Metabolic Monitoring of Postischemic Myocardium during Intermittent Warm-Blood Cardioplegic Administration

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Metabolic Monitoring of Postischemic Myocardium during Intermittent Warm-Blood Cardioplegic Administration

In 12 patients undergoing elective myocardial revascularization with intermittent administration of warm-blood cardioplegic solution for myocardial protection, we analyzed metabolic changes by assay of global ischemia indicators (pH, lactate, glucose, and potassium), which we measured in the coronary sinus and arterial blood during the ischemic and postischemic periods. A typical cumulative ischemic pattern with progressively decreasing pH values and progressively increasing lactate values could not be observed in all patients. It was not the degree of lactate washout, but the lactate concentration at the end of each reperfusion, that correlated significantly with global metabolic recovery time, which suggests the importance of effective reperfusion. (Tex Heart Inst J 2010;37(2):184–8)

During intermittent warm-blood cardioplegia as described by Calafiore and colleagues,1 progressive lactate accumulation and intracellular acidosis are well-known phenomena. Therefore, continuous gas monitoring of coronary sinus (CS) blood during the ischemic period has been recommended as an adjunct, in order to evaluate the quality of myocardial protection.2 If we assume that prolonged lactate production induced by ischemia is associated with adenosine triphosphate depletion and therefore with alteration of myocardial contractile function,3,4 continuous monitoring of myocardial recovery during the postischemic phase might prove useful in improving the management of patients undergoing coronary bypass surgery.

Patients and Methods

To monitor global metabolic imbalance during the ischemic period and to assess its impact on the postischemic period, we chose for our prospective study 12 patients (8 men and 4 women) aged 43 through 68 years (mean age, 61 yr) who were to undergo coronary artery bypass grafting (CABG), in whom intermittent warm-blood cardioplegic solution was to be used for myocardial protection. The study received approval from the Institutional Ethics Committee, University of Düsseldorf, Germany. All patients included in the study provided informed consent.

The inclusion criteria were 3-vessel disease and normal left ventricular (LV) function; 4 or more coronary grafts; use of isolated, on-pump CABG together with the intermittent antegrade administration of warm-blood cardioplegic solution according to the Calafiore protocol1 for myocardial protection; and surgery performed on an elective basis, by the same surgeon (AB). The exclusion criteria were myocardial infarction in the patient’s history, a left main stem lesion, and repeated revascularization.

All patients were operated on under extracorporeal circulation and normothermia. For the monitoring of metabolic changes, global ischemia indicators such as pH, lactate, glucose, and potassium were measured simultaneously in the CS and in the arterial blood during ischemic and postischemic periods at the beginning and at the end of each coronary reperfusion and, after declamping the aorta, every 4 to 5 minutes until the crossover point (COP) for lactate had been reached. The COP was reached when the lactate values—measured simultaneously in the CS and in the arterial blood—were equal.

For adequate sampling of the coronary blood, both venae cavae were cannulated and snared, and an Edwards Research Medical RCP014MIB catheter (Edwards Lifesciences LLC; Irvine, Calif) was placed in the CS with the tip positioned at the level of the middle cardiac vein. Samples were drawn simultaneously from the ar-
terial and CS catheters and sent for blood gas analysis by means of an ABL™ 700 (Radiometer Medical ApS, Brønshøj, Denmark). Care was also taken to keep the successive samples admixture-free by purging the aspirate from each previous sample. In order to avoid data misinterpretation, the concentration of CS metabolites was also considered in relation to the concentration of metabolites in the arterial blood.

Weaning from cardiopulmonary bypass (CPB) was undertaken when COP had been reached and the last coronary bypass anastomosis had been completed. If the last anastomosis had been completed before CPB, weaning from CPB occurred immediately after COP, and vice versa. When COP was reached before the proximal anastomoses had been completed, weaning occurred immediately after completion of the last anastomosis.

The LV function was assessed by measuring the myocardial contractility (LVdP/dt max; mmHg/s) before onset of the extracorporeal circulation (ECC) and immediately after weaning from CPB, using a Millar tipmanometer (Millar Instruments, Inc.; Houston, Tex) placed in the LV via the right upper pulmonary vein. The data then underwent multifocus analysis with the following research interests in mind: influence of global ischemia on recovery time (COP time); change-over-time analysis of lactate and pH value differences (CS vs arterial blood), and analysis of values obtained solely from CS blood, at the beginning and at the end of each reperfusion; analysis of lactate and pH value differences (CS vs arterial blood) at the beginning and at the end of each reperfusion, in correlation with the COP times; and changes of myocardial contractility in relation to COP time.

For the different analytes (lactate and pH), regression lines were calculated at the endpoints, at the beginning, and at the end of each reperfusion. In calculating the mean, we found that if the 12 regression coefficients for a value (either at the beginning or at the end) were significantly different from zero, we could expect either a positive or a negative trend (a pattern) of this analyte during ischemic time. For testing the regression coefficients of the values against zero, the one-sample *t* test was used. The regression coefficients were calculated with Excel (Office 2003), and, for the *t* test, the means procedure was used (SAS® 9.2 software, SAS Institute Inc.; Cary, NC).

### Results

The mean number of coronary grafts implanted in the 12 patients was 4.4 (range, 4–6), and the mean aortic cross-clamp time was 53 minutes (range, 44–88 min). The mean ischemic period between each reperfusion session was 9.7 minutes and ranged between 7 and 13 minutes.

