Monitoring of right ventricular function using a conventional slow response thermistor catheter

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Abstract. *Objective:* To investigate whether determination of right ventricular end-diastolic volume (RVEDV) and right ventricular ejection fraction (RVEF) can be performed with reasonable accuracy and reproducibility using a conventional slow response thermistor pulmonary artery catheter (CPAC) applying an adaptive algorithm. *Design:* To study RVEDV and RVEF simultaneously with pulmonary artery catheters equipped with slow and fast response thermistors (FRPAC) under a broad range of cardiac output. *Setting:* Laboratory of Institute of Experimental Surgery, Technical University. *Animals:* 11 anaesthetised piglets. *Interventions:* Hypovolemia (V−) was induced by withdrawal of blood up to 50 ml/kg, hypervolemia (V+) was produced by retransfusing blood and adding up to 30 ml/kg hydroxyethyl starch. In 5 animals in phases V− and V+ beta-adrenergic stimulation was achieved with dobutamine. Finally pulmonary artery hypertension was induced by infusion of small air bubbles. *Measurements and results:* Cardiac output (CO), RVEDV and RVEF were determined simultaneously with FRPAC and CPAC placed in the same pulmonary artery branch. Measurements were repeated 8 times sequentially in steady state normovolemia. A total of 130 measurements could be analysed. The coefficient of variation was $6.7 \pm 4.2\%$ for $CO_{(FRPAC)}$ and $4.6 \pm 1.7\%$ for $CO_{(CPAC)}$; for RVEF it was $9.7 \pm 6.2\%$ (FRPAC) and $9.9 \pm 3.9\%$ (CPAC); for RVEDV it was $11.6 \pm 4.8\%$ (FRPAC) and 8.54 ± 3.2 (CPAC). Mean difference (bias) was 0.06 ± 0.39 l/min for CO measured with both methods, 19 ± 35 ml for RVEDV and $-3.3 \pm 6.5\%$ for RVEF. $CO_{(CPAC)}$ displayed a strong correlation to $CO_{(FRPAC)}$ ($R = 0.97$, $p = 0.001$) as well as RVEF (R for $RVEF_{(CPAC)}$ versus $RVEF_{(FRPAC)} = 0.90$, $p = 0.001$). R for $RVEDV_{(CPAC)}$ versus $RVEDV_{(FRPAC)}$ was 0.67, $p = 0.001$.

We conclude that this animal study demonstrates good agreement between RVEF and RVEDV obtained with catheters equipped with a fast response thermistor or with a conventional slow response thermistor allowing accurate monitoring of right ventricular function with a conventional pulmonary artery catheter.

Among the different methods for monitoring right ventricular (RV) function the thermodilution based method using a fast response thermistor has gained widespread acceptance because it can be performed easily and repeatedly at the bedside [1–5]. The method requires a pulmonary artery catheter the thermistor of which is made fast by thinning the coating over the thermistor. RV volumes and ejection fraction are calculated using an algorithm which gives a single, first order, exponential washout curve indicating the residual fraction of the thermal indicator remaining in the RV [6–8]. Modulating RV function by volume shift, venous air embolism (VAE) and beta-stimulation in an experimental model we investigated whether RV function could be reliably monitored with inexpensive slow response PA catheters applying an algorithm first developed by Newman [9]. This algorithm was subjected to an empirical modulation which corrects for the thermal signal delay caused by the slow response thermistor in conventional pulmonary artery catheters. In principle this would create the possibility to use any conventional slow response PA catheter for RV monitoring provided that the thermodilution computer has been fed with this special algorithm, RV monitoring thus requiring nothing but some extra software.

