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Right ventricular dysfunction in septic shock: assessment by measurements of right ventricular ejection fraction using the thermodilution technique

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Right ventricular ejection fraction (RVEF) was measured by the thermodilution technique in a series of 127 consecutive critically ill patients monitored with a modified pulmonary artery (PA) catheter equipped with a fast response thermistor. Thermodilution RVEF was significantly lower in septic shock ($23.8 \pm 8.2\%$, 93 measurements) than in sepsis without shock ($30.3 \pm 10.1\%$, 118 measurements) or in the absence of sepsis or cardiopulmonary impairment ($32.5 \pm 7.1\%$, 62 measurements). Both myocardial depression and pulmonary hypertension could account for this impairment of RV function. RVEF decreased from 35.1 ± 9.8 to $24.2 \pm 10.4\%$ ($P<0.01$) during development of septic shock and increased from 25.0 ± 7.6 to $29.8 \pm 8.5\%$ ($P<0.05$) during recovery (14 patients). Initial RVEF in septic shock was $27.8 \pm 8.6\%$ in 11 patients who survived but only $20.9 \pm 6.7\%$ ($P<0.02$) in the 23 patients who eventually died. Thus, RV dysfunction is common during septic shock, is directly related to its severity, and can easily be recognized in patients monitored with a PA catheter.

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Decreased venous return and depressed myocardial contractility commonly alter cardiac function in septic shock (1–5). Myocardial failure has been largely incriminated in the development of low cardiac output and high filling pressures which can complicate septic shock and characterize its downhill course (1, 2). More recent studies have indicated that myocardial depression can occur very early in the course of septic shock, even when cardiac output is normal or high (3–5). In these conditions, left ventricular dysfunction can be demonstrated early by measurement of left ventricular ejection fraction (LVEF) using radionuclide techniques (3, 4). In survivors, repeated LVEF determinations show a progressive return of LVEF to normal values (3).

Assessment of right ventricular (RV) function in septic shock might be more attractive for two reasons. First, RV dysfunction can be amplified by an increase in RV afterload, represented by the pulmonary hypertension frequently observed in severe sepsis (6–9). This is in contradistinction to the usual decrease in LV afterload associated with low systemic blood pressure and systemic vascular resistance. Moreover, the right ventricle is very sensitive to afterload increases (10, 11). Using radionuclide techniques, Hoffman et al. (12) and Kimchi et al. (13) have observed that RV function could be selectively altered in patients with septic shock.

Secondly, while measurements of ventricular ejection fraction by radionuclide techniques require sophisticated equipment precluding its routine use in the intensive care unit, recent technological advances have allowed the accurate measurement of right ventricular ejection fraction (RVEF) by the thermodilution technique using slightly modified pulmonary artery (Swan-Ganz) catheters equipped with fast response thermistors (14–16). Since pulmonary artery (PA) catheters are routinely used in the management of critically ill patients during septic shock, this adaptation may represent a widely available and uncomplicated adjunct to hemodynamic monitoring. Moreover, RVEF determinations can easily be repeated at any time along with other pressure and flow measurements. The RVEF values obtained by thermodilution correlate well with values obtained by other techniques (14–17), although the normal values are usually lower, probably because of a catheter-mounting effect of the thermistor (18). Thermodilution

RVEF measurements have recently been used to assess RV function during various therapeutic interventions in acutely ill patients (19–22).

During evaluation of these modified PA catheters in a series of 127 critically ill patients consecutively monitored in our Department of Intensive Care, we observed that RVEF was significantly decreased in septic shock and that this measurement represented a valuable prognostic sign in these conditions.

PATIENTS AND METHODS

Patients

The study included 127 consecutive adult patients (77 men, 50 women) ranging in age from 19 to 86 years (mean 60 ± 16 years) in whom invasive monitoring with a PA catheter was deemed necessary during their stay in our department of medico-surgical intensive care. Sixty-six patients (52%) left the department alive.

