

# Quality of Postoperative Care after Major Orthopedic Surgery Is Correlated with Both Long-term Cardiovascular Outcome and Troponin Ic Elevation

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## ABSTRACT

**Background:** The aim of this study performed in patients undergoing major orthopedic surgery was to assess the impact of changes in practice on both the incidence of postoperative myocardial ischemia (PMI) detected by serial measurements of troponin Ic and long-term cardiac outcome.

**Methods:** During a 3-yr period, troponin Ic was measured on the first 3 days after major orthopedic surgery in a multidisciplinary hospital. After 16 months of study, postoperative care was improved. Cardiac death, myocardial infarction, and cardiac failure were considered major adverse cardiac events and were recorded during the hospital stay and the first postoperative year. The incidences of PMI and major adverse cardiac events were used as result indicators for quality of care and compared before (P1) and after (P2) quality enhancement.

**Results:** Three hundred seventy-eight surgical procedures were included (P1, 123; P2, 255). Incidences of PMI and major adverse cardiac events were 8.9 *versus* 3.9% ( $P = 0.04$ ) and 8.1 *versus* 1.9% ( $P = 0.004$ ) for P1 and P2, respectively. Using a multivariate Cox regression analysis adjusted for baseline data, independent factors associated with the occurrence of a major adverse cardiac event were phase P1 (hazard ratio = 4.5; 97.8% confidence interval [CI], 1.1–17.4) and PMI (Hazard ratio = 6.4; 97.8% CI, 1.6–26.4).

**Conclusions:** Our postoperative care policy after major orthopedic surgery strongly correlated with both short-term cardiac outcome (*i.e.*, PMI with troponin Ic release) and long-term cardiac outcome. Thus, in a given surgical population, variation of incidence of troponin Ic elevations could be used as a result indicator for postoperative care policy.

### What We Already Know about This Topic

- ❖ Major orthopedic surgery can be followed by major adverse cardiac events.
- ❖ Interventions to reduce these complications are controversial.

### What This Article Tells Us That Is New

- ❖ In 378 patients receiving major orthopedic surgery, a root cause analysis followed by application of simple changes in postoperative care were associated with a 4-fold reduction in major adverse cardiac events.

POSTOPERATIVE cardiac complications represent a major health burden.<sup>1</sup> Numerous studies indicate that these complications, which occur during the first postoperative days, can harm patients immediately but also months to years later.<sup>1,2</sup> Thus, there is a major need to find the most efficient actions to prevent postoperative myocardial ischemia (PMI) or myocardial infarction. Several studies investigating the impact of single therapeutic interventions on postoperative cardiac outcome have provided conflicting results.<sup>3–6</sup> Moreover, it remains uncertain whether interventions that prevent PMI or myocardial infarction can also decrease intermediate or long-term cardiovascular complications.<sup>7</sup>

In a previous study, we found that an unexpectedly high incidence of myocardial ischemia with TnIc release was strongly correlated with long-term cardiac outcome in a major orthope-

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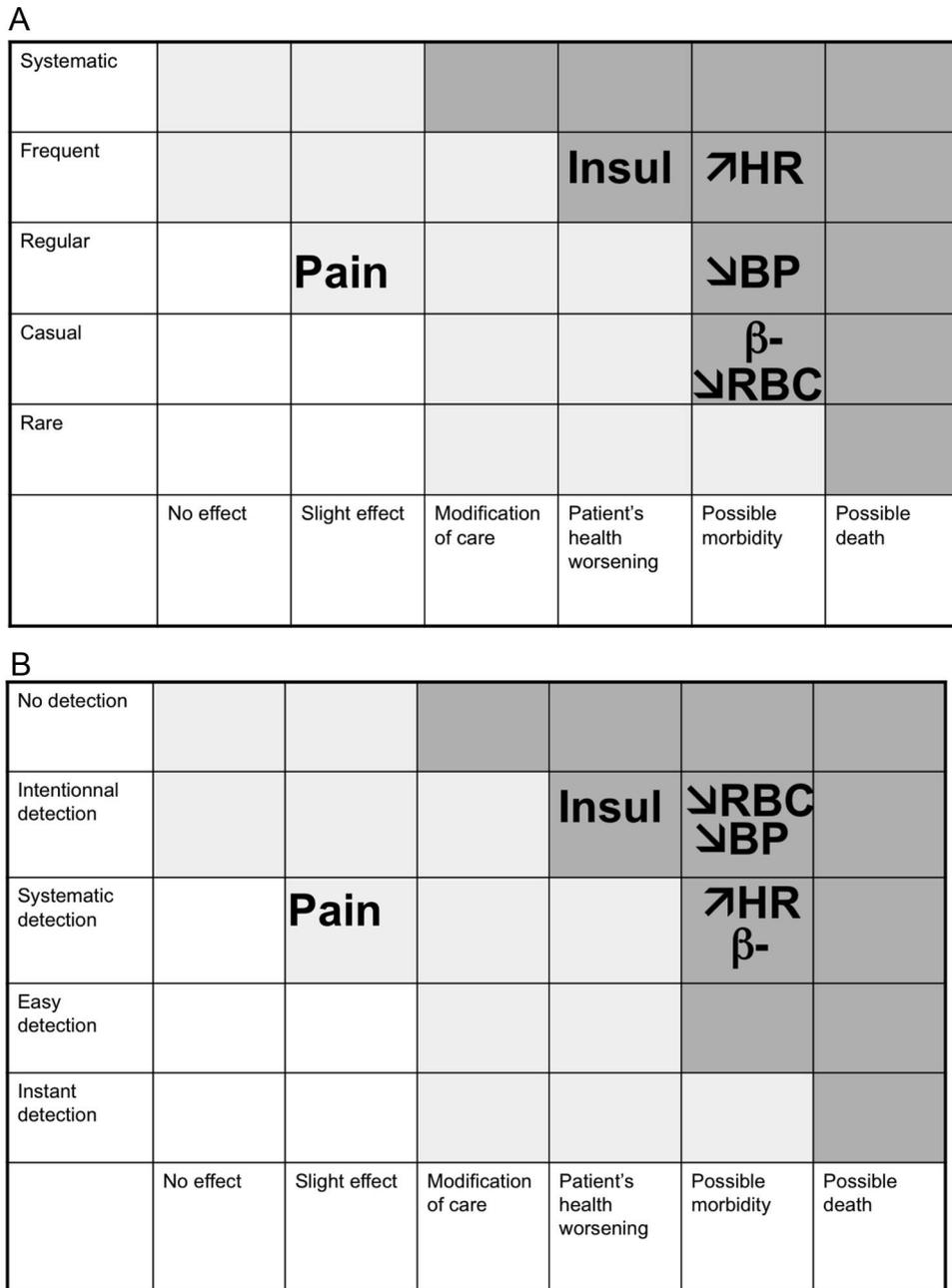
dic surgery population.<sup>8,9</sup> Because single component strategies (*i.e.*,  $\beta$ -adrenergic receptor blockers [ $\beta$ -blockers]) remain of doubtful benefit and because some studies involving a larger scope had shown a positive impact of quality of care on postoperative outcome,<sup>10,11</sup> we postulated that a strategy that would target several key factors would improve the process of postoperative care, reduce perioperative myocardial ischemia, and improve long-term cardiovascular outcome. We chose to use postoperative troponin I<sub>c</sub> (TnI<sub>c</sub>) elevation as a diagnosis tool for myocardial ischemia because it was shown previously to be correlated with long-term cardiac outcome.<sup>12-16</sup> TnI<sub>c</sub> can thus be

