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Early and Delayed Myocardial Infarction after Abdominal Aortic Surgery

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Background: **Although postoperative myocardial infarction (PMI) after vascular surgery has been described to be associated with prolonged ischemia, its exact pathophysiology remains unclear.**

Methods: **The authors used intense cardiac troponin I (cTnI) surveillance after abdominal aortic surgery in 1,136 consecutive patients to better evaluate the incidence and timing of PMI (cTnI ≥ 1.5 ng/ml) or myocardial damage (abnormal cTnI < 1.5 ng/ml).**

Results: **Abnormal cTnI concentrations was noted in 163 patients (14%), of which 106 (9%) had myocardial damage and 57 (5%) had PMI. In 34 patients (3%), PMI was preceded by a prolonged (> 24 h) period of increased cTnI (delayed PMI), and in 21 patients (2%), the increase in cTnI lasted less than 24 h (early PMI). The mean times from end of surgery to PMI were 37 ± 22 and 74 ± 39 h in the early PMI and delayed PMI groups, respectively ($P < 0.001$). The mean time between the first abnormal cTnI and PMI in the delayed PMI group was 54 ± 35 h, during which the cTnI profiles of the myocardial damage and delayed PMI groups were identical. In-hospital mortality rates were 24, 21, 7, and 3% for the early PMI, delayed PMI, myocardial damage, and normal groups, respectively.**

Conclusions: **Intense postoperative cTnI surveillance revealed two types of PMI according to time of appearance and rate of increase in cTnI. The identification of early and delayed PMI may be suggestive of different pathophysiologic mechanisms. Abnormal but low postoperative cTnI is associated with increased mortality and may lead to delayed PMI.**

THE understanding of the pathophysiology, definition, and identification of acute cardiac events is constantly improving. This is mainly due to development of assays of biomarkers that have led to a better characterization of these processes and to a better prediction of prognosis. Specifically, biomarkers such as cardiac troponin I (cTnI) have greatly enhanced our ability to identify and quantify myocardial damage (MD) in the perioperative period.[1–6] However, in spite of our improved ability to detect postoperative myocardial infarction (PMI) and to assess its impact on the outcome, the exact pathophysiology of PMI has yet to be elucidated. We still do not know whether PMI is due mostly to sudden development of a thrombotic process associated with vulnerable plaque rupture, as is the case in most nonsurgical myocardial infarction, or whether it is due to the cumulative deleterious effects on myocardial oxygenation of several factors that are present after major surgery, such as increased thrombogenicity,[7] high concentrations of circulating tissue factor, and sympathetic overactivity.[2] Does PMI occur more often as a result of sudden coronary artery occlusion followed by massive necrosis, or is it mostly due to the cumulative effects of repeated or prolonged ischemic episodes, which by themselves may not cause extensive MD, as has been suggested previously?[8,9] The answers to these questions may have both pathophysiologic and therapeutic implications that may potentially lead to the reduction of the still considerable cardiac morbidity and mortality after major vascular surgery.[10–12]

Therefore, we have attempted to better evaluate the true incidence and timing of PMI and, in particular, how often it is preceded by prolonged low cTnI concentrations, by using intense surveillance of cTnI concentrations in a large cohort of consecutive patients undergoing abdominal aortic surgery.

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Materials and Methods

Since September 1995, we have used an intensive cTnI surveillance policy in all patients undergoing infrarenal aortic surgery, to better evaluate the incidence and better understand the pathophysiology of postoperative MD. All postoperative cTnI data are included in the Pitié-Salpêtrière Vascular Surgery Registry, which is a comprehensive, prospectively recorded database describing clinical and surgical characteristics of all patients undergoing aortic surgery at our institution. A systematic audit by one of the authors (M. B.) constantly verifies the accuracy of the coded data. All patients undergoing aortic surgery have been preoperatively screened in accordance with the recommendations proposed by the American Heart Association/American Col-

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lege of Cardiology Task Force.[13,14] This study was approved by our institutional review board (Comité Consultatif de Protection des Personnes se Prêtant à la Recherche Médicale Pitié-Salpêtrière, Paris, France). Since the study data were collected, although care of patients conformed to standard procedures currently used in our institution, authorization was granted to waive informed consent for the study.

Postoperatively, cTnI was measured on arrival to the intensive care unit (time 0); 6, 12, and 24 h later; and every 24 h thereafter for 3 days. When an abnormal concentration of cTnI was observed, the measurement was repeated 12 h later. cTnI was measured by an immunoenzymofluorometric assay on a Stratus autoanalyser (Dade-Behring, Paris La Défense, France), with values above 0.5 ng/ml being considered abnormal in our institution from September 1995 to November 1999, and values above 0.2 ng/ml being considered abnormal from November 1999 until today. PMI was defined as a cTnI concentration of at least 1.5 ng/ml, as recommended by a recent consensus conference for epidemiologic and clinical research studies.[15] Two physicians classified each patient according to the pattern of cTnI measurements. In the case of a disagreement, a third physician was consulted.