Patients were divided into four groups.

Group 1 included 56 septic patients who developed fever (T > 38.5° C) and abnormal white blood count (above 13 000/mm³ or below 4000/mm³) in the presence of a documented source of sepsis or bacteremia. The sources of bacteria recovered were lungs and pleura in 22 patients, gut and biliary tract in 15 patients and other sources in 8 patients. In 11 patients, blood cultures were positive, and several sources of sepsis were considered.

Group 2 included 32 patients with cardiac failure related to advanced cardiomyopathy (14 patients), complicated myocardial infarction (9 patients), recent CPR (5 patients) or after cardiac surgery (4 patients).

Group 3 included 15 patients with pulmonary hypertension (mean PA pressure > 20 mmHg (2.7 kPa)) in the absence of heart failure or sepsis. This group included 8 patients with pulmonary edema due to the adult respiratory distress syndrome (6 patients) defined by the usual criteria (23) or to fluid overload (2 patients), 4 patients with decompensated chronic obstructive pulmonary disease and 3 patients with documented pulmonary embolism.

Group 4 included 29 patients invasively monitored essentially for difficult fluid management related to trauma, hemorrhage, extended surgery or renal failure. These critically ill patients were taken as controls because they did not present evidence of sepsis or cardiopulmonary failure.

Five patients were included in more than one group when they were monitored at clearly different times during their course.

Methods

Each patient was monitored with a modified PA catheter (Swan Ganz catheter 93A-431 H-7.5 F, Edwards Laboratories, Santa Ana, CA) equipped with a fast response (50 ms) thermistor, a modified proximal lumen ending in a 3-hole port at 21 cm from the catheter tip, and two electrodes for intracardiac ECG recording. The use of this catheter has been approved by the institutional human study committee. The PA catheter was inserted until the proximal lumen ended in the right ventricle just below the tricuspid valve, and was then withdrawn by 2–3 cm. The appropriate position of the tip of the PA catheter was also controlled by a chest roentgenogram.

Thermodilution cardiac output (CO) was measured by successive injections of 3 to 5 boluses of 10 ml cold (6–10°C) dextrose 5% in water, via a closed system (Co-set, Edwards Laboratories). In patients treated with mechanical ventilation, bolus injections were initiated at end-inspiration to improve the reproducibility of the measurement (24) and also to minimize the influence of changes in intrathoracic pressure on RVEF (25).

RVEF was measured by a modified algorithm based on exponential curve analysis, using a computer prototype (REF 1, Edwards Laboratories). The catheter and the method used have recently been described in detail elsewhere (15, 16). Measurements of CO and RVEF immediately followed measurements of intravascular pressures at end-expiration from a paper trace (recorder 7404 Hewlett Packard, Palo Alto, CA), using the mid-chest position as zero reference. Stroke volume (SV) was calculated by dividing CO by heart rate and RV end-diastolic volume (RVEDV) by dividing SV by RVEF. RV end-systolic volume (RVESV) was then obtained by subtracting SV from RVEDV.

In total, 435 measurements were performed in the 127 patients. Two thirds of the measurements (294) were obtained during mechanical ventilation. In Group 1, 211 measurements were obtained, including 93 measurements (Group 1a) obtained during circulatory shock characterized by the association of hypotension (systolic blood pressure below 90 mmHg (12 kPa)), oliguria (urine output below 20 ml/h) and lactacidemia (arterial lactate concentration above 2 mmol/l), and 118 measurements (Group 1b) obtained in the absence of signs of circulatory shock.

Totals of 112, 50 and 62 measurements were obtained in Groups 2, 3 and 4, respectively.

Results were analyzed by analysis of variance (ANOVA) and Student's *t*-test for paired (comparison between similar patients) or unpaired (comparison between different groups of patients) data. The Bonferroni adjustment was used when several groups were compared. All data are presented as mean ± s.d.

