# Risk factors for nonocclusive mesenteric ischemia after elective cardiac surgery

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**Objective:** Nonocclusive mesenteric ischemia (NOMI) may occur after cardiopulmonary bypass. It is crucial to early identify patients who are at risk of developing this complication. The aim of this prospective study was to evaluate perioperative risk factors in a large cohort of patients undergoing elective cardiac surgery.

**Methods:** From January 1, 2010, to March 31, 2011, all patients scheduled for elective cardiac surgery were screened for participation in this trial. If NOMI was suspected, arterial angiography was performed. NOMI and non-NOMI patients were compared with respect to all variables assessed in this study. Additionally, odds ratios were calculated. Linear discriminant analyses as well as logistic regression analyses were performed to develop a model that identifies patients at risk for developing NOMI.

**Results:** Eight hundred sixty-five patients were included in the study, of whom 78 developed NOMI. Among preoperative parameters, renal insufficiency, diuretic therapy, and age >70 years showed the highest odds ratios for postoperative NOMI. The highest odds ratios for development of NOMI were observed with postoperative variables. In particular, the need for intra-aortic balloon pump support and serum lactate concentrations >5 mmol/L proved to be serious risk factors. Using a linear discriminant analysis with 7 variables, 92.3% of patients were correctly classified (sensitivity 76.9%, specificity 93.8%).

**Conclusions:** A high index of suspicion for NOMI in patients with the above-mentioned risk factors may decrease the diagnostic and therapeutic delay. To identify at-risk patients the developed risk equation is a useful tool with a high specificity. (J Thorac Cardiovasc Surg 2013;145:1603-10)

Non-occlusive mesenteric ischemia (NOMI) is a rare but serious complication after cardiac surgery. NOMI was first described by Ende in 1958[1] as summarizing all forms of mesenteric ischemia without occlusion of the mesenteric arteries. NOMI has been generally defined as ''intestinal gangrene in the presence of a patent arterial tree.''[2] Although incidence rates around 1% have been reported, mortality is up to 90%.[3,4]

The exact pathophysiology of NOMI is currently not fully understood; it is assumed that the key mechanism is an extreme reduction or maldistribution of splanchnic blood flow. Intestinal ischemia results in compromised integrity of the mucosal layer with bacterial translocation, bacteremia, and the development of multiorgan failure.[3]

The clinical signs of NOMI—oliguria, increased serum lactate levels, decreased oxygenation, or hypotension—are unspecific. The same is true for abdominal pain, which in addition may be suppressed by analgosedation.[5,6]

Angiography is currently the only means of establishing the diagnosis; in addition it allows for intra-arterial application of vasodilators as the specific treatment. Angiography, however, is an invasive procedure that cannot be applied too liberally. In addition, it must be instituted early enough to be able to correct the vascular pathology. To minimize morbidity and mortality due to NOMI, it is thus crucial to identify patients who are at risk of developing this complication.[7]

A variety of risk factors have been proposed on the basis of retrospective investigations of heterogeneous patient cohorts. Among others, advanced age, renal failure, and different forms of shock as well as the use of an intra-aortic balloon pump (IABP) have been found to be associated with NOMI.[3,4,7] At this time there is no prospective identification of risk factors for NOMI.

Therefore, aim of this prospective study was to identify perioperative risk factors for NOMI in a large cohort of patients undergoing elective cardiac surgery.

## METHODS

The study was designed as a prospective cohort study and approved by the local ethics committee (Landesärztekammer des Saarlandes; ID: 199/09). From January 1, 2010, to March 31, 2011, all patients scheduled for

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**Abbreviations and Acronyms**
CABG = coronary artery bypass graft
IABP = intra-aortic balloon pump
NOMI = nonocclusive mesenteric ischemia

cardiac surgery at our institution were screened for participation in this trial. The inclusion criterion was elective cardiac surgery with cardiopulmonary bypass. Exclusion criteria were age <18 years, refusal to participate, planned off-pump surgery, urgent cardiac surgery, hemodynamic instability with emergency indication for cardiac surgery, or insufficient knowledge of the German language. Written informed consent was obtained from all patients meeting the above-mentioned criteria. The patients' demographic and perioperative data were entered in a computerized data bank in addition to the medical record chart (see Appendix 1).

### Radiographic Analysis

If NOMI was suspected arterial angiography was performed. The decision to perform angiography was based on the presence of at least 2 of 4 possible clinical indicators: new onset of oliguria (urine output < 0.5 mL/kg/hour for at least 6 hours) or anuria, abdominal distention with decreased or absent bowel sounds, serum lactate levels >5.0 mmol/L or metabolic acidosis (base excess <−5 mmol/L). In accordance to the definition of cardiogenic shock,[8] angiography was only performed in patients with a systolic blood pressure >90 mm Hg, and a cardiac index >1.8 L/minute/$m^2$.