Patients who underwent repeated surgery or had a major septic event postoperatively were excluded from the study. The overall amount of released cTnI ($ng \cdot ml^{-1} \cdot h^{-1}$) was calculated as the area under the cTnI concentration curve by the use of a curve-fitting application that generated a series of rectangles between consecutive points on the curve, with the overall area under the curve being the sum of the areas of these rectangles. To enable us to compare the duration of hospitalization in different groups while taking into account the mortality rates, we calculated the number of hospital-free days within 1 month after surgery, with all dead patients being given a score of 0 hospital-free days. In-hospital mortality was defined as all-cause mortality before hospital discharge.

Statistical Analysis

Data are expressed as mean ± SD, median, and interquartile for nongaussian variables (*e.g.*, duration, number of hospital-free days), or number and percentage with 95% confidence interval (CI). In the analysis of baseline characteristics, comparison of two proportions was performed with use of the chi-square test or Fischer exact test where appropriate, comparison of means was performed with use of the Student *t* test, and comparison of medians was performed with use of the Mann–Whitney and Kruskal–Wallis tests. Comparison of several means was performed by one-way analysis of variance. Significance was set at the 0.05 level, with all *P* values being two-tailed. The relation between cTnI concentration and short-term mortality was assessed by logistic stepwise regression. We applied the clinical risk model of Lee *et al.*[11] and collapsed the clinical risk assessment into one index variable. To compose the Lee risk index,[11] 1 point is assigned to each of the following characteristics: high-risk type of surgery, known ischemic heart disease, a history of congestive heart failure, a history of cerebrovascular disease, diabetes mellitus, and renal failure. Subsequently, the prognostic value of this risk index and the additional and additive prognostic value of age and postoperative cTnI concentration were analyzed by logistic regression analyses. Calibration of the model was assessed using Hosmer-Lemeshow statistics ($P > 0.05$ for no significant difference between predictive model and observed data). All analyses were performed using SPSS 11.5 (Chicago, IL).

Results

The data of 1,152 consecutive patients, who underwent abdominal infrarenal aortic surgery from September 1995 to November 2002, were included in the study. Sixteen patients who had an abnormal postoperative increase of cTnI were not included in the final analysis because of a need for repeated surgery (n = 7) or a major septic event (n = 9). All of these patients had increased cTnI concentrations, and 9 of them had at least one cTnI measurement above 1.5 ng/ml.

Four different patterns of postoperative cTnI measurements led us to define four groups of patients (table 1). Out of the study population of 1,136 patients, 204 patients (18%) had one missing cTnI value, and 57 patients (5%) had two missing values. Patients who had cTnI values within the normal range were allocated to the no-MD group. In the case of at least one abnormal cTnI value, patients were classified as having MD or one of the two types of PMI, according to the level of the abnormal cTnI value and its pattern. Despite the occurrence of some missing values, as mentioned above, all patients except two (see below) could be allocated into one of the four groups using the other cTnI values

Of the final study population that included 1,136 patients, 163 patients (14%) had at least one abnormal cTnI concentration. Of these patients, cTnI concentrations were always less than 1.5 ng/ml in 106 patients (10%) (MD group) and 1.5 ng/ml or greater in 57 patients (5%) who were considered to have PMI. Patients with PMI included 34 patients (3%) in the delayed PMI (DPMI) group, 21 patients (2%) in the early PMI (EPMI) group, and 2 patients in whom the cTnI profile was incomplete and precluded the definition of either EPMI or DPMI. The main preoperative clinical characteristics of the four groups of patients are summarized in table 2. History of previous myocardial infarction was significantly more frequent in the EPMI group only (table 2). Intraoperative blood loss for the whole patient population was 1,220 ±

Table 1. Definition of Groups According to Cardiac Troponin I Profile

Group	cTnI Pattern
No myocardial damage	No abnormal cTnI values during the first 3 postoperative days
Myocardial damage	Patients with abnormal values of cTnI that have not exceeded at any time a postoperative myocardial infarction threshold value of 1.5 ng/ml
Early postoperative myocardial infarction	Patients in whom the cTnI concentration exceeded the 1.5-ng/ml threshold and in whom the cTnI increase from normal or first abnormal value to the threshold value lasted 24 h or less
Delayed postoperative myocardial infarction	Patients in whom the cTnI concentration exceeded the 1.5-ng/ml threshold and in whom the cTnI increase from normal or first abnormal to the threshold value took longer than 24 h and included at least two abnormal values that were lower than 1.5 ng/ml

cTnI = cardiac troponin I.

320 ml, and aortic cross clamp lasted between 20 and 50 min.

The mean time from end of surgery to the detection of both PMI threshold and peak cTnI concentrations was significantly longer in the DPMI group compared with the EPMI group (fig. 1). The mean times to detection of threshold PMI cTnI concentrations were 37 ± 22 h in the EPMI group and 74 ± 39 h in the DPMI group ($P < 0.001$). The mean times to detection of peak cTnI concentration were 51 ± 30 and 92 ± 34 h in the EPMI and DPMI groups, respectively ($P < 0.001$). However, the mean times to the detection of the first abnormal cTnI concentration were similar in the two groups (29 ± 23 *vs.* 20 ± 20 h in the EPMI and DPMI groups, respectively) and in the MD group, as well (29 ± 18 h) (fig. 1).