used as a marker describing the efficiency of a prevention policy against cardiac complication.

**Materials and Methods**

**Study Design**

We conducted a prospective study of preintervention and postintervention periods at the orthopedic and trauma surgery ward of a 300-bed multidisciplinary academic hospital. From October 2003 to October 2006, after approval from the Local Research Ethics Committee (Percy Military Hos-



**Fig. 1.** (A) This graph describing the correlation between severity and rate of occurrence was used to determine the main failure modes of the postoperative process. (B) This graph describing the correlation between severity and capacity to detect the occurrence of a given sign was used to determine the main failure modes of the postoperative process. ↘BP = hypotension; β- =  $\beta$ -adrenergic receptor blocker withdrawal; ↗HR = tachycardia; Insul = blood glucose disorder; ↘RBC = postoperative anemia.

pital, Clamart, France), which waived the requirement for written informed consent from patients, all patients undergoing scheduled or emergency major orthopedic surgery were prospectively screened for PMI through serial postoperative TnIc measurements during the first 3 postoperative days and at follow-up during the hospital stay and after the first postoperative year.

**Study Population**

Surgical procedures considered major orthopedic surgery were hip fracture surgery, scheduled arthroplasty, and reoperation of arthroplasty. Patients already included during the previous 12 months for another surgical procedure were excluded. All patients had a preoperative anesthetic evaluation several weeks before a scheduled surgical procedure or hours before emergency surgery. In addition to the standard evaluation, each anesthetist asked for specific cardiac tests according to the medical history (e.g., nonexercise stress testing or transthoracic ultrasound), and the time interval before surgery was planned in agreement with surgeons.

Patients were screened according to predefined criteria that included components of the Revised Cardiac Risk Index as defined by Lee *et al.*<sup>17</sup> and the coronary artery disease risk factors as defined by Mangano and colleagues.<sup>18,19</sup>

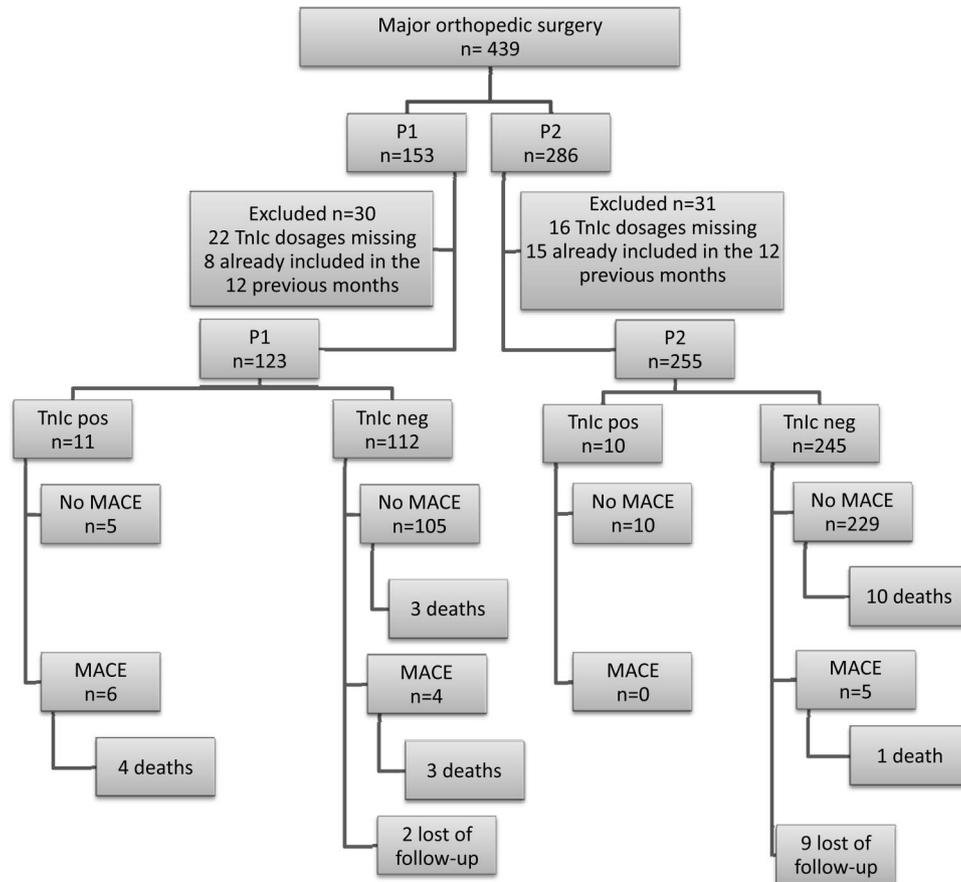
Antiplatelet medications were stopped 10 days before scheduled surgery and replaced by low molecular weight hep-

arin according to recommendations of the French Society of Anaesthesia and Intensive Care<sup>20</sup> All cardiac treatments remained unchanged until surgery, except for angiotensin-converting enzyme inhibitors, which were stopped 2 days before scheduled surgery.<sup>21,22</sup> All cardiac medications were started again on the ward after surgery.