The examinations were performed on an undercouch tube/overcouch detector angiography unit (Axiom Artis, Siemens Medical Solutions, Forchheim, Germany) with a maximum field of view of 40 cm.

In all cases the common femoral artery was accessed and a 6F sheath was inserted. The superior mesenteric artery was intubated with a 4F catheter (Cordis, Johnson & Johnson Medical Products GmbH, Vienna, Austria) with a cobra tip configuration and a digital subtraction angiography was obtained by automatic contrast medium injection (contrast medium: Imeron 300, Bracco, Milan, Italy).

All images were assessed by an experienced radiologist and an intensivist on a consensus basis. In accordance with our previously published scoring system,[9] NOMI was diagnosed whenever the total score was more than 1 (Table 1).

### Statistics

Data analysis was performed using SPSS Statistics version 19 (IBM, Ehningen, Germany). As a first step, patients with and without NOMI as confirmed by angiography were compared with respect to all variables assessed in this study (see Appendix 1). For categorical variables, $\chi^2$ tests were performed. For continuous variables the differences in manifestation (expressed as mean ± standard deviation) between NOMI and non-NOMI patients were compared with Student $t$ tests (Welch's $t$ tests in case of inhomogeneous variance). As a second step, odds ratios were calculated for all categorical dichotomized variables (with 95% confidence intervals) to describe the risk of developing NOMI.

Previous risk analyses only pointed toward differences between NOMI and non-NOMI patients regarding several variables. These analyses, however, did not exceed the description of the differences. Therefore, in a third step, linear discriminant analyses as well as logistic regression analyses were performed to develop a model that separates patients at high risk for developing NOMI from patients at low risk. To derive a medically sensitive predictive model, we stepwise excluded variables with low predictive values: After exclusion of the variable with the lowest predictive value, both linear discriminant and logistic regression analysis were calculated again to see how the coefficient loadings changed. Subsequently, the variable with the lowest predictive value by now was excluded, and analyses were iterated until the final equation was found. In addition, we partially reincluded several variables to compare different possible predictive models. This was done when variables had been excluded due to statistical reasons, but were previously reported to influence NOMI.

## RESULTS

During the study period, 1163 adult patients underwent elective cardiac surgery with extracorporeal circulation. Because 298 patients refused participation in the study the final study population consisted of 865 individuals (74%). Angiography was performed in 88 patients. Of these, 78 patients (9% of the total cohort) had the typical angiographic signs of NOMI in the absence of cardiogenic shock. Ten additional patients underwent angiography based on clinical suspicion; their findings were unremarkable. At the time of angiography systolic blood pressure was 120 ± 15 mm Hg, cardiac index was 2.7 ± 0.3 L/minute/$m^2$, and central venous saturation was 69.1% ± 1.2%. Relevant outcome data are shown in Table 2.

Patients with NOMI differed in many respects from patients without NOMI (Table 3). Among preoperative parameters, renal insufficiency, diuretic therapy, and age >70 years showed the highest odds ratios for postoperative NOMI.

Intraoperative risk factors with clearly increased odds ratios for postoperative NOMI were duration of operation >240 minutes and cardiopulmonary bypass time >100 minutes.

The highest odds ratios for development of NOMI were observed with postoperative variables. In particular, the need for IABP support, levosimendan therapy, transfusion of >1 unit packed red blood cells, and re-exploration for bleeding proved to be serious risk factors. In addition, serum lactate concentrations >5 mmol/L and norepinephrine support >0.1 μg/kg/minute were associated with a clearly increased risk to develop NOMI (Table 4).

Among the calculated models, the best classification regarding medical sensitivity and practice orientation was obtained by linear discriminant analysis. The final model included 7 variables (see below; for standardized canonical coefficients see Appendix 2). The discriminant function was highly significant (Wilks' $\Lambda$, 0.59; $\chi^2_7$, 449.41; $P < .001$). It was calculated with the following equation:

$$\begin{aligned} d = {} & 3.85 \times \text{postoperative IABP support } (0 = \text{no}; 1 = \text{yes}) \\ & + 1.91 \times \text{re} - \text{exploration for bleeding } (0 = \text{no}; 1 = \text{yes}) \\ & + 1.86 \times \text{postoperative need for more than 1 unit PRBC} \\ & (0 = \text{no}; 1 = \text{yes}) \\ & + 1.52 \times \text{postoperative serum lactate level} > 5 \text{ mmol/l} \\ & (0 = \text{no}; 1 = \text{yes}) \end{aligned}$$



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