In the EPMI group, PMI occurred in 10 patients (48%) by 24 h and in 18 patients (86%) by 48 h postoperatively (fig. 1). In the DPMI group, only 17 patients (50%) experienced PMI within the first 48 h, and only 10% experienced PMI on the fifth and sixth postoperative days (fig. 1). Abnormal cTnI concentrations were present in only 27% of all patients with PMI at 6 h postoperatively and in 93% by 48 h. The positive predictive value of an abnormal cTnI value for the development of PMI was 47% at 6 h and 36% at 48 h (table 3), implying that the earlier one has abnormal cTnI values, the higher the chance is that one already has or will have PMI. The negative predictive value of abnormal cTnI concentrations for PMI was 99.6% at 48 h, meaning that if by that time cTnI was normal, the chances of development of PMI were approximately 0.4% (95% CI, 0.2–0.6%; table 3)

Although the times to PMI in the DPMI and EPMI groups were significantly different, the areas under the cTnI concentration curves of both groups were similar (502 ± 600 *vs.* 574 ± 673 $ng \cdot ml^{-1} \cdot h^{-1}$) and significantly higher than that of the MD group (32 ± 78 $ng \cdot ml^{-1} \cdot h^{-1}$; $P < 0.001$).

Table 2. Main Clinical Characteristics of the Four Groups of Patients

	No-MD Group (n = 973)	MD Group (n = 106)	DPMI Group (n = 34)	EPMI Group (n = 21)
Age, yr	67 ± 11	68 ± 11	70 ± 11	70 ± 10
Male	875 (90)	90 (85)	33 (97)	19 (90)
Female	98 (10)	16 (15)	1 (3)	2 (10)
Coronary artery disease	339 (35)	45 (42)	19 (56)*	12 (57)*
Previous myocardial infarction	164 (17)	26 (24)	7 (21)	9 (43)*
Previous coronary revascularisation	160 (16)	19 (18)	6 (18)	7 (33)*
Previous CABG	50 (5)	3 (3)	0 (0)	1 (5)
Previous PCI	110 (11)	16 (15)	6 (18)	6 (29)
Hypertension	523 (54)	63 (59)	24 (71)	17 (81)
β Blockers	263 (27)	30 (28)	13 (38)	9 (43)
Angiotensin-converting enzyme inhibitors	250 (26)	26 (24)	11 (32)	9 (43)
Chronic obstructive pulmonary disease	391 (40)	45 (42)	13 (38)	7 (33)
Diabetes mellitus	83 (8)	6 (6)	2 (6)	1 (5)
Chronic renal failure	156 (16)	16 (15)	6 (18)	5 (24)
Abdominal aortic aneurysm	675 (69)	71 (67)	22 (65)	16 (76)
Lee Risk Score	1.6 ± 0.8	1.7 ± 0.7	1.9 ± 0.8	2.0 ± 0.7
1	543 (56)	50 (47)	9 (27)	5 (25)
2	306 (31)	40 (39)	21 (61)	13 (60)
≥ 3	124 (13)	15 (14)	4 (12)	3 (15)

Data are expressed as mean ± SD or number of patients (%).

* $P < 0.05$ *vs.* no-MD group.

CABG = coronary artery bypass graft; DPMI = delayed postoperative myocardial infarction; EPMI = early postoperative myocardial infarction (see table 1 for definitions); MD = myocardial damage; no MD = no abnormal troponin Ic values; PCI = percutaneous coronary intervention.

