ± 1.1 mmHg was measured between the central venous pressure (superior caval vein) and the pressure in a more remote venous vessel (common iliac) in anesthetized patients (8). In consequence, the diaphragm presents no remarkable waterfall in supine humans, and the differences between the studies must be attributed to the different canine and human anatomies (5, 11).

In addition, a waterfall within the large arteries can be excluded, because the peak systolic LV pressure (119 ± 19 mmHg) before VF compared well with the systolic arterial pressure (122 ± 18 mmHg) if a small pressure augmentation toward the periphery is accepted (15).

**Estimation of equilibrium pressure.** To overcome the limited time frame of VF, a true \( P_{ms} \) (as an equilibrium pressure within the systemic circulation after cardiac arrest of adequate duration) can be extrapolated by using the different compliances of the arterial and venous trees (16, 19). The venous compliance presents the major component of total vascular compliance (14, 16, 18). In the dog, the ratio between the venous and arterial compliances varies between 12 (20) and 82 (13). Using the “worst case” value for correction, i.e., 12, the central venous pressure at the end of fibrillation will increase by 1/12 of the pressure difference of 13.2 mmHg at 13 s of VF. Thus our \( P_{ms} \) would increase from 11 to ~12 mmHg for the true \( P_{ms} \), meaning that the blood volume remaining in the arterial tree after 13 s of VF does not considerably contribute to the \( P_{ms} \).

The pressure of 12 mmHg found in our anesthetized patients is clearly higher than the value of 5.6 mmHg found earlier in human corpses (23). Our equilibrium pressure, in turn, is possibly an overestimate, because some sympathetic reflex venoconstriction during falling arterial pressure might even persist during anesthesia and because patients with heart failure, as in the present study, might have increased circulatory blood volume secondary to sodium and water retention.
In conclusion, in the present study, a pressure gradient between the arterial and central venous pressure of 13.2 mmHg remained at the end of, on average, a 13-s episode of VF in anesthetized patients. Even after 20 s, no true equilibrium was achieved. The persisting pressure difference could be suggestive of a vascular waterfall. We provide experimental evidence that such a waterfall is located neither within the large arteries nor at the diaphragm.

APPENDIX

Some historical aspects and methods to assess pressures after cessation of cardiac pump action are summarized in this appendix.

Static filling pressure. After the first theoretical description of static filling pressure as the equilibrium pressure in the entire circulatory system, Weber (24) wanted to experimentally assess its value in humans by infusing water into dead bodies. However, the experiments failed because the role of the colloid osmotic pressure was unknown at that time (5a). About 100 years later, investigations were resumed on dead human bodies (23a). Starr’s static blood pressure in very recently deceased humans without a prior history of cardiac or circulatory problems equaled 5.6 mmHg in various vascular segments (23). This pressure was clearly increased to 14.7 mmHg in patients with chronic cardiac disease during their lifetime resulting from a discrepancy between the compliance of the vascular bed and the increased blood volume.

Mean circulatory and mean systemic filling pressure. Starling recognized the concept and importance of a pressure that would occur throughout the circulation if the pressures could be brought to equilibrium and coined the term “mean circulatory filling pressure” (MCFP) (22a). So far, static filling pressure and MCFP are used synonymously, although the latter term has the advantage of not suggesting an “unchanging” pressure. Once the MCFP is representative for the entire circulatory system, “mean systemic (filling) pressure” and “mean pulmonary (filling) pressure” would be applicable to the systemic and pulmonary systems, respectively (7a).

Guyton et al. (7), and later others (16, 19), assessed the MCFP in experimental animals immediately after circulatory arrest by rapidly pumping blood from the arterial to venous system (from the aorta to jugular vein) at the point where arterial and venous pressure cross. Guyton et al. reported values of 6.5 ± 1.0 mmHg in control dogs and a maximum of 16.9 mmHg after the administration of epinephrine. As pressures in the pulmonary system were not considered, Guyton’s values relate in the strict sense not to the MCFP but to the mean systemic pressure.

Mean systemic pressures (4a, 6a, 17a) or Pms (23c) have been assessed in different species by using different techniques, most of which imply a momentary circulatory arrest via inflation of a right atrial balloon (14a, 23b), occlusion of the pulmonary artery (19), administration of acetylcholine (11a, 16), stimulation of the vagal nerve (9a), or electrical induction of fibrillation (5, 7, 7a). Although these pressures apply to the entire peripheral circulatory system, most of the above studies assessed pressures solely in the central venous system. Despite a helpful review (18), the semantics of equilibrium pressures remain somewhat unclear to now.

Independent from the semantics, the importance of the above pressures is clear, as they reflect venous tone (9b, 16a, 17b) and provide an estimate of the distending pressure in the small veins and venules (18). In turn, the particular amount of the pressures depends on the compliance of the vascular system, the volume contained in that system, and the pressures surrounding it (7, 23c).

The expert secretarial help of E. Brandomisio, R. Rummel, and T. Stuff is greatly appreciated. We are indebted to Dr. P. Nacke for the cooperative support in preparing the figures.

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