Intense Cardiac Troponin Surveillance for Long-Term Benefits Is Cost-Effective in Patients Undergoing Open Abdominal Aortic Surgery: A Decision Analysis Model

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BACKGROUND: Strategies to limit adverse cardiac events after vascular surgery continue to evolve. Early recognition and treatment of myocardial ischemia may be a key to improving postoperative survival rates. Cardiac troponin I (cTnI) screening is an effective means of surveillance for postoperative myocardial ischemic injury and has long-term prognostic value.

METHODS: We designed a Markov-based decision analysis model to determine the cost-effectiveness of routine surveillance with cTnI on postoperative Days 0, 1, 2, and 3, with an aim to institute tight heart rate control (60–65 bpm) with close monitoring and coronary care in the intensive care unit for 5 days in patients with cTnI >1.5 ng/mL. The key input variables obtained from published literature were as follows: probability of myocardial infarction, 0.049; cost of cTnI surveillance, $357; cost and efficacy of interventions, $13,145 and 0.55, respectively. The time horizon was lifetime and the target population being individuals aged 65 yr (median) undergoing elective open abdominal aortic surgery.

The perspective for analysis was third-party payer.

RESULTS: The incremental cost-effectiveness ratio for cTnI surveillance was $12,641 per quality-adjusted life year compared with standard care without cTnI surveillance. During one-way sensitivity analysis, probability of myocardial infarction and efficacy of interventions were found to influence the cost-effectiveness. Multivariate sensitivity analysis with second-order Monte Carlo simulation revealed that cTnI surveillance was favored in 90.75% of simulations at a commonly used threshold of $50,000 per quality-adjusted life year.

CONCLUSIONS: In patients presenting for elective open abdominal aortic surgery, intensive surveillance with cTnI and early institution of aggressive β-blockade is cost-effective.

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Strategies to limit adverse cardiac events after vascular surgery continue to evolve as usefulness of traditional approaches of preoperative cardiac testing and revascularization have been questioned (1–6). Patients who suffer perioperative nonfatal events have reduced intermediate and long-term survival (7). After major vascular surgery, the first 48 to 72 postoperative hours, when adverse cardiac complications can develop, are the most dangerous (8,9). Cardiac troponin I (cTnI) screening is an effective means of surveillance for postoperative myocardial ischemia (10). The routine cTnI surveillance on Days 0, 1, 2, and 3 has allowed recognition of two distinct types of perioperative myocardial infarction (PMI): "early" and "delayed" (11). Early PMI occurs in the early postoperative period and is not preceded by subinfarction myocardial damage, whereas the delayed PMI occurs later and is preceded by a long period (>24 h) of myocardial damage during which cTnI levels are increased. Early PMI resembles that of acute nonsurgical MI, and is probably because of acute coronary occlusion resulting from plaque rupture and thrombosis. The delayed PMI resembles that resulting from an increase in oxygen demand in the setting of fixed coronary stenosis. Le Manach et al. (11) believed that monitoring cTnI concentrations postoperatively may allow the institution of early aggressive interventions to prevent the evolution of PMI during the "golden period" of approximately 2 days before the development of delayed PMI.

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Early invasive therapy involving interventional procedures and anticoagulants is beneficial in the management of acute coronary syndromes (12). However, the immediate postoperative state may preclude the use of such a therapy. Heart rate control with use of β-blockers may seem to be a reasonable approach in this setting. Reduction in heart rate tends to restore the oxygen supply-demand balance and also reduce the risk of plaque disruption. Additional benefits regardless of the PMI types are prolongation of coronary diastolic filling time and reduction in risk of ischemic ventricular arrhythmias (13). The initial financial burden of such monitoring and treatment strategy could be substantial. For example, troponin surveillance (four tests) incurs an additional expenditure of $357 on every patient (14). Additional expenditures will be incurred for aggressive treatment in a fraction of patients manifesting increased cTnI concentrations. An important question that may be asked in such a situation is, "Is increased cost of monitoring worth any potential reductions in morbidity?" (15).