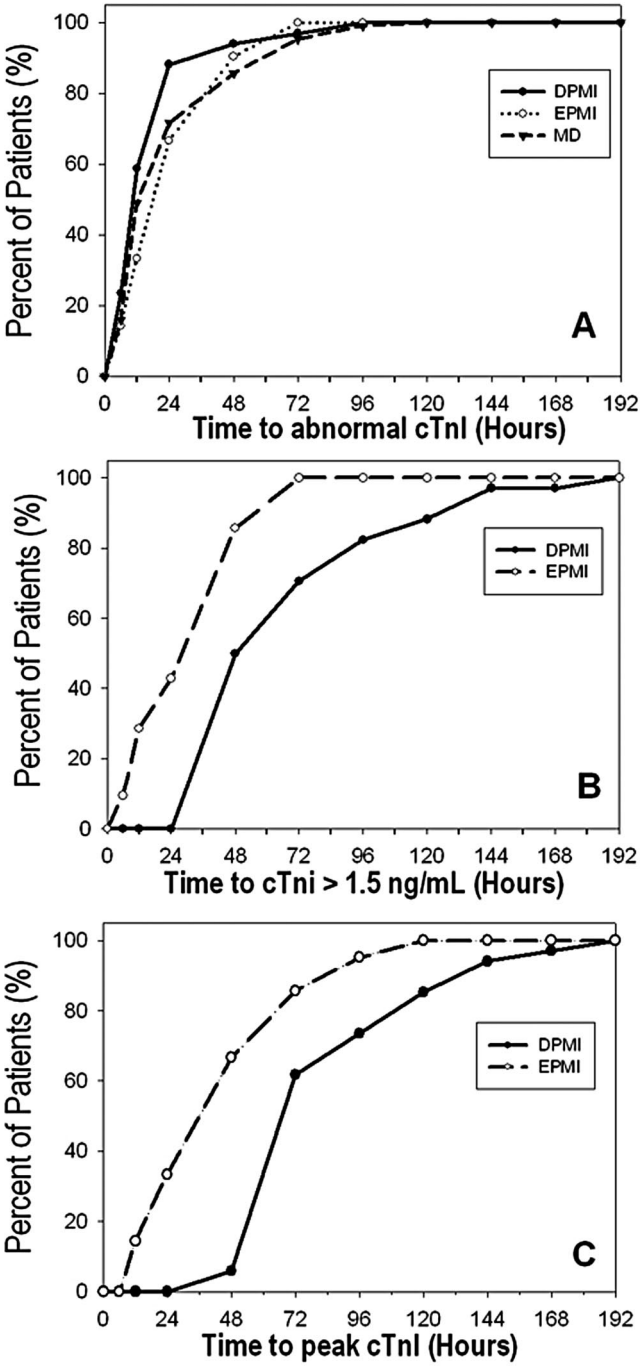

Fig. 1. Cardiac troponin I (cTnI) time profiles since arrival at the intensive care unit in the early (EPMI) or delayed (DPMI) postoperative myocardial infarction and myocardial damage (MD) groups. (*A*) Time to detection of first abnormal cTnI value. (*B*) Time to postoperative myocardial infraction (cTnI value ≥ 1.5 ng/ml). (*C*) Time to peak cTnI concentration.

In the DPMI group, the mean time between the first abnormal cTnI value and the development of PMI was 54 ± 35 h. During this period, the cTnI profiles of the MD and DPMI groups were comparable, as can be seen from the representative cTnI concentration curves of two patients from the MD and DPMI groups (fig. 2).

Global in-hospital mortality for the whole patient population was 4%. Mortality rates in the EPMI (24%; 95% CI, 8–47%) and DPMI (21%; 95% CI, 9–38%) groups were not different. Mortality in the PMI group (22%; 95% CI, 12–35%) was significantly higher than that of the MD group (7%; 95% CI, 2–12%), which in turn was significantly higher than the mortality of patients with normal cTnI concentrations (3%; 95% CI, 2–4%) (fig. 3). Increased postoperative cTnI, even at a low level, was an independent predictor of increased in-hospital mortality (table 4) and was associated with a significant decrease in the number of postoperative hospital-free days within 1 month after surgery (fig. 3)

Table 3. Predictive Value of Abnormal Troponin Ic Concentrations of Postoperative Myocardial Infarction over Time

Time,* h	Sensitivity, %	Specificity, %	PPV, %	NPV, %
6	27	98	47	96
12	60	95	39	98
24	80	93	37	99
48	93	91	36	99
72	98	91	35	99
96	100	90	34	100

* Time from end of surgery.

NPV = negative predictive value; PPV = positive predictive value.

Discussion

The postoperative cTnI profiles of our large group of consecutive patients undergoing aortic surgery suggest that there are two types of PMI that are different in their timing and biomarker pattern. EPMI occurs in the early

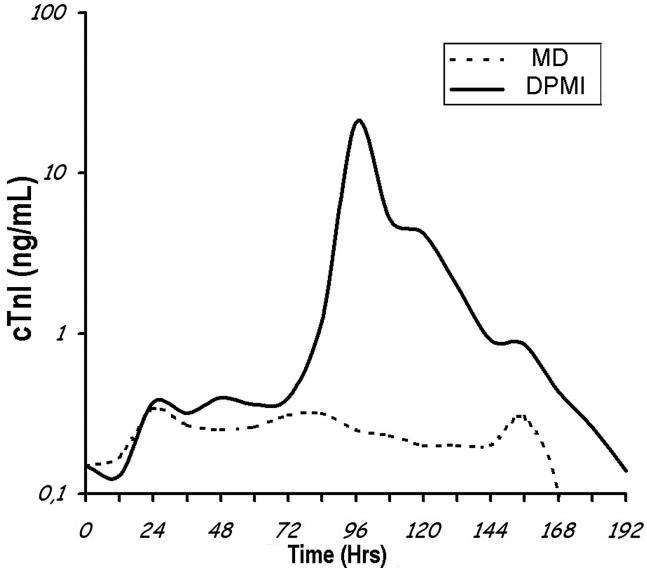

Fig. 2. Cardiac troponin I (cTnI) profiles over time of two representative patients with myocardial damage (MD) or delayed postoperative myocardial infarction (DPMI). Note that during the period of subinfarction MD in the DPMI patient, the cTnI profile is similar to that of the patient with MD only. Log scale is used for cTnI values.