Surgical procedures were performed under general, spinal, or combined anesthesia (epidural plus light general anesthesia). After hip surgery, postoperative analgesia relied on acetaminophen given every 6 h and intravenous morphine administered *via* a patient-controlled analgesia system. After knee surgery, continuous femoral nerve blockade was used instead of patient-controlled analgesia. In the absence of contraindication, 50 mg of ketoprofen every 6 h was added during the first 2 postoperative days.

**Therapeutic Intervention (Quality of Care Improvement)**

The intervention involved a two-step improvement of quality of care through Failure Modes, Effects, and Criticality Analysis (FMECA). FMECA is a methodology used by reliability engineers that is designed to identify potential failure modes for a product or process, to assess the risk associated with those failure modes, and to carry out corrective actions to address the most serious concerns. First, we performed an in-depth analysis of factors possibly implicated in the genesis of PMI.<sup>19,23-29</sup> Thereafter, factors identified were reported



**Fig. 2.** Trial profile. MACE = major adverse cardiac event. TnIc = troponin Ic.

on a worksheet according to their severity, occurrence, and clinical capacity of detection (fig. 1). Areas related to increasing levels of risk were created to determine the main failure modes of the postoperative process. These main failure modes were then represented on the patient's clinical pathway to determine the best opportunity to deal with them. The preoperative and postoperative periods in which useful targeted interventions could be implemented were identified. Postoperative orders were modified to reduce the occurrence of the main failure modes identified by FMECA (*i.e.*, hypoxemia, anemia, hypotension, tachycardia, and hyperglycemia) by agreement among all members of the anesthetic team after several medical meetings. These postoperative orders were thereafter placed in the orthopedic operating rooms and the recovery room and were explained to the orthopedic ward's nursing staff during several meetings. This protocol was also available on the hospital electronic network that holds all the medical protocols at our institution.

The therapeutic interventions in this protocol were deliberately very simple and addressed only basic issues such as hypovolemia, hypoxemia, and hyperglycemia (appendix 1). When the FMECA was completed, the only issue identified that could require a more sophisticated approach was tachycardia and the use of  $\beta$ -blockers. However, because of the scarcity of the data available at the time and because no study had been performed in the orthopedic surgery setting, we decided not to use such a policy. In contrast, it appeared that the critical issues identified on the FMECA could be addressed through simple therapeutic measures if those issues were readily detected. Thus, the main part of the protocol was a close monitoring of vital signs, glycemia, and hemoglobin levels. The need to monitor so closely a surgical population who was perceived as low risk was difficult to understand for the medical and nursing staff. Disclosing the high incidence of PMI before the improvement of postoperative care (P1) was the key evidence needed to obtain adhesion of the team. After the improvement of postoperative care (P2), the evolution of the incidence of TnIc elevation was communicated annually to the team (and all hospital staff) through a poster campaign. At the first analysis after the changes in postoperative care policy, the incidence of PMI had already decreased significantly compared with P1. The second analysis (October 2006) showed the same results, and 1 yr later, the analysis of the patients' follow-up showed a statistically significant difference in long-term cardiac outcome.

**End Points**

The primary end points were the occurrence of a PMI during the first 3 postoperative days and the occurrence of a major adverse cardiac event (MACE) during the year after surgery, as indicated at a 1-yr follow-up. PMI was defined as the elevation of TnIc beyond the reference threshold and MACE was defined as one of the following events: cardiac death, acute coronary syndrome, need for coronary revascularization or cardiac surgery, and congestive heart failure. The secondary endpoint was all-cause death.

**Table 1.** Patient Characteristics and Intraoperative Data

	P1	P2	P Value
Sex ratio (male/female)	54/75	112/134	0.5
Type of surgery			
Scheduled arthroplasties	79 (61)	175 (71)	0.022
Hip fracture	30 (23)	54 (22)	
Reoperations of arthroplasties	20 (15.5)	17 (7)	
Age (yr)	73 (11.8)	72 (13.3)	0.477
Medical history			
Coronary artery disease	15 (12)	30 (13)	0.796
Renal failure	23 (18)	15 (6)	0.0005
Cardiac failure	4 (3)	5 (2)	0.640
History of stroke	7 (5)	14 (6)	0.865
Dyslipidemia	37 (29)	64 (27)	0.663
Diabetes	10 (8)	26 (11)	0.474
Current smoking	11 (9)	22 (9)	0.898
Hypertension	62 (50)	112 (47)	0.616
Revised cardiac risk index			
Class I	93 (72)	159 (67)	0.612
Class II	22 (17)	54 (23)	
Class III	11 (9)	21 (8)	
Class IV	3 (2)	4 (2)	
ASA classification			
1	13 (10)	26 (11)	0.422
2	76 (59)	147 (62)	
3	35 (27)	63 (26)	
4	5 (4)	3 (1)	
Medications			
$\beta$ -blocking agent	27 (21)	43 (18)	0.493
Calcium channel-blocking agent	25 (20)	44 (18)	0.793
Angiotensin II antagonist	9 (7)	24 (10)	0.419
ACE inhibitor	29 (22)	51 (21)	0.8
Nitrates	7 (5)	11 (5)	0.714
Antiplatelet agent	23 (18)	55 (23)	0.260
Type of anesthesia			
General	112	280 (97)	—
Regional	2	5 (1.7)	—
Perioperative blood losses, median ml of erythrocytes ( $\pm$ interquartile range)			
Scheduled arthroplasties	655 ( $\pm$ 316)	612 ( $\pm$ 248)	0.141
Reoperation of arthroplasties	622 ( $\pm$ 364)	644 ( $\pm$ 338)	0.6058*
Hip fracture	425 ( $\pm$ 362)	434 ( $\pm$ 500)	0.843

P values are from *t* test for mean blood losses, from Kruskal-Wallis test for type of surgery, revised cardiac risk index, and ASA status, or from chi-square test.

\* P value from Mann-Whitney *U* test.

ACE = angiotensin-converting enzyme; ASA = American Society of Anesthesiologists;  $\beta$ -blocking =  $\beta$ -adrenergic receptor blocking.