We sought to determine, through a decision analysis model, whether postoperative cTnI surveillance on Days 0, 1, 2, and 3, and institution of MI risk-reducing strategies in those patients having a value >1.5 ng/mL, would be cost-effective when long-term benefits are considered. Specific management strategies that were perceived to be beneficial in ameliorating the adverse impact of PMI were tight heart rate control coupled with close monitoring of heart rate and routine coronary care in intensive care unit (ICU) (4,5,16). The target population is patients aged 65 yr with intermediate risk (1–2 clinical risk factors) undergoing open abdominal aortic surgery. As cTnI surveillance has intermediate and long-term prognostic value (17,18), we hypothesize that potential long-term benefits of early recognition and management could outweigh the disadvantages of initial cost burden.

METHODS

Overview

We constructed a Markov-based decision analysis model (19,20) incorporating the costs and survival benefits that were captured by intensive cTnI monitoring and intervention compared to a base-case strategy of standard care in patients undergoing elective open abdominal aortic surgery (aortic aneurysm repair and aorto-bifemoral bypass surgery). The model inputs were derived from the literature published in English as of October 2006 using PubMed database search. The model was designed to assess health outcomes, i.e., quality-adjusted life years (QALYs) and costs (present value of future expenditures) that result from base-case strategy and intense cTnI monitoring strategy. All costs were converted to 2003 US$ using the medical care component of the Consumer Price Index. The primary outcome measure was incremental cost per QALY (21) evaluated by calculating the incremental cost-effectiveness ratio (ICER). Our analysis assumed a third-party perspective and a lifetime time horizon using yearly cycles of the Markov process. Annual mortality data from United States life tables for both genders and all races were incorporated in the analysis while using an annual excess mortality rate of 0.014 for peripheral vascular disease (22) for the entire cohort. In accordance with standard principles of economic analysis, future costs, and health outcomes (QALYs) were discounted at a yearly rate of 3% (21). Such discounting allows one to assign a higher value for current dollars and health outcomes to those accrued in the future. Sensitivity analysis included one-way sensitivity analysis calculated by systematically varying on all data inputs in clinically plausible ranges. In addition, multivariate probabilistic Monte Carlo simulation was also used to evaluate the stability of our model parameters (23). The ICER value of $50,000/QALY was used as a threshold for defining cost-effectiveness (24). The output of the Monte Carlo simulation was summarized using the recommended cost-effectiveness acceptability curve (25). Decision analysis was facilitated using DATAPro 2006 (TreeAge Software, Williamstown, MA).

Literature Search Methodology

The model inputs were derived from the literature published in English as of October 2006 using PubMed database search. The search was made using the key words: "troponin," "vascular surgery" in one set and using the key words: "perioperative," "myocardial infarction," "vascular surgery," "treatment" in another. The abstracts of retrieved articles were read by one author (S.M.) and full-length articles were obtained for those determined to be suitable for the model by another author (J.E.E.). In addition, relevant articles on the subject were also identified from the personal files of both of these authors to identify any articles that could have missed the initial defined search.

Target Population

The target population was to have a median age of 65 yr and at least two clinical risk factors for adverse cardiac events. Such inclusion typically categorizes the patients as "intermediate risk." The clinical risk factors include the following: current or previous angina pectoris, previous MI, compensated or previous congestive heart failure (CHF), diabetes mellitus, severely limited exercise tolerance, and renal insufficiency (serum creatinine >2.0 mg%) (4,26). Patients with major risk factors, i.e., acute MI (<7 days), recent MI (7–30 days), unstable angina, decompensated CHF, and significant arrhythmias, were excluded from the model. Patients having conditions that preclude use of tight heart rate control with β-blockers were also excluded. In the intense cTnI strategy, patients would be screened for cTnI on Days 0, 1, 2, and 3, and those patients with a cTnI value ≥1.5 ng/mL would have