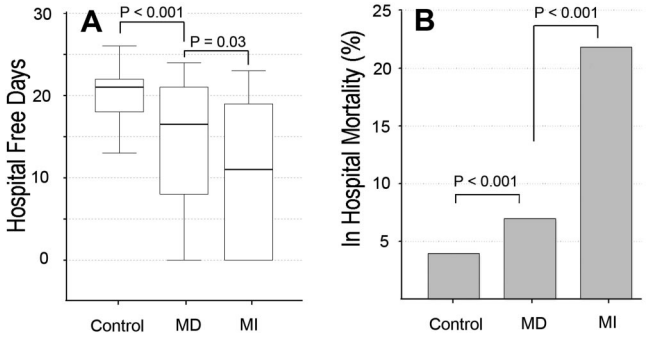

Fig. 3. (*A*) Number of postoperative hospital free days within 1 month after surgery in normal cardiac troponin I, myocardial damage (MD), and postoperative myocardial infarction (MI) groups. (*B*) In-hospital mortality of the postoperative MI, MD, and normal cardiac troponin I (control) groups.

postoperative period and is not preceded by subinfarction MD, whereas DPMI occurs later and is preceded by a long period (> 24 h) of MD in which cTnI values are increased. Because these two distinct PMI profiles were identified in a large population with an overall incidence of PMI similar to that previously reported,[1,10,12] we believe that our findings may have a significant clinical relevance because they allow a better understanding of the pathophysiology of PMI. In addition, these findings highlight the significance of the presence of low cTnI values after major vascular surgery.

Approximately 60% of the patients who had PMI had their infarction preceded by a prolonged period of MD (DPMI group). This delayed pattern of PMI is consistent with previous observations by Mangano *et al.*,[16] in which a clear association has been demonstrated between postoperative ischemia and PMI. Landesberg *et al.*[9] have later shown that there is a close correlation between the duration of postoperative ischemia, as reflected by the electrocardiogram, and MD reflected by cTnI concentrations. These authors have postulated that prolonged ischemia, in the presence of severe but stable coronary artery disease, may be a causative factor for PMI, rather than acute coronary occlusion.[9] The causative role of prolonged ischemia in the development of PMI has been previously postulated as well.[8]

However, our findings do suggest that, in addition to the well-recognized entity of DPMI, there is another PMI entity, namely EPMI, which may have been hitherto unrecognized in the postoperative setting. EPMI occurs quite early in the postoperative period, is not preceded by prolonged MD, and is associated with a sudden increase in cTnI. Therefore, the cTnI profile of EPMI resembles that of acute nonsurgical myocardial infarction and is most probably due to acute coronary occlusion resulting from plaque hemorrhage, rupture, and thrombus formation, as has been observed in autopsies of fatal PMI.[17]

We may therefore postulate that the mechanism underlying EPMI is that of the "vulnerable plaque," which includes all thrombosis-prone plaques and plaques prone to undergo rapid progression.[18,19] The postoperative inflammatory syndrome may greatly contribute to this process because increased C-reactive protein plasma concentrations have been shown to provoke plaque rupture.[20] Although the vulnerability of the plaque is defined by its structural and functional properties, patient-related factors may play a role in the outcome that will result from its disruption.[18,19] In this context, it is interesting to note that the EPMI population in our study had a significantly higher incidence of previous myocardial infarction compared with the patients who experienced DPMI, reflecting a possible higher patient-vulnerability.[21] The cTnI pattern of DPMI is more similar to that observed during prolonged unstable angina culminating in myocardial infarction. This pattern has been recently defined as unstable angina class IIIA, which develops in the presence of extracardiac conditions that intensify myocardial ischemia (secondary unstable angina).[22]

Although the pathophysiology of EPMI and DPMI may be different, we have found the extent of MD and the associated mortality to be the same for the two types of PMI, although PMI-related mortality was significantly higher than that of the MD group (MD not reaching the cTnI threshold of PMI). In this regard, postoperative abnormal sub-PMI threshold cTnI concentrations may be considered as a marker of unstable coronary artery disease, explaining their association with lower survival compared with patients who had normal cTnI values (no-MD group). These findings, which are in accord with previous reports in which mortality after vascular surgery was found to correlate with cTnI concentrations,[1–3] demonstrate that even postoperative abnormal although sub-PMI threshold cTnI concentrations may worsen outcome.

Although EPMI and DPMI seem to have a similar extent

Table 4. Multivariate Model for the Prediction of In-hospital Mortality by Lee Risk Index, Age, and Postoperative Peak Cardiac Troponin I Concentration

Variables	OR	95% CI for OR		*P* Value
		Lower	Upper	
Postoperative peak cardiac troponin I				
Abnormal and ≥ 1.5 ng/ml	8.1	2.9	22.8	< 0.001
Abnormal and < 1.5 ng/ml	3.9	1.8	8.4	< 0.001
Normal	1.0	—	—	—
Age (per 1-yr increase)	1.05	1.03	1.14	0.003
Lee Risk Index* (per 1-point increase)	2.7	1.6	4.7	0.001

Hosmer-Lemeshow statistic associated with this model is 5.84 ($P = 0.66$; $df = 8$).