Material and methods

The experiments were performed in 11 German house piglets, mean body weight (bw) 31 ± 4 kg (± 1 SD). Premedication was 8 mg/kg

azaperone and 1 mg atropine intramuscularly. Anaesthesia was induced with 0.5 – 0.8 mg/kg etomidate intravenously and maintained by continuous intravenous infusion of pentobarbital 10 mg/kg/h and inhalation of N_2O. The animals were paralysed with 0.3 mg/kg/h alcuronium chloride. They were ventilated with a volume-controlled pattern with positive end expiratory pressure (PEEP) of 5 cmH_2O (Servo Ventilator 900C Siemens Elema, Solna, Sweden) at a respiratory rate of 20/min, inspiration to expiration ratio (I : E) 1 : 2. Tidal volume was adjusted to maintain $PaCO_2$ between 35 – 45 mmHg and the inspiratory oxygen fraction (FIO_2) to keep PaO_2 between 70 – 100 mmHg except for the venous air embolism period, when FIO_2 was 1.0. The following catheters were inserted:

Both a fast response PA catheter (FRPAC) (93 A-431 H-7.5 F, Baxter Edwards, Santa Ana CA; USA; response time 50 ms) and a conventional slow response PA catheter (CPAC) (SP 5107, 7.5 F, Spectramed, response time 1200 ms) were placed in the same pulmonary artery branch. A large bore catheter for blood withdrawal was positioned in the femoral artery and one for fast volume infusion in the femoral vein. Additional catheters were placed in the femoral artery for systemic blood pressure measurement and another triple-lumen catheter in the superior vena cava for fluid replacement, CVP measurement and injection of the thermal-dye-indicator. Pressures in the pulmonary artery were obtained from the CPAC. Exact position of the catheters was confirmed by pressure tracing and by X-ray. All pressures were referenced to midthorax and displayed on a bedside monitor (KONE 560A, Espoo, Finland). Heart rate, derived from the ECG, was displayed continuously on the same monitor. Each of the pulmonary catheters was connected to the appropriate computer: the FRPAC to REF-1 (Baxter Edwards, Santa Ana, CA) and the CPAC to COLD Z-021 System (Pulsion Medizintechnik, München, Germany).

The REF-1 computer uses an algorithm which does not recognise specific plateaus, but is based on a model of a single pulsatile chamber's response to a pulsed input bolus. This mathematical system gives rise to a single, first order exponential washout curve, the downslope of which is used to calculate the residual fraction occurring within each RR-interval. The algorithm for the FRPAC follows the general formula:

$$y = A \times e^{-t/\tau}$$

with A = constant. The algorithm fed to the COLD-computer follows the formula:

$$v = A \times e^{-t/f(\tau)}$$

with A = constant, flow being assumed constant after injection, and f(t) = empirical algorithm which corrects for thermodilution curve delay caused by sensor response time. As shown in Fig. 1 with a fast decay of temperature curve (= low RVEDV and high RVEF) the slow response time of the CPAC limits the detection of fast temperature changes, while with a slow decay of temperature changes (= high RVEDV and low RVEF) (see Fig. 1) the slow response thermistor is fast enough. The algorithm corrects for the slower response time by increasing the steepness of the thermal downslope, when the measured downslope approaches the catheter's response time.

The double indicator bolus, i.e. 10 mg indocyanine green mixed in 10 ml glucose 5% in water (temperature: 2 – 5 °C) was injected into the superior vena cava via the triple-lumen catheter. The injectate was delivered at a constant rate of 10 ml/sec by an automatic thermodilution injector (ZI-O3, Pulsion, Medizintechnik, München FRG). The same injection of the thermal indicator triggered the measurement start of both thermodilution computers connected to the FRPAC and the CPAC. Injections were not timed to respiratory cycle. Both computers calculate CO, RVEDV and RVEF. In order to obtain RVEF, HR has to be entered manually into the COLD-Z-021 system, whereas the REF-1 uses the HR obtained from the FRPAC's intracardiac leads.

The following variables were measured: HR; systemic and pulmonary arterial and venous pressures; cardiac output and RVEDV and RVEF.