RESULTS

In the 56 septic patients, RVEF was significantly lower in the presence than in the absence of circulatory shock (23.8 ± 8.2 vs 30.3 ± 10.1%, $P < 0.01$, Fig. 1). In septic shock, the lower RVEF was associated with lower stroke volumes and higher RV end-systolic volumes (Table 1). As expected, arterial pressure was significantly lower in septic shock. However, pulmonary artery pressures and right atrial pressures were only slightly lower in the presence than in the absence

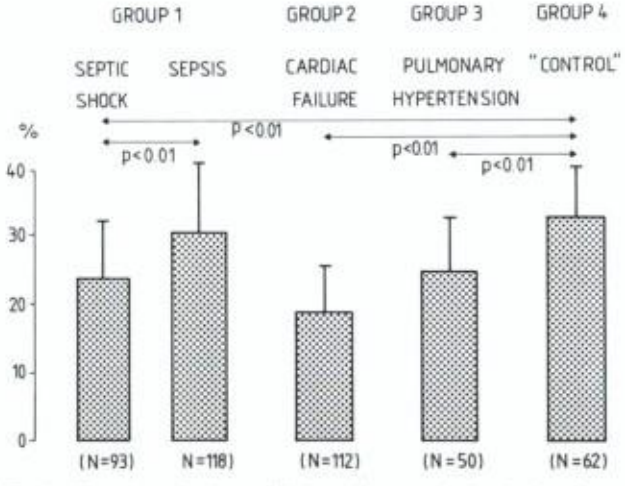

Fig. 1. Mean (± s.d.) thermodilution right ventricular ejection fractions (RVEF) measured in the four groups of patients. The number of measurements is indicated in parentheses.

of septic shock (Table 1). When compared to the 29 control patients, septic patients without signs of circulatory shock had significantly higher RV end-systolic and end-diastolic volumes, but their RVEF was not significantly depressed. Pulmonary artery pressures were significantly elevated in all septic patients (Table 1).

Signs of septic shock resolved in 14 patients, whose RVEF increased from 25.0 ± 7.6 to $29.8 \pm 8.5\%$ ($P < 0.05$) after resolution of the shock state. On the other hand, in 7 septic patients monitored during the development of septic shock, RVEF dramatically decreased from 35.1 ± 9.8 to $24.2 \pm 10.4\%$ ($P < 0.01$).

As anticipated, RVEF was significantly reduced in the 47 patients with cardiac failure or pulmonary hypertension related to other causes. In these groups RV end-systolic and end-diastolic volumes were both increased, but stroke volume was significantly depressed only in patients with cardiac failure (Table 1 and Fig. 1).

In septic shock, RVEF also had a prognostic value, since the initial RVEF was $27.8 \pm 8.6\%$ in the 11 patients who were ultimately discharged but only $20.9 \pm 6.7\%$ in the 23 patients who died from protracted sepsis ($P < 0.02$). Initial RVEF was above 25% in 8 of the 11 patients who were discharged alive from the intensive care unit, but only in 5 of the 23 fatalities ($P < 0.01$). The other hemodynamic parameters did not have a similar predictive value (Fig. 2).

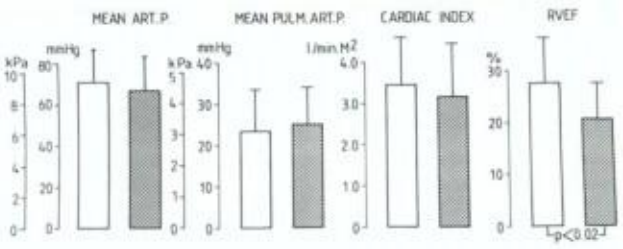

Fig. 2. Initial values of mean arterial pressure, mean pulmonary arterial pressure, cardiac index and right ventricular ejection fraction in patients in septic shock, including 11 ultimate survivors (open columns) and 23 fatalities (shaded columns).