* To compose the Lee Risk Index, 1 point was assigned to each of the following characteristics: high-risk type of surgery, known ischemic heart disease, history of congestive heart failure, history of cerebrovascular disease, diabetes mellitus, and renal failure.

CI = confidence interval; OR = odds ratio.

of MD and to carry similar mortalities, the identification of these two different types of PMI may have some therapeutic implications. In patients who are prone to development of PMI, and especially in those who are prone to development of EPMI, prevention might be achieved by better preoperative identification of the vulnerable plaque and by better plaque stabilization, either metabolically (*e.g.*, statins) or by actual coronary stenting. However, the patients who have DPMI do present an additional opportunity for the prevention of PMI during the period of increased biomarkers of myocardial injury. Because this period of subinfarction MD lasts for approximately 60 h, it should be regarded as a "golden period" in which various interventions (*e.g.*, intensive β-blocker therapy, adequate analgesia, correction of anemia) may potentially prevent PMI. Our finding that close to 50% of the patients with abnormal cTnI concentrations at 6 h either have or will have PMI indicates that these patients might get the benefit of optimal monitoring and care until cTnI concentrations normalize. These data complement previous studies in which the majority of ischemic events, including those culminating in PMI, started immediately at the end of surgery[9] or within 12–24 h after surgery.[23,24] The very strong negative predictive value of cTnI suggests that, in the presence of normal cTnI values, the chance of development of PMI is 3.6% at 6 h and only 0.4% after 48 h.

Our study has a few potential shortcomings, of which our definition of PMI is a major one. The introduction of cTnI as a biomarker of MD has dramatically increased our ability to detect even small amounts of damage and is far superior to the use of sophisticated but cumbersome electrocardiogram interpretation. However, the use of such a sensitive biomarker has made MD to be a continuum that still necessitates the definition of discreet cardiac events as well as the redefinition of PMI.[25,26] According to the recent definitions proposed by the American Heart Association, any abnormal increases of cTnI should be considered myocardial infarction.[15] Because higher cTnI concentrations have been repeatedly shown to be associated with worse outcome, it seems practical to define more specific cTnI threshold values for the diagnosis of PMI. The different cutoff levels that were previously proposed as signifying myocardial infarction include 1.5,[2] 2.0,[27,28] 2.5,[29] and 3.1 ng/ml.[1,9] We have chosen to remain with the 1.5-ng/ml cutoff value for cTnI because this value has been well established in the literature,[26] has been used in studies similar to ours, and was shown to be markedly associated with both short- and medium-term outcome after vascular surgery.[1,3]

Another potential shortcoming of our study is the degree by which our own definitions of EPMI and DPMI have contributed to the differences between the two groups. However, the main variable that was used to differentiate between EPMI and DPMI was the duration of the preceding MD as evidenced by abnormal cTnI concentrations. This differentiation is not different than the one used for the definitions of acute myocardial infarction on one hand and unstable angina leading to myocardial infarction on the other.[22] Using this criterion alone has resulted in the separation of all patients with PMI into our two subgroups, with the mean time to reach threshold cTnI values in the DPMI group being 37 h (or twice) longer than that of EPMI patients. This difference is even more significant if one considers the fact that in both DPMI and EPMI, the mean time to the first abnormal cTnI concentration was similar.

Although highly suggestive of the fact that PMI may be caused by two different mechanisms, our study was not designed to explore the specific pathophysiology of PMI, and further studies are necessary to elucidate whether different cTnI profiles are indeed due to different mechanisms of PMI. In addition, caution is advised in interpreting our results to the postoperative period of surgery other than major vascular, because the latter is characterized by a high percentage of patients with coronary artery disease. Although moderately increased cTnI concentrations were reported to be associated with increased mortality and morbidity in surgical intensive care unit patients,[30] flow-limiting coronary artery disease was not found at autopsy or stress echocardiography in the majority of cTnI-positive critically ill patients.[31] It is therefore clear that the prognostic implications of increased cTnI concentrations may be different in other patient groups.[26]

In conclusion, based on intense cTnI surveillance, we have identified, in patients undergoing vascular surgery, two cTnI patterns that correspond to an early and a delayed PMI. Monitoring cTnI in the postoperative period after aortic surgery enables the identification of patients with abnormal but low postoperative cTnI concentrations. This may have an important clinical implication because these low cTnI concentrations are associated with increased mortality and may lead to delayed PMI. In addition, monitoring cTnI concentrations postoperatively may allow the institution of early aggressive intervention to prevent the evolution of PMI during the "golden period" of approximately 2 days before the development of delayed PMI. Further understanding of the mechanisms underlying PMI, as well as its early identification, may contribute to the reduction of the incidence of PMI and its associated morality in the future.