In the first four out of 11 animals we ruled out valve insufficiency qualitatively. After positioning the first PA-catheter, the second PA-catheter was inserted to have its distal lumen in the Right Ventricle. Injection of contrast medium confirmed that insufficiency of the tricuspid valve had not been induced by the second catheter. The PA-
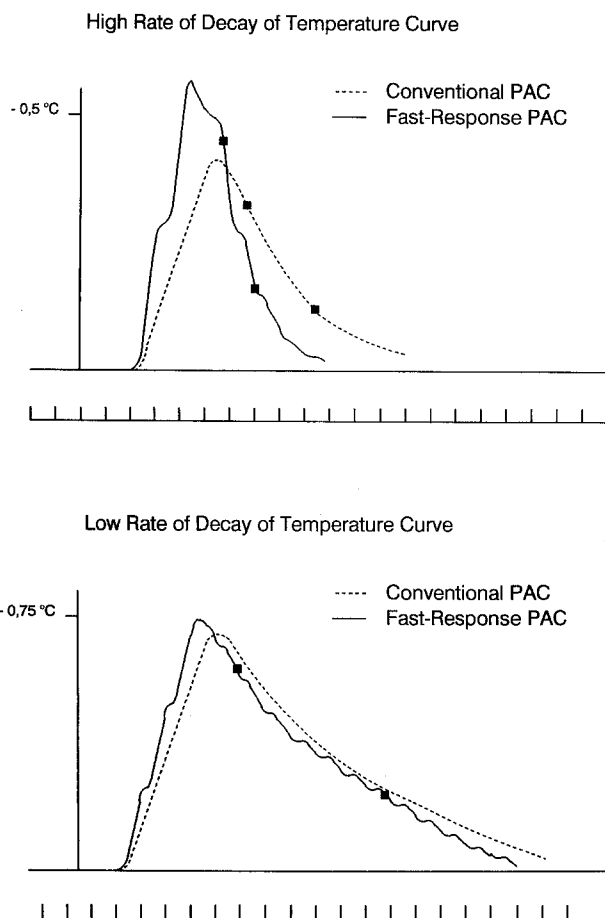

Fig. 1. Principle effect of the slow response thermistor, if rate of thermal decay approaches the response time of the catheter. The empirical algorithm gradually corrects the steepness of the measured thermal signal the more the rate of thermal decay approaches the thermisor response time. Thermistor response time is not a limiting factor if rate of thermal decay is slow (as it is with high RVEDV and low RVEF)

catheter was then advanced to the main pulmonary artery. Injection of contrast medium confirmed that insufficiency of the pulmonary valve had not been induced by the second catheter. With these results we felt justified not to continue performing selective angiography in the remaining 7 animals.

Experimental protocol

After positioning of the catheters the animals were turned to the prone position. In order to change cardiac output, RVEDV and RVEF over a wide range, measurements were taken in normovolemia (NV), hypovolemia(V–), hypervolemia(V+), beta-stimulation(b) and venous air embolism(VAE). The different conditions were brought about in the following order:
1. NV: 8 measurements in normovolemia were performed in order to determine the coefficient of variation for both methods.
2. V–: up to 50 ml/kg blood was withdrawn. The withdrawal was performed as quickly as possible provided that the mean arterial pressure could be kept above 40 mmHg. Within 1 min after completion of the withdrawal a measurement was started.
3. V+: after retransfusion of the withdrawn blood additional volume (10% hydroxyethyl starch) in steps of 15, 20 and finally up to 30 ml/kg was given. After each of these 3 steps a measurement was performed starting within 1 min after completion of volume expansion.
4. b: in 5 animals in phases V– and V+ beta-adrenergic stimulation was achieved by infusion of 5 – 10 µg/min*kg dobutamine. A measurement

Table 1. CO, RVEDV and RVEF with fast response pulmonary artery catheter (FRPAC) and conventional pulmonary artery catheter (CPAC) (slow response thermistor). Values represent mean ± 1 SD, minimum and maximum values obtained under all experimental conditions (normovolemia, hypovolemia, hypervolemia, beta-stimulation and venous air embolism) and minimum/maximum given as % of the normovolemic (NV) level ($n = 11$ animals)

	Mean	1 SD	Minimum	Maximum	Minimum in % of NV	Maximum in % of NV
FRPAC CO [l/min]	4.34	± 1.66	0.46	8.6	10	191
RVEDV [ml]	121	± 37	59	212	62	223
RVEF [%]	42	± 15	5	71	10	145
CPAC CO [l/min]	4.61	± 1.85	0.47	9.79	10	218
RVEDV [ml]	101	± 34	35	227	34	220
RVEF [%]	36	± 16	1	82	12	195

was started 1 min after the increase of hemodynamic performance had reached a stable level.