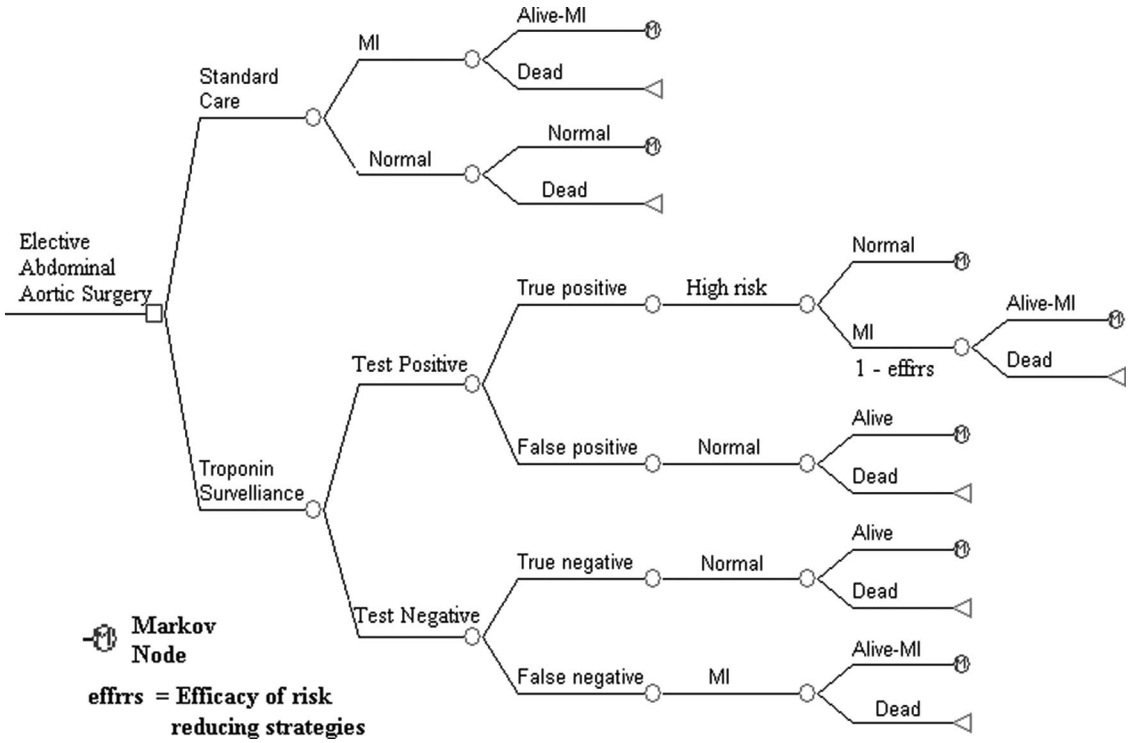

Figure 1. The basic decision tree designed for modeling short-term events. In the postoperative (cTnI) surveillance strategy, patients having cTnI values >1.5 ng/mL would have interventions in the form of tight heart rate control with close hemodynamic monitoring and coronary care in the intensive care unit (ICU) for 5 days. Based on the relative efficacy of such interventions, the risk of progression to myocardial infarction (MI) would be reduced.

aggressive β-blockade therapy with close heart rate monitoring and routine coronary care in the ICU for an average period of 5 days. The base-case alternative strategy was standard care without cTnI surveillance.

Model Structure

Our model included PMI and 30-day mortality as short-term events and, future MI, future requirement of coronary revascularization (coronary artery bypass graft [CABG], percutaneous coronary angioplasty with stenting [PTCA]) as long-term events. We also considered MI and mortality after PTCA and MI, stroke and mortality after CABG. The decision analysis model adopted in this study could be summarized in two tree structures, i.e., basic tree (Fig. 1) and Markov tree (Fig. 2).

In the basic tree for short-term events, we modeled the differential mortality rates in those with and without PMI (11). In the cTnI surveillance limb, patients having a cTnI level >1.5 ng/mL would have risk-reducing strategies adopted in the form of tight heart rate control with close hemodynamic monitoring and coronary care in the ICU for 5 days. The goal of tight heart rate control is to maintain a heart rate of 60–65 bpm. Based on the efficacy of such an intervention, the risk of progression to PMI would be decreased. The Markov tree (Fig. 2) depicts modeling for the long-term events, i.e., future MI and future coronary revascularization after hospital discharge. In long-term Markov modeling, we modeled differential rates of future MI and coronary revascularization in those with and without PMI (7). Annual rates of future MI and coronary revascularization in those who suffered PMI were 0.076 and 0.037, and in those who did not suffer PMI, rates were 0.012 and 0.012, respectively (7). Finally, annual excess mortality rates for each of the following disease states: stroke (0.083) (27), MI with associated cTnI increase for each of the first 4 yr (0.22) (28).