No correlation was found between global ischemic and COP times (data not shown). It is of interest that, in most patients, we observed a conspicuous congruence between arterial and CS blood in regard to lactate content and pH value, with 3 directions of movement: upward or downward movement, or constant-value behavior (data not shown).

The regression analysis revealed that only 2 *t* values—that for lactate value differences and that for pH value differences (both registered at the end of reperfusions)—showed a significance in favor of the alternatives of increasing values over time (*P* = 0.02548 and *P* = 0.03139, 11 degrees of freedom, 1-sided alternatives). All other *P* values were greater than 0.05 (Fig. 1).

The analyses of lactate, glucose, and potassium levels during the postischemic period revealed a striking congruence: similar COP times for all 3 analytes in all patients. A representative tracing (in patient 1) of simultaneously sampled lactate, glucose, and potassium values, in CS and in arterial blood, is presented in Figure 2. In this patient, 39 minutes after declamping the aorta, values of all 3, measured in CS blood, reached the levels of values measured in arterial blood.

Figure 3 shows scatter plots of the mean lactate and pH differences in simultaneously sampled CS and arterial blood in relation to the corresponding COP times: for each individual patient, mean values from all reperusions were registered at the beginning and again at the end of each reperfusion, and single values for each patient were registered at the end of the last reperfusion.

We observed no correlation between mean values from all lactate samples and COP times at the beginning of reperfusion, but we did observe a positive correlation at the end of reperfusion. In regard to pH values, we found a slight correlation between mean pH values from all samples and COP times at the beginning of reperfusion, but not at the end (see Figs. 3A and 3B).

The analysis of lactate and pH value differences (CS vs arterial blood) at the beginning of the last reperfusion (data not shown) showed no correlation with COP times, but there was a positive correlation between lactate values and COP times at the end of the last reperfusion (Fig. 3C). No correlation was found between pH value differences and COP times at the end of the last reperfusion (Fig. 3C).

Left ventricular contractility (LVdP/dt max; mmHg/s) measured before the onset of extracorporeal circulation and immediately after weaning from CPB is presented with corresponding COP times in Figure 4. The declines in LV performance in the 3 patients (patients 1, 3, and 12) who presented with the longest COP times (39, 27, and 26 min, respectively) are shown on the graph.

### Discussion

Graffigna and colleagues investigated the metabolic state of ischemic myocardium in 19 patients who underwent CABG or valve surgery (or both) with myocardial...
Fig. 1 These regression lines depict value differences in lactate and pH values between coronary sinus and arterial blood at the beginning (A) and the end (B) of each reperfusion; and they depict values registered solely in coronary sinus blood at the beginning (C) and the end (D) of each reperfusion. Significance was calculated from regression coefficients. Numbers 1 through 5 indicate successive reperfusions.
Fig. 2 Representative tracings (from patient 1) of lactate, glucose, and potassium values registered during the ischemic and post-ischemic periods. Numbers 5 through 40 indicate postischemic time in minutes.

Art = arterial blood; CS = coronary sinus blood; P = successive reperfusions during ischemic period

Fig. 3 Scatter plots present the mean lactate and pH differences in simultaneously sampled arterial and coronary sinus blood in relation to crossover-point time. For each individual patient, mean values from all reperfusions were registered at the beginning (A) and again at the end (B) of each reperfusion, and single values (C) for each patient were registered at the end of the last reperfusion.
protection afforded by the intermittent administration of warm-blood cardioplegic solution, antegrade or retrograde (or both). They detected a typical pattern of blood-gas change with progressive deterioration of PCO₂ and pH values: at subsequent intermittent doses of warm-blood cardioplegic solution, pH and PCO₂ failed to return to previous levels, so that at the end of every ischemic period progressively lower pH levels and higher PCO₂ values were recorded.

In contrast with the observations of Graffigna, we found, in our study group, no clear pattern of progressively decreasing pH values and progressively increasing lactate values. Generally, we observed, during the ischemic period, changes of lactate and pH content in CS blood that were congruent with changes in the arterial blood. Even in patients who underwent longer ischemic periods, constant lactate and pH values could be registered at the end of reperfusion. Furthermore, longer ischemic periods were not necessarily associated with cumulative patterns of ischemic metabolites and longer COP times. Neither the degree of lactate washout nor the pH values measured at the beginning of each reperfusion correlated significantly with COP times. However, our regression analysis revealed a significant change over time for lactate and pH values obtained at the end of all reperusions. We also observed a positive correlation between the mean lactate concentration at the end of all reperusions (including the last) and COP times. These data indicate the importance of effective reperfusion.

According to a report published by Johnson and coauthors, an immediate increase of contractility after CABG can be expected in patients who have good preoperative LV function. We observed this phenomenon in all but 3 patients—those in whom the longest COP times were registered. Despite metabolic recovery with demonstrably normal lactate metabolism, diminished contractility persisted in all 3 patients even longer than 20 minutes after declamping the aorta. Therefore, lactate monitoring seems to be useful in the assessment of myocardial protection quality and hence in the management of the postischemic heart. In our study group, a cumulative ischemic pattern could not be observed in all patients, which suggests differences in reperfusion efficiency. Additional research is warranted to prove the notion that changing reperfusion conditions (for example, pressure, volume, or duration) can contribute to the improvement of quality of myocardial protection.

References