DISCUSSION

The present study explored the usefulness of routine RVEF measurement by the thermodilution technique, especially in septic patients requiring PA catheterization for their intensive care management. The design of the study had inherent limitations. First, categorization of patients with diverse underlying conditions is arbitrary in nature. Secondly, various therapeutic interventions can influence RV function and RVEF. Thirdly, the control group did not represent normal individuals, as these patients could have right ventricular dysfunction associated with their ongoing disease process. In these control patients, RVEF was decreased below the normal value of 40 to 45% (15). In view of these limitations, the present study must be considered as a preliminary evaluation of RVEF in septic patients.

RVEF is an index of right ventricular function, which is influenced by contractility, afterload and to a lesser extent by preload (10, 11). There is a negative correlation between RVEF and pulmonary artery pressures or pulmonary vascular resistance (10, 11, 15, 16), which is related to the great sensitivity of the right

Table 1

Hemodynamic data in the four groups of patients (mean ± s.d.).

	Group 1		Group 2	Group 3	Group 4
	Septic shock (a)	Sepsis (b)	Heart failure	Pulm. hypertens.	"control"
N	93	118	112	50	62
RVEF, %	23.8 ± 8.2*†	30.3 ± 10.1	18.7 ± 7.0*	25.0 ± 7.6*	32.5 ± 7.1
SI, ml/M²	29.0 ± 10.5*†	37.2 ± 13.5	23.5 ± 9.1*	33.8 ± 12.9	34.3 ± 12.5
ESVI, ml/M²	104 ± 43*†	88 ± 34*	115 ± 50*	111 ± 55*	73 ± 30
EDVI, ml/M²	135 ± 48*	125 ± 36*	141 ± 62*	143 ± 55*	107 ± 38
AP, mmHg	68 ± 16*†	79 ± 14	81 ± 19	94 ± 15*	83 ± 18
(kPa)	(9.1 ± 2.1)	(10.5 ± 1.9)	(10.8 ± 2.5)	(12.5 ± 2.0)	(11.1 ± 2.4)
PAP, mmHg	25.6 ± 8.0*	27.4 ± 8.3*	27.5 ± 7.6*	25.1 ± 5.7*	18.5 ± 6.6
(kPa)	(3.4 ± 1.1)	(3.7 ± 1.1)	(3.7 ± 1.0)	(3.3 ± 0.8)	(2.5 ± 0.9)
RAP, mmHg	11.9 ± 5.8*	13.1 ± 6.7*	13.1 ± 6.4*	12.1 ± 5.8*	7.7 ± 4.2
(kPa)	(1.6 ± 0.8)	(1.7 ± 0.9)	(1.7 ± 0.9)	(1.6 ± 0.8)	(1.0 ± 0.6)
PAOP, mmHg	12.7 ± 4.8*	13.6 ± 5.7*	16.0 ± 5.5*	13.6 ± 5.2*	9.4 ± 4.2
(kPa)	(1.7 ± 0.6)	(1.8 ± 0.8)	(2.1 ± 0.7)	(1.8 ± 0.7)	(1.3 ± 0.6)

* $P < 0.05$ from Group 4. † $P < 0.05$ between Group 1a and 1b.

RVEF: right ventricular ejection fraction; SI; stroke index; ESVI: end-systolic volume index; EDVI: end-diastolic volume index; AP: mean arterial pressure; PAP: pulmonary arterial pressure; RAP: right atrial pressure; PAOP: pulmonary artery balloon-occluded pressure.

ventricle to an increase in afterload.

Both a decrease in myocardial contractility and an increase in RV afterload are common in severe sepsis. Various experimental and clinical studies have indicated that myocardial depression can occur early during the course of septic shock (1–5). The causes can be intracardiac ionic and fluid disturbances, altered coronary blood supply, and circulation of cardiodepressant substances (5, 26). Also common in severe sepsis is pulmonary hypertension, which has been related to the release of bacterial toxins and the activation of various mediators with secondary vasoconstriction and formation of microthrombi in the pulmonary vasculature (6–9, 11). Severe pulmonary hypertension can also be associated with myocardial depression, possibly by altering RV coronary perfusion (11).