5. VAE: graded RV-dysfunction was induced by continuous infusion of small air bubbles into the right atrium causing a rise of mean arterial pulmonary pressure up to 60 mmHg. To this end up to 250 ml of air had to be infused for 10–20 min. A measurement was performed within 1 min after mean arterial pulmonary pressure had reached 60 mmHg or when extrasystoles and/or rapidly decreasing mean arterial pressure indicated life threatening RV dysfunction.

Repeated measurements were performed in NV and in V+ because it was only under these conditions that hemodynamic stability was present.

Exclusion criteria

Measurements with heart rates above $150 \, min^{-1}$ had to be excluded, because the REF-1 does not detect these high heart rates correctly. In some animals in VAE pulmonary hypertension with MPAP > 60 mmHg occurred. These animals were excluded because in these cases the animals died without delay and measurement could not be completed.

A total of 130 measurements could be included in the statistical analysis. At the end of the experiment the animals were sacrificed with an overdose of pentobarbital.

All values are presented as mean ± 1 standard deviation. Regression analysis (best fit) was performed where appropriate. The coefficients of variation were compared with a paired t-test. A p-value of ≤ 0.05 was considered statistically significant. Bias (the mean difference between the two methods) was presented according to [10].

The experiments were performed at the laboratory of the Institute of Experimental Surgery of the Technical University of Munich (Germany). The ethics committee for animal experimentation of the state of Bavaria reviewed and consented to the protocol.

Results

The results are summarised in Tables 1–3 and Fig. 2–3. CO was modulated over a wide range of 10–191% of its control value in normovolemia (FRPAC), whereas the range of RVEDV and RVEF modulation could not be extended as much (see Table 1).

The coefficient of variation for 8 sequential measurements obtained in each of 11 animals in steady state conditions under normovolemia did not significantly differ, whether measured with FRPAC or CPAC (although the coefficient of variation displayed a higher scatter with FRPAC). It was 6.7 ± 4.2% for $CO_{(FRPAC)}$ and 4.6 ± 1.7% for $CO_{(CPAC)}$; for RVEF it was 9.7 ± 6.2% (FRPAC) and 9.9 ± 3.9% (CPAC); for RVEDV it was 11.6 ± 4.8% (FRPAC) and 8.54 ± 3.2 (CPAC) (see Table 2).

Table 2. Coefficient of variation (%) for the measurement with fast response pulmonary artery catheter (FRPAC) and conventional pulmonary artery catheter (CPAC) (slow response thermistor) (values are mean ± 1 SD; $n = 8$ measurements for each animal in normovolemia)

Coefficient of variation [%]	CO	RVEDV	RVEF
FRPAC	6.7 ± 4.2	11.6 ± 4.8	9.7 ± 6.2
CPAC	4.6 ± 1.7	8.54 ± 3.2	9.9 ± 3.9

CO measured with the conventional slow response catheter displayed a strong correlation to CO measured with the fast response thermistor ($R = 0.97$; $p = 0.001$), as well as did RVEF (R for $RVEF_{(CPAC)}$ versus $RVEF_{(FRPAC)} = 0.90$; $p = 0.001$) while the RVEDV correlation was less strong (R for $RVEDV_{CPAC}$ versus $RVEDV_{(FRPAC)} = 0.67$; $p = 0.001$) (see Table 3 and Fig. 2–3).

Mean difference (bias) was 0.06 ± 0.39 l/min for CO measured with both methods, 19 ± 35 ml for RVEDV and −3.3 ± 6.5% for RVEF. RVEF and RVEDV differences displayed a minor increase in scatter with increasing RVEF and RVEDV, agreement between both methods remained reasonably good over the whole range (see Table 3 and Fig. 2).