### Data Analysis

Patients' clinical features, type of surgery, myocardial ischemia, and long-term MACE incidences were prospectively recorded, and the two phases of the study were compared (*i.e.*, before [P1] or after [P2] quality enhancement). The quality of postoperative monitoring was measured and compared between P1 and P2 by comparing the use of pulse oximetry, blood pressure monitoring, and glucose monitoring. The quality of postoperative care at P1 and P2 was also measured and compared according to the number of patients receiving oxygen, insulin, or transfusion. In addition, the patients' mean lowest postoperative hemoglobin values in the two phases of the study were compared.

**Measurement.** The TnIc level was measured on the morning of each of the first 3 postoperative days using a commercially available kit (Ortho Vitros ECI; Ortho-Clinical Diagnostics, Raritan, NJ). The upper reference limit (0.08 ng/ml) was specified by the manufacturer to be the 99th percentile concentration of a reference population.<sup>30</sup>

### Follow-up.

**In-hospital.** Data were collected prospectively. Patients were clinically assessed daily by the anesthetist in charge of the orthopedic ward. A standardized form that included evaluation of chest pain and signs of cardiac failure was used to record results of the daily examination.

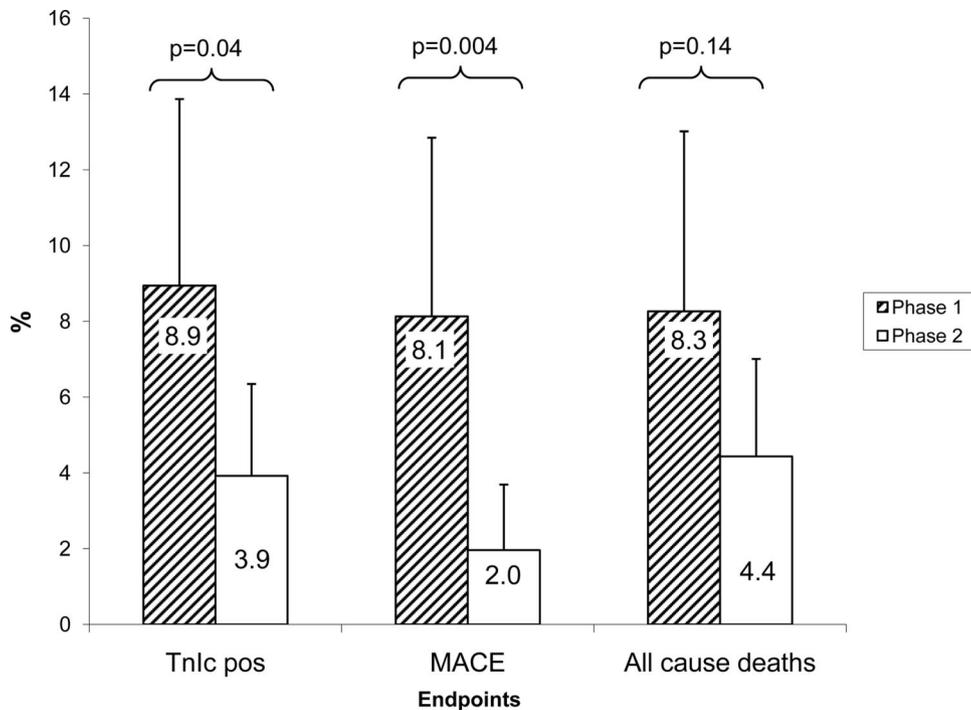
**Long-term.** Semistructured telephone interviews were performed by one of two authors (Dr. Ausset or Dr. Cirotte). The patient, his or her family, or the physician in charge of the nursing home were phoned 1 yr after surgery to learn of major cardiac events, determine mortality and its cause, and record any further hospitalizations. A standardized form was used that in-

cluded evaluation of chest pain, signs of cardiac failure, and any additional hospitalization or change of medication. The outcome measure combined the following events: cardiac death, myocardial infarction, unstable angina, need for coronary revascularization or cardiac surgery, and congestive heart failure. When such an event was suspected, the medical record was accessed and the case finally categorized as MACE or not after a peer review (by Dr. Ausset and Dr. Auroy).

**Statistical Analysis.** The patient's baseline data and the incidences of PMI, MACE, and all-cause deaths were compared between the two phases. Continuous variables were compared using the unpaired *t* test and dichotomous data with the chi-square test or Fisher exact test.

Univariate and multivariate Cox regression models were used to compare survival in the two phases and to define predictors of long-term cardiac outcome. All potential preoperative predictors with  $P < 0.2$  on univariate survival analysis were included in the Cox multivariate regression analysis. The same analysis design was used to compare MACE in the two phases.

We used propensity score stratification to assess the association between the study phase and death (or MACE). A propensity score, defined as the probability of the period before or after the quality enhancement (P2 *vs.* P1) as predicted from all available baseline and intraoperative variables (age, gender, type of surgery, history of coronary artery disease, renal failure, cardiac failure, stroke, dyslipidemia, diabetes, current smoking, hypertension, use of  $\beta$ -blocking agent, American Society of Anesthesiology physical status classification [ASA status], and TnIc elevation), was calculated for each patient using logistic regression. No significance criterion was used to remove variables and all were



**Fig. 3.** Incidence of postoperative myocardial ischemia with Troponin I release (TnIc pos), major adverse cardiac events (MACE), and all-cause deaths according to the phase of the study. The vertical bars indicate 95% CI.

retained. We stratified patients in five groups using quintiles, the first quintile corresponding to the lowest probability of being included after the quality enhancement and the fifth quintile corresponding to the highest probability. Results of multivariate Cox regression models were stratified on the five groups of propensity score.

We used adjusted confidence intervals for all analysis (adjusting for the two-interim analysis), which were set as 97.8% confidence intervals (CI), because the type I error rate was  $\alpha = 0.022$ , according to the Pocock method.<sup>31</sup> All analyses were performed using STATA software (version 10.0; Stata Corp LP, College Station, TX).

### Results

During the study period, 439 patients underwent major orthopedic surgery during the study period, of whom 61 were excluded: 23 patients already included in the prior 12 months and 38 as a result of incomplete data (no TnIc dosage available). Thus, a total of 378 surgical procedures in 355 patients was analyzed, 123 for P1 and 255 for P2 (fig. 2). Patients' distribution for ASA status, age, sex, and cardiac risk index were similar for P1 and P2 (table 1).