Interestingly, no significant RV impairment was observed during sepsis in the absence of circulatory shock, even though these patients also had elevated pulmonary artery pressures. Hence, the increased RV afterload was counterbalanced by an enhanced contractility, probably related to a high sympatho-adrenergic influence (27).

The present results confirm previous data using RVEF measurements by radionuclide techniques indicating that RV function could be significantly depressed in patients with septic shock (12, 13). In the present study, sequential observations showed that RVEF significantly decreased when septic shock developed. Serial measurements of RVEF also indicated that RV function improved in survivors. This was previously suggested by Hoffman et al. (12) in a limited number of observations. A progressive increase in LVEF in survivors from septic shock was also observed by Parker et al. (3).

Our present data further indicate that the initial RVEF already has a prognostic value in septic shock. This has not been observed with measurements of LVEF in septic shock patients (3), probably because profound sepsis is also associated with more severe peripheral alterations (29), so that the effects on left ventricular function of an altered contractility and a reduced left ventricular afterload can counterbalance each other. In contrast, both pulmonary hypertension and myocardial depression have been directly related to the severity of sepsis (8, 9, 28). In the present study, however, pulmonary hypertension was similar in survivors and non-survivors, so that a more severe myocardial depression was the essential factor accounting for the lower RVEF in the fatalities.

In contrast to measurements of ejection fraction by radionuclide techniques, RVEF measurements by the thermodilution technique have the advantage of being very simple, convenient and inexpensive. Moreover, they can be repeated at any time with each cardiac output measurement. Determinations of RVEF with these modified PA catheters might have therapeutic applications in the guidance of fluid infusion, drug administration, or ventilator therapy (19–22).

The present study indicates that the RV function is altered early in the course of septic shock and that RVEF measurement has a prognostic value in these conditions. Since RVEF can easily be monitored by the thermodilution technique, it can represent a useful adjunct to hemodynamic monitoring in critically ill patients.

REFERENCES

1. Siegel J G, Cerra F B, Coleman B, et al. Physiological and metabolic correlations in human sepsis. *Surgery* 1979: **86**: 163–193.
2. Vincent J L, Weil M H, Puri V, Carlson R W. Circulatory shock associated with purulent peritonitis. *Am J Surg* 1981: **142**: 262–270.
3. Parker M M, Shelhamer J H, Bacharach S L, et al. Profound but reversible myocardial depression in patients with septic shock. *Ann Intern Med* 1984: **100**: 483–490.
4. Ellrodt A G, Riedinger M S, Kimchi, et al. Left ventricular performance in septic shock: reversible segmental and global abnormalities. *Am Heart J* 1985: **10**: 402–409.
5. Archer L T. Myocardial dysfunction in endotoxin and *E. coli*-induced shock: pathophysiological mechanisms. *Circ Shock* 1985: **5**: 261–280.
6. Clowes G H A Jr, Farrington G H, Zuschneid W, Cossett G R, Saravis C. Circulating factors in the etiology of pulmonary insufficiency and right heart failure accompanying severe sepsis (peritonitis). *Ann Surg* 1970: **171**: 663–678.
7. Zapol W M, Snider M T. Pulmonary hypertension in severe acute respiratory failure. *N Engl J Med* 1977: **296**: 476–480.
8. Marland A M, Glauser F L. Significance of the pulmonary artery diastolic-pulmonary wedge pressure gradient in sepsis. *Crit Care Med* 1982: **10**: 658–661.
9. Brigham K L, Meyrick B. Endotoxin and lung injury. *Am Rev Respir Dis* 1986: **133**: 913–927.
10. Brent B N, Mahler D, Matthay R A, Berger H J, Zaret B L. Noninvasive diagnosis of pulmonary arterial hypertension in chronic obstructive pulmonary disease: right ventricular ejection fraction at rest. *Am J Cardiol* 1984: **53**: 1349–1353.
11. Sibbald W J, Driedger A A, Cunningham D G, Cheung H. Right and left ventricular performance in acute hypoxemic respiration failure. *Crit Care Med* 1986: **14**: 852–857.
12. Hoffman M J, Greenfield L J, Sugerman H J, Tatum J L. Unsuspected right ventricular dysfunction in shock and sepsis. *Ann Surg* 1983: **198**: 307–319.
13. Kimchi A, Ellrodt G, Berman D S, Riedinger M S, Swan H J C, Murata G H. Right ventricular performance in septic shock: a combined radionuclide and hemodynamic study. *J Am Coll Cardiol* 1984: **4**: 945–951.
14. Kay H R, Afshari M, Barash P, et al. Measurement of ejection fraction by thermal dilution techniques. *J Surg Res* 1983: **34**: 337–346.
15. Vincent J L, Thirion M, Brimioulle S, Lejeune P, Kahn R J. Thermodilution measurement of right ventricular ejection fraction with a modified pulmonary artery catheter. *Intensive Care Med* 1986: **12**: 33–38.