Discussion

We could show that using a conventional (slow) response thermodilution catheter in an experimental model, right ventricular volumes and ejection fraction can be measured with a degree of accuracy which satisfies clinical purpose. Agreement between the slow and fast response thermistor method was high. The graphical display for the relationship between RVEF measured with both methods shows, that the correlation was even stronger in the low range of RVEF < 0.5, i.e. with compromised RV function.

The question of the "gold standard" for RVEF and RVEDV-measurement is not completely solved until now (for review see [11] and [12]). As pointed out by Jardin [13] the echocardiographic technique yields reliable results for RV volumes and performance. It depends on geometric assumptions, needs especially trained person-

Table 3. Agreement between cardiac output (CO), right ventricular enddiastolic volume (RVEDV) and right ventricular ejection fraction (RVEF) obtained with fast response pulmonary artery catheter (FRPAC) versus conventional pulmonary artery catheter (CPAC) (best fit regression equation, correlation coefficient R, p value, Bias)

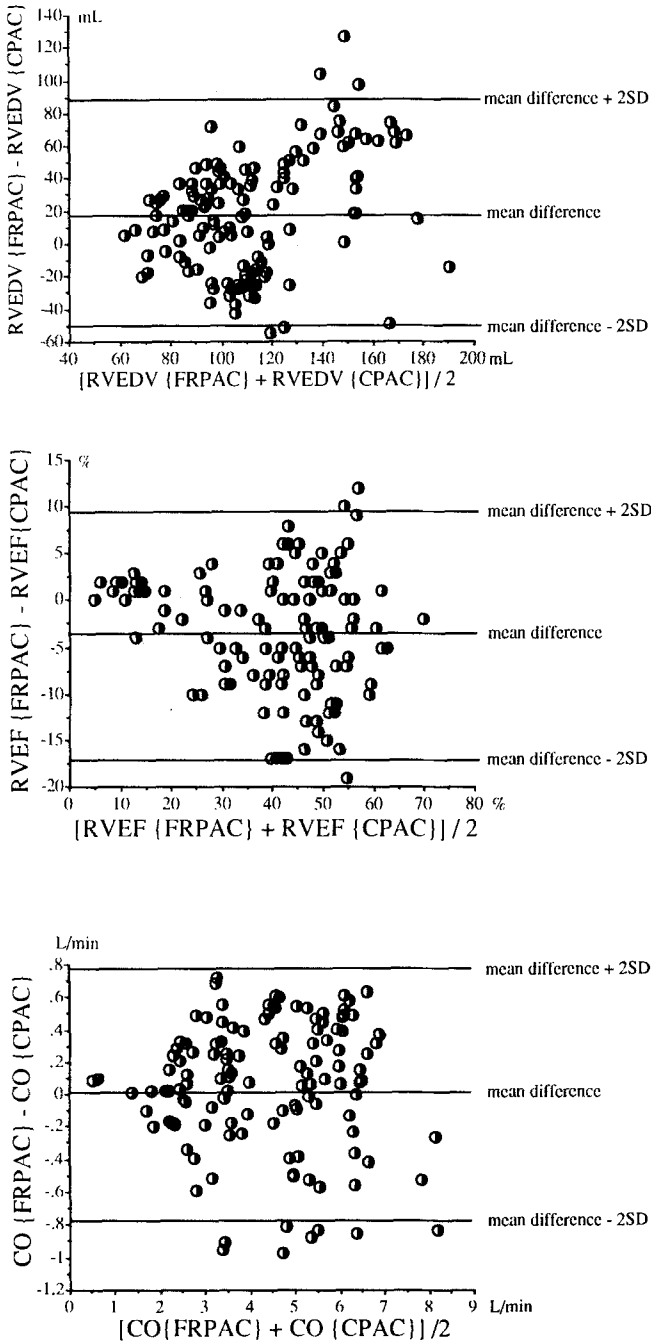|	Best fit regression equation	R	p	Bias		Units	Data sets
CO	$CO_{(FRPAC)} = 1.00 \times CO_{(CPAC)} + 0.06$	0.97	0.001	$(CO_{FRPAC} - CO_{CPAC}) \pm SD =$	0.06 ± 0.39	[l/min]	130
RVEDV	$RVEDV_{(FRPAC)} = 1.95 \times RVEDV_{(CPAC)} - 77.9$	0.67	0.001	$(RVEDV_{FRPAC} - RVEDV_{CPAC}) \pm SD =$	19 ± 35	[ml]	130
RVEF	$RVEF_{(FRPAC)} = 1.09 - RVEF_{(CPAC)} + 0.03$	0.90	0.001	$(RVEF_{FRPAC} - RVEF_{CPAC}) \pm SD =$	-3.3 ± 6.5	[%]	130