Overall, a TnIc elevation beyond the significance threshold was observed after 21 procedures (5.5%) in any of the first 3 postoperative days. The incidence of PMI with TnIc elevation was 8.9 versus 3.9% ( $P = 0.04$ ) for P1 and P2, respectively (fig. 3).

Analysis at 1 yr was performed after 367 surgical procedures, because 11 patients were lost to follow-up (fig. 2). Among the 15 (3.9%) patients who suffered a MACE during the first postoperative year, 10 (8.1%) incidents occurred during P1 and 5 (1.9%) during P2 ( $P = 0.004$ ). Six of those patients presented with a TnIc elevation (table 2, fig. 4). Factors correlated with a MACE during the first postoperative year are summarized in table 3. Using a Cox model including TnIc level, age, type of surgery, ASA status, Revised Cardiac Risk Index, and study phase, independent factors associated with the occurrence of MACE were TnIc value greater than or equal to threshold (hazard ratio [HR] = 6.4; 97.8% CI, 1.6–26.4) and study phase (HR = 4.5; 97.8% CI, 1.1–17.4).

The overall 1-yr mortality rate was 21 of 378 (5.5%). The 1-yr mortality rates were 10 of 123 (8.3%) for P1 and 11 of 255 (4.4%) for P2 ( $P = 0.14$ ). Factors correlated with all-cause death during the first postoperative year are summarized in table 4. Using a Cox model including TnIc level, age, type of surgery, ASA status, Revised Cardiac Risk Index, and study phase, independent factors associated with all-cause death were ASA status class III (HR = 5.2; 97.8% CI, 1.1–25.3), IV (HR = 22.6; 97.8% CI, 3.5–147.7), and hip fracture (HR 6.4; 97.8% CI, 1.3–32.5). The Kaplan–Meier survival curve of all-cause mortality at 1 yr according to TnIc level and phase of the study is shown in figure 4.

A propensity score was used to control for confounding factors between phase 1 and phase 2 subjects. In the multiple lo-

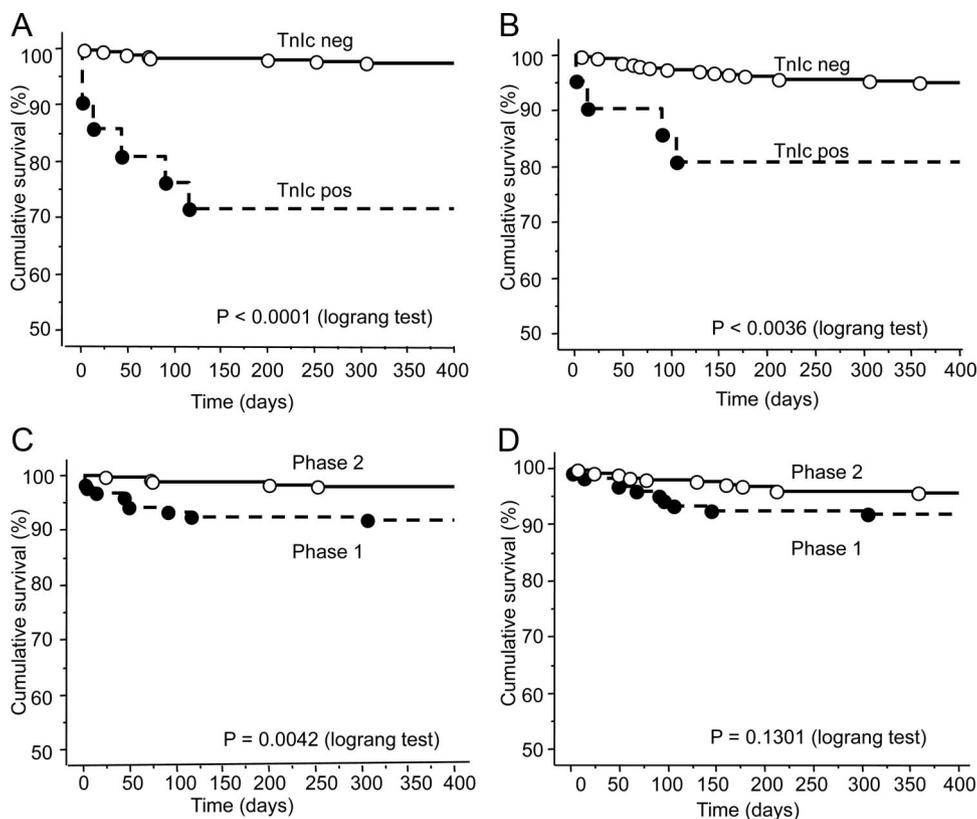
**Table 2.** Description of Cardiac Events during Follow-up

Patient Clinical Features	Type of Surgery	TnIc Positive	Cardiac Event and Time after Surgery
<b>Phase 1</b>			
Man, 65 yr, ASA 2, RCRI 1	HR	Yes	ACS 43 days
Woman, 89 yr, ASA 4, RCRI 4	HFR	Yes	CD 2 days
Man, 97 yr, ASA 3, RCRI 3	HFR	No	CD 305 days
Woman, 96 yr, ASA 3, RCRI 3	RHR	No	CD 49 days
Woman, 94 yr, ASA 3, RCRI 4	HFR	No	CD 49 days
Woman, 92 yr, ASA 2, RCRI 2	HFR	Yes	CD 90 days
Man, 54 yr, ASA 3, RCRI 1	KO	Yes	AVR 116 days
Man, 75 yr, ASA 4, RCRI 2	HFR	Yes	ACS 2 days
Man, 82 yr, ASA 4, RCRI 3	RHR	Yes	CD 13 days
Man, 75 yr, ASA 3, RCRI 2	HR	No	CHF 4 days
<b>Phase 2</b>			
Woman, 93 yr, ASA 3, RCRI 2	HFR	No	Death after ACF 24 days
Man, 63 yr, ASA 2, RCRI 1	RKR	No	PTCA after ACS 199 days
Woman, 80 yr, ASA 2, RCRI 2	KR	No	ACS 74 days
Woman, 96 yr, ASA 3, RCRI 3	HFR	No	ACS and CHF 252 days
Man, 98 yr, ASA 2, RCRI 1	KR	No	PTCA after ACS 73 days