Model Inputs

The model inputs were derived from the literature published in English as of October 2006. We did not conduct any meta-analysis to get the aggregate values for incorporating in the model. Rather, we selected data from a study that closely matched the design features of the present model. Because we used the data from one study for baseline analysis, we took care to ensure that the ranges for sensitivity analysis included data from other related studies. In addition, we ensured that the clinically plausible ranges corresponded with the target population and interventions that were modeled. The baseline variables and ranges used in sensitivity analysis are summarized in Table 1 in the following categories:

Probabilities (3,11,27)

Probability of PMI could be influenced by preoperative clinical risk status and surgical type. The present model attempted to simulate intermediate-risk clinical risk patients aged 65 yr undergoing abdominal aortic

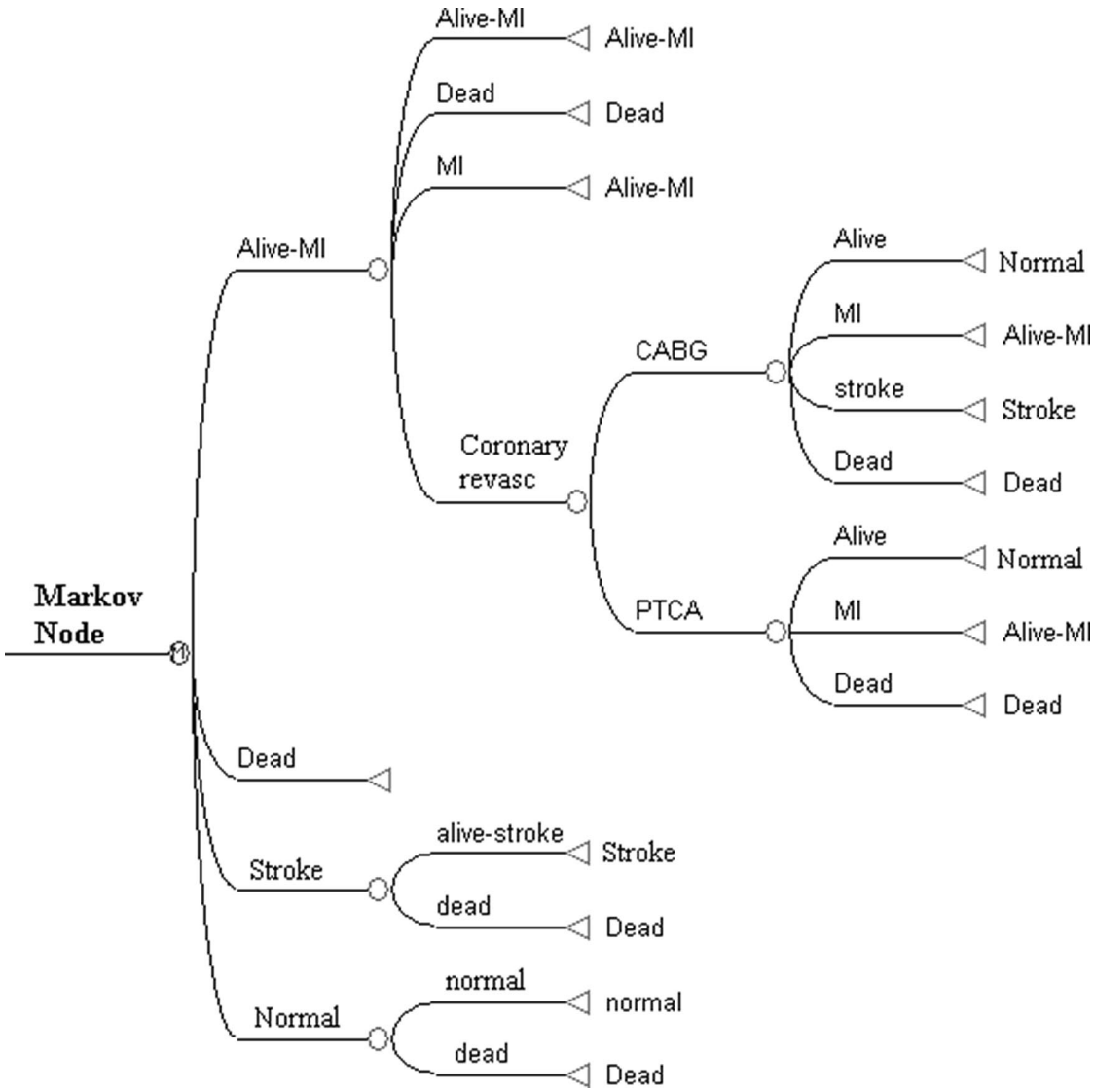

Figure 2. The Markov tree designed for modeling long-term events after the short-term events, i.e., future myocardial infarction (MI) and future coronary revascularization, i.e., coronary artery bypass graft (CABG) and percutaneous transluminal coronary angioplasty with stenting (PTCA). In the Markov tree, differential rates for future MI and coronary revascularization in those with and without postoperative MI were incorporated. In cost-effectiveness analysis, quality adjustments are required to derive quality-adjusted life years (QALYs). Such adjustment factors may range from 0 (death) to 1 (perfect health). We used a factor of 0.47 for major disabling stroke that can occur after CABG. An individual surviving 10 yr with such a stroke would accrue 4.7 QALYs. For events and procedures that did not result in durable changes in the health state of the individual, we used disutility tolls based on the average duration of hospitalization. We used yearly cycles of Markov process to capture long-term costs and QALYs after discounting at a yearly rate of 3%.

surgery by inclusion of cTnI performance data and perioperative morbidity and mortality from a single large study with similar features (11). PMI probability was assumed to be 0.049. The mortality in those suffering PMI was 22% vs 3.3% in those not suffering PMI (11). Morbidity and mortality data for CABG and PTCA were derived from a large randomized trial in vascular surgery patients (3).