Fig. 2. Agreement of variables derived from fast response thermistor catheter with variables derived from conventional pulmonary artery catheter: mean difference (bias) and mean difference±2SD are represented as horizontal lines. *Top*: $RVEDV_{(FRPAC)}$ versus $RVEDV_{(CPAC)}$. *Middle*: $RVEF_{(FRPAC)}$ versus $RVEF_{(CPAC)}$. *Bottom*: $CO_{(FRPAC)}$ versus $CO_{(CPAC)}$

nel and does not always trace RV endocardium [14]. The scintigraphic techniques using radioactive isotopes as well as the angiographic techniques suffer from the risk from accumulated radiation or from repetitive angiographic dye injections. Thus, with these techniques it is difficult to obtain serial measurements in patients which are necessary to trace the physiologically modulated RV function [15, 16]. First pass angiography seems less subject to errors in measurement. It is therefore often considered to be the "gold standard" for RVEDV measurement. The thermodilution based technique has been extensively studied and the conclusion of Kay et al. [5] that thermal techniques provide a convenient, safe, reproducible and accurate method of measuring cardiac output, RVEF and RV volumes is widely accepted. It must be recognised, however, that some investigators could not confirm the accuracy of the fast response thermistor method when compared to other methods [17] and therefore see only limited value for this method. When evaluating a technique for RV monitoring one must be aware of the fact stated by Dhainaut [18] that no "gold standard" is available to assess the accuracy of the RVEF and RV volume measurement by thermal technique. The fast response thermistor technique, which for good reasons is clinically accepted, can be used instead to evaluate the slow response thermistor thermal technique as we did in this study.

The coefficient of variation for 8 serial measurements for CO, RVEDV and RVEF was in the same range for both, the CPAC and FRPAC methods. It was for practical reasons only that we used PA catheters from different
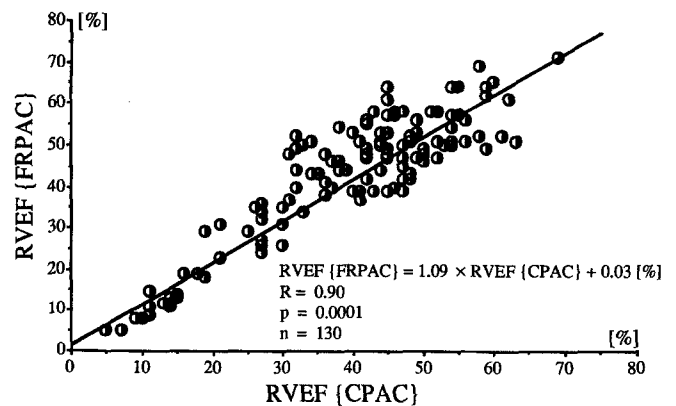

Fig. 3. Regression analysis for the relationship between right ventricular ejection fraction (RVEF) measured with conventional pulmonary artery catheter (*CPAC*) (slow response thermistor) and RVEF measured with fast response thermistor (*FRPAC*)