ACS = acute coronary syndrome; ASA = American Society of Anesthesiologists; AVR = aortic valve replacement; CD = cardiac death; CHF = congestive heart failure; HFR = hip fracture repair; HR = hip replacement; KO = knee osteotomy; KR = knee replacement; PTCA = percutaneous transluminal coronary angioplasty; RCRI = Revised Cardiac Risk Index; RHR = reoperation of hip replacement; RKR = reoperation of knee replacement.

gistic regression model for the propensity score, the following covariates were used: age, sex, type of surgery, medical history of coronary artery disease, renal failure, cardiac failure, stroke, dyslipidemia, diabetes, current smoking, hypertension, use of  $\beta$ -blocking agent, ASA status, and TnIc elevation. For the MACE criterion, the HR of phase 1 changed from 4.5 (97.8% CI, 1.1–17.4) in adjusted analysis to 4.3 (97.8% CI, 1.0–18.1) in the same analysis stratified on the propensity score. For the all-cause death criterion, the HR of phase 1 changed from 1.7 (97.8% CI, 0.5–5.2) in adjusted analysis to 1.5 (97.8% CI, 0.5–4.7) in the same analysis stratified on the propensity score.

Prescribers' adherence to the protocol varied from 33.5 to 91% according to the items identified by FMECA. Each item was significantly improved from P1 to P2 (table 5).



**Fig. 4.** (A) Incidence of patients free from major adverse cardiac event (cardiac death, acute coronary syndrome, need for coronary revascularization, or cardiac surgery and congestive heart failure) during follow-up according to postoperative troponin I (TnIc) levels. (B) Cumulative survival rate during follow-up according to postoperative TnIc levels. (C) Incidence of patients free from major adverse cardiac event (cardiac death, acute coronary syndrome, need for coronary revascularization, or cardiac surgery and congestive heart failure) during follow-up according to study phase. (D) Cumulative survival rate during follow-up according to study phase.

## Discussion

The major findings of this study can be summarized as follows: 1) an overall 5.5% incidence of PMI with TnIc release was found after major orthopedic surgery; 2) a decreased incidence of both PMI and late MACE was achieved with a program aimed at improving quality of postoperative care; 3) the occurrence of PMI with TnIc release was confirmed to be correlated with poor long-term cardiac outcome, as described previously for high-risk patients,<sup>14,32</sup> mainly after vascular surgery<sup>12,15,33</sup> and after major orthopedic surgery.<sup>8,9,34</sup>

The relationship between quality of care and postoperative outcome that we found is consistent with data showing variations of mortality according to the day of surgical procedure (Friday *vs.* rest of the week<sup>35</sup> or weekdays *vs.* weekends and holidays).<sup>36</sup> However, this correlation, which indicates that quality of immediate postoperative care results in a reduced incidence of early PMI and late cardiac outcome, is a new finding. To our knowledge, only a few studies have assessed the impact of “global” intervention on outcome,<sup>36</sup> and none has previously focused on cardiac outcome. Even if some studies have shown that “minor” issues such as hypotension or tachycardia could have an impact on the incidence of myocardial ischemia,<sup>37–40</sup> most of the studies on preventive policies against myocardial ischemia were designed to

test the efficacy of pharmacological therapies (*i.e.*, techniques such as epidural analgesia or monitoring devices such as pulmonary artery catheters). For our study, we defined a strategy in which quality of care could be improved by a combination of interventions rather than by implementing a single therapeutic intervention. We were aware that efficacy data on such interventions were scarce and mainly focused on vascular surgery.<sup>3,4,41,42</sup> Moreover, because TnIc elevation after surgery most often has no associated clinical symptoms and is of limited intensity, our program should not have introduced potentially harmful therapies. Our protocol fits with the recent European Society of Cardiology<sup>43</sup> guidelines concerning blood glucose control in the intensive care unit. That society recommends that “...the management of blood glucose in the intensive care unit [should] be optimized, avoiding the extremes of hyperglycaemia and also hypoglycaemia,” but these guidelines do not discuss the control of blood glucose concentration during the perioperative period in patients who are undergoing noncardiac surgical procedures without planned intensive care unit admission. Neither do they elucidate clear guidelines concerning hypotension and tachycardia, although they state: “...postoperative tachycardia should result in the first instance in the treatment of the

**Table 3.** Factors Associated with MACE within 12 Months

	Incidence of MACE		Univariate (Crude Measures)		Multivariate*		Multivariate†	
	n	%	HR	97.8% CI	HR	97.8% CI	HR	97.8% CI
Phase								
1	10	8.1	4.2	1.2–14.8	4.5	1.1–17.4	4.3	1.0–18.1
2	5	1.9	Ref.	—	—	—	—	—
Sex								
Female	7	3.4	Ref.	—	—	—	—	—
Male	8	4.7	1.4	0.4–4.5	—	—	—	—
Type of surgery								
Scheduled arthroplasty	4	1.6	Ref.	—	—	—	—	—
Hip fracture	8	9	6.3	1.6–25.7	1.4	0.3–8.2	2.0	0.4–10.9
Reoperation of arthroplasty	3	8.8	5.9	1.0–34.0	1.6	0.2–12.1	0.8	0.1–7.6
Age			1.1	1.0–1.2	1.0	1.0–1.1	1.0	1.0–1.1
RCRI class								
I	4	1.5	Ref.	—	—	—	—	—
II	5	6.7	4.6	1.0–21.2	2.7	0.5–15.9	2.3	0.4–13.8
III	4	11.8	8.4	1.7–42.5	3.0	0.4–23.1	2.0	0.2–18.8
IV	2	28.6	24.7	3.4–180.2	6.6	0.5–84.8	3.4	0.2–48.6
ASA classification								
1–2	5	1.8	Ref.	—	—	—	—	—
3	7	6.9	4.0	1.0–15.3	1.5	0.3–7.1	1.7	0.4–7.6
4	3	33.3	27.8	5.2–149.4	5.7	0.6–51.9	2.9	0.1–62.3
Postoperative TnIc elevation	6	28.6	13.1	3.9–43.7	6.4	1.6–26.4	2.8	0.5–15.1

\* Adjusted for age, RCRI, ASA, type of surgery, and postoperative TnIc elevation, stratified on propensity score. † Adjusted for age, RCRI, ASA, type of surgery, and postoperative TnIc elevation, stratified on propensity score.