Efficacy of cTnI Surveillance (11,16)

For cTnI performance evaluation, sensitivity and specificity data on Day 1 of serial measurements in a cohort of vascular surgery patients were taken as a baseline estimate (11). The efficacy of early interventions in the ICU to reduce MI in patients with a positive cTnI screen in the perioperative period was 0.55 (16). The efficacy formula is given by the following equation:

Efficacy = 1 − (frequency of an event with intervention/frequency of the event without intervention).

Quality adjustment (29–31)

In cost-effectiveness analyses, quality adjustments are required to derive the QALYs. The quality-adjustment factor may range from 0 (death) to 1 (perfect health). We used published population-based utilities, representing either time-trade-off or standard-gamble

Table 1. Values for Variables Used in the Decision Analysis Model

Variable	Baseline value (plausible range)[a]	References
Probabilities for perioperative/periprocedure morbidity and mortality		
MI after vascular surgery	0.049 (0.01–0.1)	(11)
MI after CABG	0.071 (0.01–0.1)	(3)
MI after PTCA	0.05 (0.025–0.075)	(3)
Stroke after CABG	0.016 (0.01–0.02)	(27)
Mortality after vascular surgery without MI	0.033 (0.01–0.06)	(11)
Mortality after vascular surgery with MI	0.22 (0.01–0.5)	(11)
Mortality after CABG	0.02 (0.01–0.03)	(3)
Mortality after PTCA	0.014 (0.007–0.021)	(3)
Proportion of CABG among patients undergoing revascularization in the future	0.41 (0.3–0.5)	(3)
Efficacy of cTnI surveillance		
Sensitivity	0.8 (0.6–1)	(11)
Specificity	0.93 (0.6–1)	(11)
Efficacy of risk-reducing strategies	0.55 (0.1–0.9)	(16)
Quality adjustment (utilities and disutilities)		
Utility stroke	0.47 (0.3–0.6)	(29)
Disutility stroke	−45 d (−20 to −60 d)	(30)
Disutility MI	−7 d (−3 to −10 d)	(31)
Disutility CABG	−30 d (−15 to −45 d)	(31)
Disutility PTCA	−7 d (−3 to −10 d)	(31)
Cost variables (2003 US$)		
Cost of troponin (4 tests)	357.56 (180–540)	(14)
Cost of MI	11,329.75 (6000–18,000)	(32)
Cost of risk-reducing strategies	13,145.46 (6500–19,500)	(33), Red book[b]
Cost of death	16,431.25 (8000–24,000)	(32)
Cost CABG	25,455 (20,000–30,000)	(34)
Cost of PTCA	17,668 (9000–27,000)	(35)
Cost of stroke	17,688 (9000–27,000)	(36)
Annual cost s/p CABG	2088 (1000–3000)	(34)
Annual cost after stroke	37,174 (19,000–56,000)	(36)
Annual cost s/p MI	2052 (1000–3000)	(14)

[a] Plausible ranges used in the sensitivity analysis.

[b] Refer to Table 2 for details on interventions and their costs.