manufacturers. We are not aware of data showing that the differences between PA catheters from different manufacturers are more important than the differences between PA catheters from the same manufacturer. For the RVEF measurements this confirms the findings of other investigators for the reproducibility of the thermodilution method. Kay et al. [5] in humans found that the reproducibility of RVEF measurement was±5%, RA injections being more reproducible than RV injections. Vincent et al. [4] found a variability coefficient in patients of 7.6%. Imai et al. [19] found in patients that RVEF measurement depended on the site of injection (a question which is not addressed in our investigation) and on whether the first, second or third measurement out of 3 serial measurements was taken. The coefficient of variation varied (taken as the mean of the whole population) from $22.1 \pm 14.3\%$ for the first RVEF determination with RV-injection to $7.7 \pm 8.7\%$ for the first RVEF determination with RA injection. Assmann et al. [20], in patients mechanically ventilated with low frequency (8 cycles/min), found that the mean amplitude of modulation of RVEF extended to 48% of a patient's mean value during the ventilatory cycle (24 cycles/min: 11%). Similar reductions were observed for CO and RVEDV.

We did expect the good agreement and low coefficient of variation for the CO determination. The accuracy and reproducibility of the determination of CO is not limited by the response time of the catheters used. We also expected the good agreement in the RVEF measurements, as the RVEF under conditions of low RV afterload (which was true except for VAE) is quite stable and not primarily determined by failing RV function. With high RVEF the response time of the conventional pulmonary artery catheter could limit the accuracy of the measurement. In practice this is of little importance, because the patient whose RV function is to be monitored is the patient at risk of right ventricular failure. The use of the CPAC with modified algorithm will be inferior for monitoring normal and supranormal RVEF occurring for example in pharmacological studies.

The RVEDV measurements with both methods do not correlate as strongly as the RVEF measurements. We see two reasons for this weaker agreement between the two methods concerning RVEDV: 1) The coefficient of variation reflects a somewhat important scatter in both methods (more pronounced with the fast response thermistor) and in the physiological variation of RVEDV due to mechanical ventilation. The amount of agreement between the two methods is limited by the variation in repeated measurements of RVEDV with either FRPAC or CPAC (Fig. 2). FRPAC measures a volume which is slightly different from the volume measured with CPAC because the latter uses a longer interval of the decay curve than the FRPAC does (Fig. 1).

Inherent methodological limitations exist for the reproducibility of RVEDV measurement when looking for a "true mean" RVEDV. As extensively discussed in the literature RV flow varies due to the cyclic intrathoracic pressure changes caused by mechanical ventilation (for review see [21]). It must be expected then that cardiac output and, even to a higher degree, RVEDV values will differ

with the injection time relative to the respiratory phase and depend on respiratory rate [22]. Various strategies have been proposed in order to get a "true mean" for cardiac output (and hence RVEDV). They rely on increasing the number of injections and timing the injections precisely relative to the respiratory phase [23–25].

We did not apply one of these strategies in this study. As we intended to study the agreement between two different types of catheters we focused on the synchronisation of measurement start for both catheters. Practical reasons consequently excluded the timing to different phases of the respiratory cycle. In addition no commercially available device exists for timing injections to respiratory phase. Thus this manoeuvre cannot be reliably and accurately performed in clinical routine.

Considering the task of the RV which has to cope with beat-to-beat changes of systemic venous return [26] the size of RVEDV must be expected to change from beat to beat too, a fact which will be easier detected with a fast response catheter of course. The scatter of RVEDV might thus be reduced by increasing the number of thermal injections but not below the point of physiologically already high variability. During the course of a (mechanical) ventilatory cycle RVEDV is sequentially increased and decreased in synchrony with rhythmic modulation of intrathoracic pressure. This bevaviour of the RV is difficult to monitor because of methodological limitations [19]. In view of the fact that the response time of the fast response thermistor might be slowed down by thrombus formation and that the thrombogenicity of PA catheters might not be reliably reduced by heparin coating [27] we question whether the additional costs for fast response thermistors are justified in all cases. The results of our study suggest that the use of conventional PA catheters in combination with the empirical algorithm allows access to similar informations on RV function at lower costs.

We conclude that this animal study shows good agreement between RVEF and RVEDV obtained with catheters equipped with a fast response thermistor or with a conventional slow response thermistor. We infer that RV function can be reliably monitored within a wide range of cardiac output using a conventional inexpensive pulmonary catheter with a modified algorithm. The presented data justify validation of this method in critically ill patients.

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