References

1. Landesberg G, Shatz V, Akopnik I, Wolf YG, Mayer M, Berlatzky Y, Weissman C, Mosseri M: Association of cardiac troponin, CK-MB, and postoperative myocardial ischemia with long-term survival after major vascular surgery. J Am Coll Cardiol 2003; 42:1547–54

2. Kim LJ, Martinez EA, Faraday N, Dorman T, Fleisher LA, Perler BA, Williams GM, Chan D, Pronovost PJ: Cardiac troponin I predicts short-term mortality in vascular surgery patients. Circulation 2002; 106:2366–71

3. Godet G, Dumerat M, Baillard C, Ben Ayed S, Bernard MA, Bertrand M,

Kieffer E, Coriat P: Cardiac troponin I is reliable with immediate but not medium-term cardiac complications after abdominal aortic repair. Acta Anaesthesiol Scand 2000; 44:592–7

4. Edouard AR, Felten ML, Hebert JL, Cosson C, Martin L, Benhamou D: Incidence and significance of cardiac troponin I release in severe trauma patients. ANESTHESIOLOGY 2004; 101:1262–8

5. Karpati PC, Rossignol M, Pirot M, Cholley B, Vicaut E, Henry P, Kevorkian JP, Schurando P, Peynet J, Jacob D, Payen D, Mebazaa A: High incidence of myocardial ischemia during postpartum hemorrhage. ANESTHESIOLOGY 2004; 100: 30–6.

6. Riou B: Troponin: Important in severe trauma and a first step in the biological marker revolution. ANESTHESIOLOGY 2004; 101:1259–60

7. Samama CM, Thiry D, Elalamy I, Diaby M, Guillosson JJ, Kieffer E, Coriat P: Perioperative activation of hemostasis in vascular surgery patients. ANESTHESIOLOGY 2001; 94:74–8

8. Kloner RA, Bolli R, Marban E, Reinlib L, Braunwald E: Medical and cellular implications of stunning, hibernation, and preconditioning: an NHLBI workshop. Circulation 1998; 97:1848–67

9. Landesberg G, Mosseri M, Zahger D, Wolf Y, Perouansky M, Anner H, Drenger B, Hasin Y, Berlatzky Y, Weissman C: Myocardial infarction after vascular surgery: The role of prolonged stress-induced, ST depression-type ischemia. J Am Coll Cardiol 2001; 37:1839–45

10. Browner WS, Li J, Mangano DT: In-hospital and long-term mortality in male veterans following noncardiac surgery. Study of Perioperative Ischemia Research Group. JAMA 1992; 268:228–32

11. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, Sugarbaker DJ, Donaldson MC, Poss R, Ho KK, Ludwig LE, Pedan A, Goldman L: Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation 1999; 100:1043–9

12. Sprung J, Abdelmalak B, Gottlieb A, Mayhew C, Hammel J, Levy PJ, O'Hara P, Hertzer NR: Analysis of risk factors for myocardial infarction and cardiac mortality after major vascular surgery. ANESTHESIOLOGY 2000; 93:129–40

13. Eagle KA, Berger PB, Calkins H, Chaitman BR, Ewy GA, Fleischmann KE, Fleisher LA, Froehlich JB, Gusberg RJ, Leppo JA, Ryan T, Schlant RC, Winters WL, Gibbons RJ, Antman EM, Alpert JS, Faxon DP, Fuster V, Gregoratos G, Jacobs AK, Hiratzka LF, Russell RO, Smith SC.: ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery: Executive summary. Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Circulation 2002; 105:1257–67

14. Eagle KA, Brundage BH, Chaitman BR, Ewy GA, Fleisher LA, Hertzer NR, Leppo JA, Ryan T, Schlant RC, Spencer WH, Spittell JA, Twiss RD, Ritchie JL, Cheitlin MD, Gardner TJ, Garson A Jr, Lewis RP, Gibbons RJ, O'Rourke RA, Ryan TJ: Guidelines for perioperative cardiovascular evaluation for noncardiac surgery. Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Committee on Perioperative Cardiovascular Evaluation for Noncardiac Surgery. Circulation 1996; 93:1278–317

15. Luepker RV, Apple FS, Christenson RH, Crow RS, Fortmann SP, Goff D, Goldberg RJ, Hand MM, Jaffe AS, Julian DG, Levy D, Manolio T, Mendis S, Mensah G, Pajak A, Prineas RJ, Reddy KS, Roger VL, Rosamond WD, Shahar E, Sharrett AR, Sorlie P, Tunstall-Pedoe H: Case definitions for acute coronary heart disease in epidemiology and clinical research studies: A statement from the AHA Council on Epidemiology and Prevention; AHA Statistics Committee; World Heart Federation Council on Epidemiology and Prevention; the European Society of Cardiology Working Group on Epidemiology and Prevention; Centers for Disease Control and Prevention; and the National Heart, Lung, and Blood Institute. Circulation 2003; 108:2543–9

16. Mangano DT, Browner WS, Hollenberg M, London MJ, Tubau JF, Tateo IM: Association of perioperative myocardial ischemia with cardiac morbidity and mortality in men undergoing noncardiac surgery. Study of Perioperative Ischemia Research Group. N Engl J Med 1990; 323:1781–8

17. Dawood MM, Gutpa DK, Southern J, Walia A, Atkinson JB, Eagle KA: Pathology of fatal perioperative myocardial infarction: Implications regarding pathophysiology and prevention. Int J Cardiol 1996; 57:37–44