CABG = coronary artery bypass graft; CAD = coronary artery disease; MI = myocardial infarction; s/p = status post; PTCA = percutaneous coronary angioplasty; cTnI = cardiac troponin I.

techniques. For example, a utility value of 0.47 for major disabling stroke implies that an individual surviving 10 yr with stroke would accrue 4.7 QALYs. For events and procedures that did not result in durable changes in the health state of the individual, we used disutility tolls based on the average duration of hospitalization (37).

Costs (14,32–36)

Direct medical costs were used and, where available, Medicare reimbursement cost data were used to reflect the cohort modeled in this study. Tight heart rate control was modeled by using the cost data for maximum allowable doses of esmolol during the first 48 h and high doses of oral and IV metoprolol therapy in the next 48 h. Close monitoring for heart rate and routine coronary care was modeled by using the ICU costs of DRG 122 (33). Total duration of hospital stay was assumed to be 12 days (38). The details of interventions, along with their costs, are listed in Table 2. A cost of $21,089 was assigned for vascular surgery for the entire cohort (32).

Sensitivity Analysis

To assess the degree to which variation in any variable altered our results, we performed a one-way sensitivity analyses for each model input. Noncost data were varied systematically in the clinically plausible ranges, and cost data were varied by 50% in each direction in the sensitivity analysis, as described in Table 1. We performed a two-way sensitivity analysis on key variables identified on the one-way sensitivity analysis. To further evaluate the stability of our model, we performed a second-order Monte Carlo simulation (23). The distribution type used for different variables is of primary importance in probabilistic sensitivity analysis. Beta distribution is ideal for variables that are bound on the 0–1 interval, e.g., transition probabilities, utilities and efficacy data. Because of concerns of skewness to the right of cost data in medical studies (39), the use of Log-Normal or truncated normal or γ distributions are recommended for cost parameters (40,41). Triangular distribution is applicable for data presented as means with minimum and maximum values (42). In the present study, the type

Table 2. Details of Interventions and Their Costs in Patients With Increased Cardiac Troponin I (cTnI)

Item component	Cost per day	Duration and time of intervention[a]	Total cost	References
DRG122 in the ICU[b]	$2520	5 d (Day 1 to Day 5)	$12,600	(33)
Esmolol (maximum dose 300 $\mu gm \cdot kg^{-1} \cdot min^{-1}$	$255.37	2 d (Day 1 to Day 2)	$510.74	Red book[c]
Oral metoprolol 100 mg twice daily	$2.08	2 d (Day 3 to Day 4)	$4.16	Red book
Oral metoprolol 50 mg twice daily	$1.04	7 d (Day 5 to Day 11)	$7.28	Red book
Grand cost			$13,145.46	

[a] Time implies time from first increase in cTnI concentrations >1.5 ng/mL.

[b] DRG 122 = circulatory disorders with acute myocardial infarction without major complications discharged alive; ICU = intensive care unit.

[c] Red book (2005). Lists whole sale costs for the year 2005. The drug costs as shown are the costs when converted to 2003 US$. Cost of esmolol was computed considering a 70-kg individual.

Table 3. Results of the Model With Baseline Values

Strategy	Direct medical costs	QALYs	ICER (cost/QALY)
Standard care	$27,964	10.4577	
cTnI surveillance	$29,639	10.5902	$12,641

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year.

of distribution used was influenced by the availability of information in the relevant source studies. When the information required to generate appropriate distribution was not available, we used triangular distribution. For example, we used β-distribution for probability data and triangular distribution for the rest of the variables listed in Table 1. Details of the distributions used for different variables in the model are available at www.anesthesia-analgesia.org.

In the present model, we used 10,000 iterations during Monte Carlo simulation. During each of the 10,000 iterations, different values were randomly and simultaneously chosen from a wide range of all the variables generated from their respective distributions. We constructed a cost-effectiveness acceptability curve by calculating the average net monetary benefit for each strategy, i.e., standard care and cTnI surveillance in each simulation over thresholds ranging from $0 to $100,000 for each QALY gained. The net monetary benefit (μ_t) is given by the following formula:

$$\mu_t = (\lambda \times \text{QALY}_t) - \text{Cost}_t,$$

where λ is externally set threshold limit and t is the treatment strategy. Incremental net monetary benefit is given by the following formula:

$$\text{Incremental net benefit} = \mu_{t1} - \mu_{t2},$$

where t_1 is the intervention of interest and t_2 is the comparator (25). We then determined the proportion of simulations for which cTnI surveillance resulted in greater net monetary benefit at each cost-effectiveness threshold.