16. Dhainaut J F, Brunet F, Monsallier J F, et al. Bedside evaluation of right ventricular performance using a rapid computerized thermodilution method. *Crit Care Med* 1987: **15**: 148–152.
17. Jardin F, Gueret P, Dubourg O, Farcot J C, Margairaz A, Bourdarias J P. Right ventricular volumes by thermodilution in the adult respiratory distress syndrome: a comparative study using two-dimensional echocardiography as a reference method. *Chest* 1985: **88**: 34–39.
18. Maruschak G F, Schauble J F. Limitation of thermodilution ejection fraction: degradation of frequency response by catheter mounting of fast-response thermistors. *Crit Care Med* 1985: **17**: 679–682.
19. Martyn J, Wilson R S, Burke J F. Right ventricular function and pulmonary hemodynamics during dopamine infusion in burned patients. *Chest* 1986: **89**: 357–360.
20. Vincent J L, Reuse C, Kahn R R. Effects on right ventricular function of a change from dopamine to dobutamine in critically ill patients. *Crit Care Med* 1988: **16**: 659–662.
21. Hines R L, Barash P G. Protamine: does it alter right ventricular function? *Anesth Analg* 1986: **65**: 1271–1274.
22. Martin C, Saux P, Albanese J, Bonneru J J, Gouin F. Right ventricular function during positive end-expiratory pressure: thermodilution evaluation and clinical application. *Chest* 1987: **92**: 999–1004.
23. Vincent J L, Brimioulle S, Berré J, Kahn R J. Prevention of the adult respiratory distress syndrome with dipyridamole. *Crit Care Med* 1985: **13**: 783–785.
24. Daper A, Parquier J N, Preiser J C, Contempré B, Vincent J L. Timing of cardiac output measurements during mechanical ventilation. *Acute Care* 1986: **12**: 113–116.
25. Vincent J L, Reuse Ch. Thermodilution for measurement of cardiac output during artificial ventilation (Letter). *Intensive Care Med* 1988: **14**: 252–254.
26. Parrillo J E, Burch C, Shelhamer J H, Parker M M, Natanson C, Schuette W. A circulating myocardial depressant substance in humans with septic shock. *J Clin Invest* 1985: **76**: 1539–1553.
27. Little R A, Frayn K N, Randall P E, Stoner H B, Maycock P F. Plasma catecholamine concentrations in acute states of stress and trauma. *Arch Emerg Med* 1985: **2**: 46–47.
28. Mc Donough K H, Brumfield B A, Lang C H. *In vitro* myocardial performance after lethal and nonlethal doses of endotoxin. *Am J Physiol* 1986: **250** (*Heart Circ Physiol* **19**): H240–H246.
29. Groeneveld A B J, Bronsveld W, Thijs L G. Hemodynamic determinants of mortality in human septic shock. *Surgery* 1985: **99**: 140–152.

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