ASA = American Society of Anesthesiologists; CI = confidence interval; HR = hazard ratio; MACE = major adverse cardiac event; RCRI = Revised Cardiac Risk Index; Ref. = reference; TnIc = troponin I c.

underlying cause, for example hypovolaemia, pain, blood loss, or infection....”

Despite the fact that the incidence of PMI varies widely according to the type of surgery, we decided to implement

this policy with all types of major orthopedic procedures, because we believed that better adherence from the medical team and nurses could be obtained if the protocol was straightforward, simple, and applied similarly to a variety of clinical

**Table 4.** Factors Associated with All-Cause Death within 12 Months

	Death		Univariate (Crude Measures)		Multivariate*		Multivariate†	
	n	%	HR	97.8% CI	HR	97.8% CI	HR	97.8% CI
Phase								
1	10	8.3	1.9	0.7–5.3	1.7	0.5–5.2	1.5	0.5–4.7
2	11	4.4	Ref.	—	—	—	—	—
Gender								
Female	7	12	5.9	Ref.	—	—	—	—
Male	8	9	5.4	0.9	—	—	—	—
Type of surgery								
Scheduled arthroplasty or arthroplasty redux	3	1.0	Ref.	—	—	—	—	—
Hip fracture	18	21.4	21.8	5.2–91.1	6.4	1.3–32.4	9.0	1.7–48.4
Age			1.1	1.1–1.2	1.0	1.0–1.1	1.0	1.0–1.1
RCRI class								
I	4	2.3	Ref.	—	—	—	—	—
II	6	6.9	3.0	0.8–12.2	1.5	0.3–6.9	1.5	0.3–8.9
III	5	18.8	8.5	2.3–32.1	1.0	0.2–4.2	0.7	0.1–3.2
IV	6	57.1	36.2	8.2–159.2	4.5	0.8–24.7	3.0	0.5–16.8
ASA classification								
1–2	3	1.1	Ref.	—	—	—	—	—
3	12	12.2	11.3	2.6–49.6	5.2	1.1–25.3	5.9	1.2–27.9
4	6	66.7	95.2	18.7–485.1	22.6	3.5–147.7	25.7	3.2–208.0
Postoperative TnIc elevation	4	19	4.4	1.2–15.8	1.2	0.3–5.1	0.3	0.1–2.2

\* Adjusted for age, RCRI, ASA, type of surgery, and postoperative TnIc elevation, stratified on propensity score. † Adjusted for age, RCRI, ASA, type of surgery, and postoperative TnIc elevation, stratified on propensity score.

ASA = American Society of Anesthesiologists; CI = confidence interval; HR = hazard ratio; RCRI = Revised Cardiac Risk Index; Ref. = reference; TnIc = troponin I c.

**Table 5.** Quality of Care during the First 3 Postoperative Days

	P1	P2	P Value*
<b>Prescribed</b>			
Oxygen administration, %	60	81	<0.0001
Repeated blood glucose measurements, %	9	91	<0.0001
Insulin therapy according to blood glucose level, %	8	48	<0.0001
Vascular filling according to blood pressure, %	0.8	33.5	<0.0001
<b>Performed</b>			
Patients with blood glucose level monitoring, %	54	78	<0.0001
Patients receiving oxygen, %	79	90	0.0067
Patients receiving insulin, %	3	31	<0.0001
Patients receiving volume expansion, %	7	4	0.259
Blood pressure measurements, mean no.	10	12.3	0.0003
Spo <sub>2</sub> measurements J0–J3, average	9.8	12.3	<0.0001
Duration of oxygen administration, hr	25	30	0.113
Blood glucose measurements, mean no.	1.8	3.2	0.006
Insulin therapy, mean days	3.2	0.9	0.663
Insulin therapy, mean units	4.9	4.3	0.724
RBCs transfused, mean units ± SD	1.6 ± 2.4	1 ± 1.5	0.0031
<b>Intermediate outcomes</b>			
Patients with at least one episode of hypotension, % SBP <100 mmHg	38	39	0.865
Patients with at least one episode of hypoxemia, % Spo <sub>2</sub> <95 mmHg	58	45	0.021
Spo <sub>2</sub> value <95%, n, mean no.	1.2	0.9	0.08
Lowest hemoglobin	8.9	9.4	0.0041
≤7 g/dl, n (%)	6 (4.9)	9 (3.9)	0.0027
>7 ≤8 g/dl, n (%)	27 (22.1)	32 (13.7)	
>8 ≤9 g/dl, n (%)	39 (32)	48 (20)	
≥9 g/dl, n (%)	50 (41)	144 (61.8)	

\* P values are from Kruskal-Wallis test for the lowest hemoglobin value and Student t test for number of RBC units transfused. All other P values are from chi-square test.

RBC = erythrocytes; SBP = systolic blood pressure; Spo<sub>2</sub> = oxygen saturation measured by pulse oximetry.

conditions. Its implementation significantly improved each prescription item considered relevant by the FMECA. The rate of prescription during P2 became high for oxygen and blood glucose monitoring (81 and 91%, respectively); by contrast it

stayed low for insulin therapy and vascular filling (48 and 33.5%, respectively). The implementation of standardized prescriptions during P2 was shown to lead to clear improvement compared with P1 for all prescription items considered relevant by the FMECA. This emphasizes the importance of having clear protocols for postoperative prescription. Closer patient monitoring was also observed, with more patients receiving oxygen, insulin, and blood transfusions. By contrast, vascular filling products remained seldom administered (table 5). This may explain why, although fewer patients were hypoxicemic or anemic, there was no difference in the number of hypotension episodes. The interpretation of these results must take into account the idea that intensification of vital signs monitoring during P2 might have been associated with a greater probability to detect an abnormality. Although we believe that improvement of postoperative care resulted in a decrease of both early and late MACE, the possibility cannot be excluded that the benefit observed was due to the Hawthorne effect (*i.e.*, improved performance as a result of the subjects' knowledge of being observed).

