Myocardial ischemia, one of the major causes for postoperative cardiac dysfunction in patients undergoing cardiac surgery, can be defined as a condition when \( O_2 \) supply is not sufficient to meet the rate of mitochondrial oxidation. Bardenheuer et al have demonstrated that the adenosine concentration was enhanced in close proportion to the duration of coronary occlusion during PTCA, and was regarded as a sensitive marker to diagnose myocardial ischemia. The purposes of this study are to demonstrate: is adenosine still a sensitive myocardial ischemic parameter during cardiac interventions such as CABG, to reflect the status of \( O_2 \) supply and \( O_2 \) consumption?

**Methods:** Twenty one patients undergoing elective CABG operations under stable hemodynamic conditions were investigated in this study. Anesthesia and cardiovascular surgery were performed according to standard procedures. The following parameters were measured: 1. hemodynamics and respiratory parameters; 2. coronary sinus blood flow; 3. blood gas analysis in systemic and in coronary sinus blood; 4. purine compounds (adenosine, hypoxanthine, uric acid) and lactate in arterial, pulmonary arterial as well as in coronary sinus blood samples.

The blood samples from arterial and pulmonary arterial catheters were obtained at the following 7 time points: T1: 15 - 20 min after start of anesthesia; T2: 15 - 20 min after start of operation; T3: 15 - 20 min after the aortic crossclamping; T4: 45 - 50 min after the aortic crossclamping; T5: just before the release of aortic crossclamping; T6: 25 - 30 min after the release of aortic crossclamping; T7: 15 - 20 min after the end of CPB. Time schedule for coronary sinus blood sampling during reperfusion was as follows: as soon as the ascending aorta was declamped, the coronary sinus blood was collected from coronary circulation over the next 105 sec in intervals of 5 sec each (21 time points), and was additionally collected for 5 sec each at 3, 9, and 15 min, respectively, after reperfusion. The nucleosides were assayed by a fully automated HPLC system equipped with a dual pump system, Nova-Pak C18 reversed-phase column and a photodiode array detector. Absorbency of adenosine and hypoxanthine was monitored at 254 nm. Plasma uric acid concentrations were assayed at 293 nm. Sample peaks were integrated and quantitated using a computer- assisted program. Results are analyzed by the statistical program SPSS. Statistical significance is at the \( p \leq 0.05 \) level.

**Results:** All patients [18/3 male/female, 66 ± 1.4 years, ASA II-IV] showed coronary obstructions of 2-3 coronary vessels with an EF \( \geq 50\% \). In all patients CABG of 3-4 vessels
was performed. The average bypass time, the aortic clamping time, and the reperfusion time were 112 ± 7 (59-195), 67 ± 6 (36-155), and 36 ± 3 (23-75) min, respectively.

During CPB the adenosine concentrations in arterial and pulmonary arterial blood were 2.6- and 2.3-fold increased in comparison to the corresponding control conditions, respectively (p < 0.01). Before CPB the concentration differences between arterial and pulmonary arterial adenosine (A – Pa ado) showed negative. The A – Pa ado differences were reversed (A – Pa ado positive) during CPB, and lasted until the period of partial bypass. In the post-bypass period, however, pulmonary-arterial adenosine exceeded the arterial concentrations again (A – Pa ado negative). No significant changes in arterial and pulmonary arterial concentrations of hypoxanthine and uric acid were obtained throughout the total surgical intervention. Significant increases of arterial and pulmonary arterial lactate concentrations were found during cardioplegic arrest, which might be caused by the infusion of Ringer-Lactate solution. Following coronary reperfusion the net release rates of adenosine exhibited transient changes reaching the maximum (334 ± 47 nmole/min) within 15 sec, after reperfusion was started. The peak adenosine release rate at 15 sec presented a 6.5 fold increase in comparison with the control release rate at 15 min. In contrast to the changes of adenosine the changes in cardiac hypoxanthine were less sensitive during the reperfusion period with a 3.7-fold maximum enhancement in net release rate 60 sec after reperfusion was started. The total loss of cardiac adenosine and hypoxanthine during the reperfusion period (15 min) was calculated to be 1086 µmole which is almost 15 % of total adenine nucleotides in cardiac tissue.

The coronary sinus uric acid concentrations significantly increased from 121 ± 23 at 5 sec to 169 ± 23 µmol/L at 90 sec of reperfusion, respectively. Its release rates showed a biphasic (at first negative and then positive) phenomenon.

The quantitative changes of coronary lactate net release rates, although increased significantly, were by far lower in comparing to adenosine (3-fold versus 6.5-fold).

**Discussion and conclusion:** ATP degradation during ischemia leads to a concomitant rise in tissue purine catabolites. The quantitative changes of cardiac adenosine were by far much more sensitive in comparing to lactate, although the time related changes of lactate were similar to adenosine. It definitely demonstrated that the ratio of ATP production to ATP utilization is more sensitive to disturbances in tissue oxygenation than the rate of anaerobic glycolysis. Furthermore, It strongly suggests that the degradation of ATP exceeded its production during CABG surgery, although cold cardioplegic solution is used for cardiac protection.

The changes in concentrations difference between the arterial and pulmonary arterial adenosine (A-Pa ado) ) reflect the clearance function of pulmonary endothelial cells for adenosine under physiologic conditions.

The negative net release of uric acid during early reperfusion indicated the consumption of uric acid by the human heart. This phenomenon is most likely explained by chemical reaction of uric acid with hydroxyl radicals and HOCL[ radical scavenger function].

From the present study the following conclusions can be reached: a. Cardiac adenosine increased significantly in systemic and especially in coronary sinus blood samples during CPB and reperfusion period. Adenosine is much more sensitive in contrast to lactate to predict myocardial ischemia. The rank order of sensitivity is: adenosine > hypoxanthine > lactate. b. During CPB and early period of reperfusion the physiologic clearance function of the pulmonary endothelium for adenosine is decreased. c. Despite sufficient cardioplegic arrest, substantial amounts of energy rich compounds (15%) are lost during reperfusion, which may contribute to post-operative heart dysfunction. d. During early period of reperfusion the uric acid is consumed by the human heart. Which may suggest the chemical reaction of uric acid with hydroxyl radicals and HOCL ( radical scavenger function ).