RESULTS

Our defined search from PubMed database yielded 190 references for troponin in vascular surgery and 613 references for treatment of MI after vascular surgery.

Baseline Analysis

The results of the model with baseline values are depicted in Table 3. The ICER value of $12,641/QLAY implies that cTnI surveillance is cost-effective when interpreted with threshold value of $50,000/QALY.

One- and Two-Way Sensitivity Analysis

One-way sensitivity analysis revealed that the model was stable to changes in all the variables except probability of MI and efficacy of risk-reducing strategies (Fig. 3) with values 0.01 (precisely 0.0100625) and 0.1425, respectively, below which the ICER value increases beyond $50,000/QALY. One-way sensitivity analysis at other discount rates, i.e., 0%, 4%, 5%, and 7% revealed ICER values of $9,365, $13,829, $15,069, and $17,679, respectively. The Panel on Cost-effectiveness in Health and Medicine recommended the use of 3% discount rate for baseline analysis and suggested the use of other discount rates in the range from 0% to 7% in sensitivity analysis (21). Hence, the ICER values at the other discount rates are reported as well. Figure 4 shows the two-way sensitivity analysis of the two critical variables, i.e., probability of MI and efficacy of risk-reducing strategies, identified during one-way sensitivity analysis. The results of two-way sensitivity analysis depict a complex interaction of the two variables.

Probabilistic Sensitivity Analysis

This analysis examines the model by estimating the percent of trials that would be favorable at progressively increasing cost-effectiveness thresholds. At a cost-effectiveness level of zero, the least expensive strategy will always be selected. As we increased the cost-effectiveness threshold, i.e., society's willingness to pay for improved quality and quantity of life, the cTnI surveillance strategy became progressively more attractive. In other words, the percentage of trials expected to have favorable cost-effectiveness for the cTnI surveillance strategy

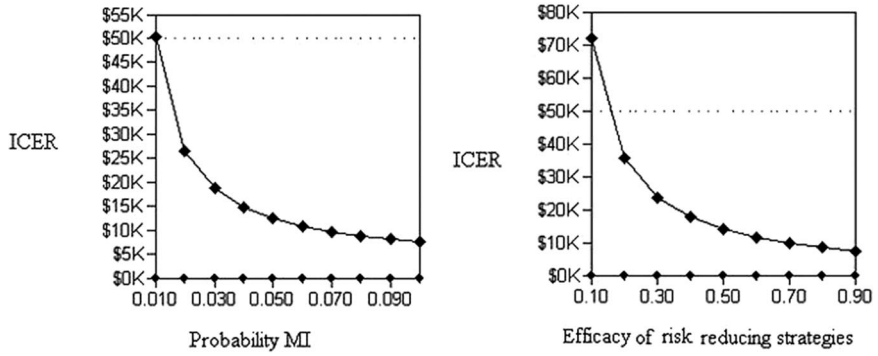

Figure 3. One-way sensitivity analysis graphs on probability of myocardial infarction (MI) and efficacy of MI risk-reducing strategies. The horizontal dotted line represents the threshold for cost-effectiveness, i.e., $50,000 per quality-adjusted life year (QALY) gained. The critical values for probability of MI and efficacy of risk-reducing strategies below the ICER value increases beyond the threshold, i.e., troponin surveillance strategy loses cost-effectiveness, were 0.01 (precisely 0.0100625) and 0.1425, respectively. ICER = incremental cost-effectiveness ratio.