18. Naghavi M, Libby P, Falk E, Casscells SW, Litovsky S, Rumberger J, Badimon JJ, Stefanadis C, Moreno P, Pasterkamp G, Fayad Z, Stone PH, Waxman S, Raggi P, Madjid M, Zarrabi A, Burke A, Yuan C, Fitzgerald PJ, Siscovick DS, de Korte CL, Aikawa M, Airaksinen KE, Assmann G, Becker CR, Chesebro JH, Farb A, Galis ZS, Jackson C, Jang IK, Koenig W, Lodder RA, March K, Demirovic J, Navab M, Priori SG, Rekhter MD, Bahr R, Grundy SM, Mehran R, Colombo A, Boerwinkle E, Ballantyne C, Insull W, Schwartz RS, Vogel R, Serruys PW, Hansson GK, Faxon DP, Kaul S, Drexler H, Greenland P, Muller JE, Virmani R, Ridker PM, Zipes DP, Shah PK, Willerson JT: From vulnerable plaque to vulnerable patient: A call for new definitions and risk assessment strategies: II. Circulation 2003; 108:1772–8

19. Naghavi M, Libby P, Falk E, Casscells SW, Litovsky S, Rumberger J, Badimon JJ, Stefanadis C, Moreno P, Pasterkamp G, Fayad Z, Stone PH, Waxman S, Raggi P, Madjid M, Zarrabi A, Burke A, Yuan C, Fitzgerald PJ, Siscovick DS, de Korte CL, Aikawa M, Juhani Airaksinen KE, Assmann G, Becker CR, Chesebro JH, Farb A, Galis ZS, Jackson C, Jang IK, Koenig W, Lodder RA, March K, Demirovic J, Navab M, Priori SG, Rekhter MD, Bahr R, Grundy SM, Mehran R, Colombo A, Boerwinkle E, Ballantyne C, Insull W Jr, Schwartz RS, Vogel R, Serruys PW, Hansson GK, Faxon DP, Kaul S, Drexler H, Greenland P, Muller JE, Virmani R, Ridker PM, Zipes DP, Shah PK, Willerson JT: From vulnerable plaque to vulnerable patient: A call for new definitions and risk assessment strategies: I. Circulation 2003; 108:1664–72

20. Libby P: Current concepts of the pathogenesis of the acute coronary syndromes. Circulation 2001; 104:365–72

21. Baron JF, Mundler O, Bertrand M, Vicaut E, Barre E, Godet G, Samama CM, Coriat P, Kieffer E, Viars P: Dipyridamole-thallium scintigraphy and gated radionuclide angiography to assess cardiac risk before abdominal aortic surgery. N Engl J Med 1994; 330:663–9

22. Hamm CW, Braunwald E: A classification of unstable angina revisited. Circulation 2000; 102:118–22

23. Badner NH, Knill RL, Brown JE, Novick TV, Gelb AW: Myocardial infarction after noncardiac surgery. ANESTHESIOLOGY 1998; 88:572–8

24. Adams JE III, Sicard GA, Allen BT, Bridwell KH, Lenke LG, Davila-Roman VG, Bodor GS, Ladenson JH, Jaffe AS: Diagnosis of perioperative myocardial infarction with measurement of cardiac troponin I. N Engl J Med 1994; 330: 670–4

25. Jaffe AS, Katus H: Acute coronary syndrome biomarkers: The need for more adequate reporting. Circulation 2004; 110:104–6

26. Jaffe AS: A small step for man, a leap forward for postoperative management. J Am Coll Cardiol 2003; 42:1555–7

27. Luscher MS, Thygesen K, Ravkilde J, Heickendorff L: Applicability of cardiac troponin T and I for early risk stratification in unstable coronary artery disease. TRIM Study Group. Thrombin Inhibition in Myocardial ischemia. Circulation 1997; 96:2578–85

28. Apple FS, Maturen AJ, Mullins RE, Painter PC, Pessin-Minsley MS, Webster RA, Spray Flores J, DeCresce R, Fink DJ, Buckley PM, Marsh J, Ricchiuti V, Christenson RH: Multicenter clinical and analytical evaluation of the AxSYM troponin-I immunoassay to assist in the diagnosis of myocardial infarction. Clin Chem 1999; 45:206–12

29. Pervaiz S, Anderson FP, Lohmann TP, Lawson CJ, Feng YJ, Waskiewicz D, Contois JH, Wu AH: Comparative analysis of cardiac troponin I and creating kinase-MB as markers of acute myocardial infarction. Clin Cardiol 1997; 20: 269–71

30. Relos RP, Hasinoff IK, Beilman GJ: Moderately elevated serum troponin concentrations are associated with increased morbidity and mortality rates in surgical intensive care unit patients. Crit Care Med 2003; 31:2598–603

31. Ammann P, Maggiorini M, Bertel O, Haenseler E, Joller-Jemelka HI, Oechslin E, Minder EI, Rickli H, Fehr T: Troponin as a risk factor for mortality in critically ill patients without acute coronary syndromes. J Am Coll Cardiol 2003; 41:2004–9