Our study confirms that late MACE can arise from complications of the early postoperative period. Similar data have been reported by numerous previous studies.<sup>15,23,42,44–54</sup> One could argue that the fact that cardiac morbidity is higher for patients who had PMI does not imply that PMI was the cause of the late MACE. It could be a marker of severe underlying cardiovascular disease and could thus be associated with a worse cardiac outcome even without being the causation. Nonetheless, several studies support the hypothesized pathway that PMI may lead to MACE months to years later.<sup>8,9,12,13,15,16,34,55–57</sup> Although it is difficult to draw firm conclusions on the basis of these studies, the consistency of perioperative studies and the strong evidence that myocardial infarctions alter the intermediate and long-term outcome in the nonoperative setting suggests that perioperative events may cause worse long-term cardiac outcome.<sup>7</sup> Therefore, the fact that interventions that prevent PMI result in a decrease in long-term cardiac complications strongly suggests that aiming to decrease PMI is a sound strategy for improving long-term cardiac outcome. These data are consistent with those of Feringa *et al.*,<sup>57</sup> who showed, in 272 vascular surgery patients, that heart rate control produced similar variations of incidences of myocardial infarction, troponin release, and long-term mortality. Thus, we believe that the variation of the incidence of troponin elevation in a given surgical population can be used as a marker of the efficiency of preventive policies.

The question of the cost-effectiveness of our intervention is complex. The benefit is 6 MACE avoided for 100 patients. The raw cost could be estimated through the cost of systematic biologic follow-up; that is, the cost of three TnIc measurements and three full blood counts: (17.55 € + 9.45 €) × 3 = 81 €/patient. However, to be exhaustive, extra investigations (10% of positive TnIc had a cardiologic consultation and 7% required a coronary angiography), and intensive care unit admissions induced by the results of TnIc screening (25% of patients with a positive TnIc) should be taken into account.

Our study presents several weaknesses. First, the number of clinical events is relatively small; nonetheless, this number

was large enough for statistical analysis.<sup>58</sup> We did not perform *post hoc* power calculations because they are based on questionable assumptions and reflect only the observed *P* value of the comparison.<sup>59</sup> Moreover, this small number is likely the consequence of the risk reduction of our program, because during P1, the incidence of both MACE and PMI was higher. Second, for ethical reasons, it was impossible to allocate quality of care in a randomized fashion. Instead, we chose to compare preintervention and postintervention data using recruitment of the two groups of patients from the same surgical ward at the same hospital being treated by a similar group of physicians. Furthermore, it is now accepted that some assessment methods developed in engineering and used in quality improvement, such as statistical process control and time series analysis, are more powerful than randomized control trials to assess improvement of quality of care.<sup>60</sup> The recent example of a surgical safety checklist perfectly demonstrates this evolution.<sup>61</sup> The third limitation of our study is the possibility of a Hawthorne effect; that is, the improvement of care was due to subjects' knowledge of being observed rather than to the effect of a protocol of care.<sup>62,63</sup> However, whatever the cause of its improvement, the quality of care remains correlated with both PMI and late cardiac outcome.

In summary, we found that improved quality of care after major orthopedic surgery can have a significant impact on both cardiac outcome and PMI with TnIc release. This may have two implications: First, postoperative TnIc measurements can be used as a relevant result indicator of quality of care. Second, because a simple and combined preventive policy aimed at lowering early ischemic complications risk can induce improved long-term cardiac outcomes, late cardiac outcomes can be partly modulated by perioperative care.<sup>3</sup>

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## Appendix 1: Postoperative Prescriptions for Hip and Knee Arthroplasties, Reoperations of Arthroplasties, and Hip Fractures

### Monitoring

1. Vital signs: Check heart rate, blood pressure, SpO<sub>2</sub>, visual analog scale every 4 h during the first 2 postoperative days.
2. Wound monitoring: Measurement of liquid in the suction drains and inspection of dressings every 4 h during the first 2 postoperative days.
3. Glycemic checking: Glucometer analysis of capillary blood via fingerstick every 4 h during the first 2 postoperative days (stop after 24 h if all measurements are equal to 7 mm). Recheck 1 h after each subcutaneous insulin injection.

### Fluid Therapy

During the first two postoperative days:

- 25–30 ml/kg of rehydration fluid (68.4 mM sodium, 26.8 mM potassium, 278 mM glucose)
- In case of BP below a threshold defined by the attending anesthesiologist: 250–500 ml of colloids infused in 20 min

Reintroduction of antiplatelet medication

Used in primary prevention

- Arthroplasties and reoperations of arthroplasties, between days 3 and 5 according to surgeon’s wishes.
- Hip fractures without arthroplasty (dynamic hip screw, gamma nailing, hip pinning): on the first postoperative day.

Used in secondary prevention

- On the first postoperative day

Oxygen therapy

- O<sub>2</sub> 3 l/min for 24 h, 48 h when revised cardiac risk is equal to 2.

Insulin therapy

- Subcutaneous injection of regular insulin every 4 h according to blood glucose level as follows: 4.4–7.4 mM, 0 IU; 7.5–8.9 mM, 2 IU; 8.9–11 mM, 5 IU; 11–13.5 mM, 10 IU; 13.6–16.5 mM, 15 IU; 16.6–20 mM, 20 IU; and >20 mM, 5 IU and call physician. Reperform glucometer analysis 1 h after each insulin subcutaneous injection. If glycemia is 4.4 mM, then (1) IV injection of 20 ml of glucose, 0.3 g/l, and (2) perform glucometer analysis 15 min later and resume the protocol.

### Lab Tests

- Hemoglobin and troponin Ic in the recovery room and on the morning of the first 3 postoperative days.
- Platelet count twice a week during low-molecular-weight heparin treatment.

### Antibiotics

- Arthroplasties and reoperation of arthroplasties: 2 g cefazolin at induction of anesthesia and 2 g every 8 h for 48 h.
- Hip fractures without arthroplasty (dynamic hip screw, gamma nailing, hip pinning): 2 g cefazolin at induction of anesthesia.

### Thromboprophylaxis

- Enoxaparin 40 mg/day started 12 h after the end of surgery.
- In patients with creatinine clearance of <30 ml/min, unfractionated heparin targeting activated partial thromboplastin time in the range of 1.5–2 times the control value.

### Postoperative Analgesia

- Acetaminophen ± nefopam ± ketoprofen in the absence of contraindication.
- For knee surgery, continuous femoral nerve block using 6–8 ml/l ropivacaine, 2 mg/l IV morphine via patient-controlled analgesia in case of block failure or contraindication.