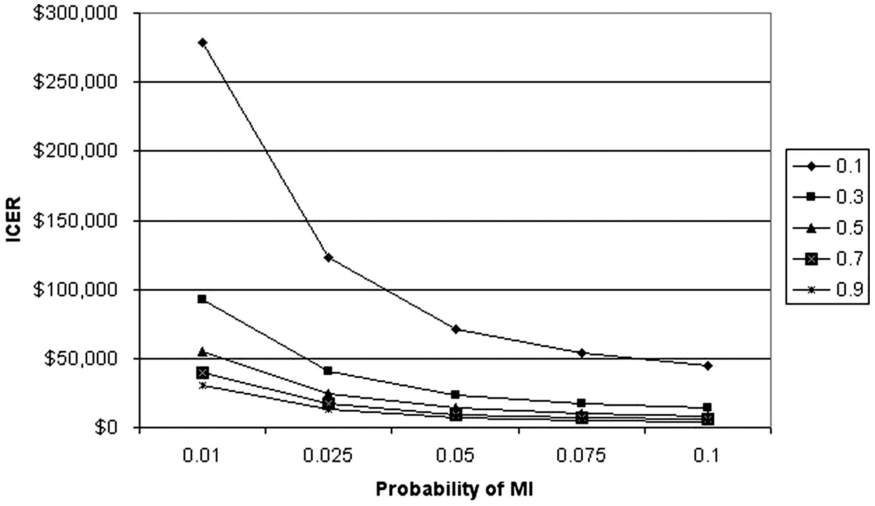

Figure 4. Two-way sensitivity analysis on efficacy of myocardial infarction (MI) risk-reducing strategies and different values of previous probability of MI. The *x* axis represents the previous probability of MI and five values for efficacy, i.e., 0.1, 0.3, 0.5, 0.7, and 0.9 were examined. The results depict the complex interaction of the two variables. The present study used 0.55 as a baseline estimate for the efficacy. ICER = incremental cost-effectiveness ratio; MI = myocardial infarction.

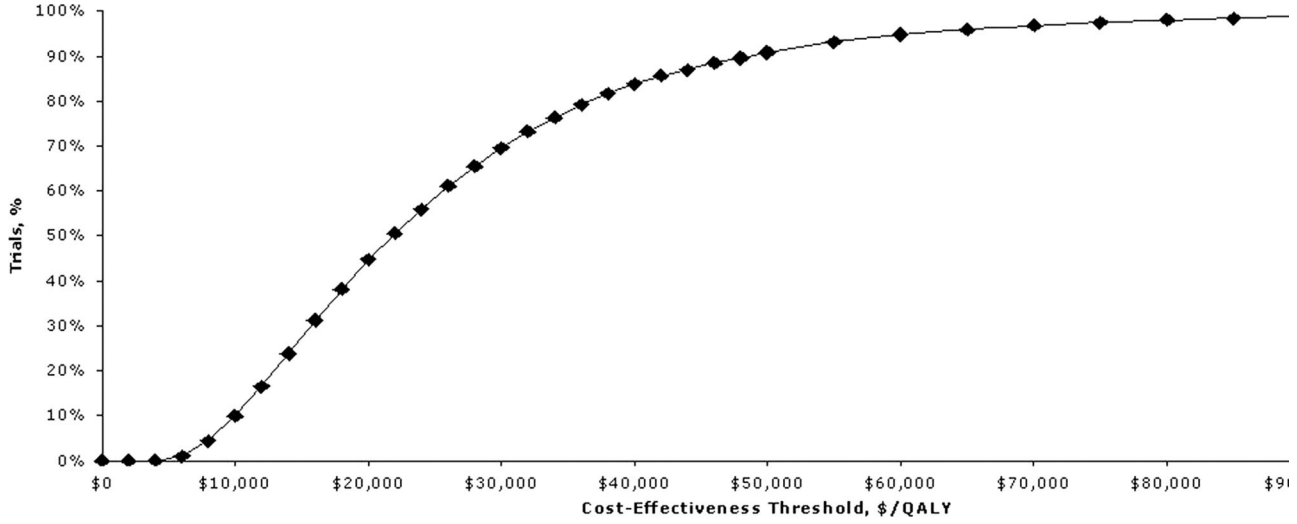

Figure 5. Cost-effectiveness acceptability curve based on the output of 10,000-simulation Monte Carlo analysis comparing cardiac troponin I (cTnI) surveillance with standard care. The *y* axis depicts the proportion of trials for which cTnI surveillance resulted in net monetary benefit rather than standard care. QALY = quality-adjusted life year.

increased progressively (Fig. 5). For example, at a cost-effectiveness threshold of $25,000 per QALY, the cTnI surveillance was favored in 58.65% of simulations. The cTnI surveillance was favored in 90.75% of simulations at a threshold of $50,000 per QALY. The data values from the distributions that were randomly and simultaneously chosen during each iteration of the first 500 of the 10,000 simulations are available at www.anesthesia-analgesia.org.

DISCUSSION

PMI is associated with increased resource utilization and the consequent financial implications (38). Furthermore, nonfatal PMI is associated with increased incidence of cardiovascular events and reduced long-term survival (7,18,43). Research in the past decade has focused on preoperative risk stratification and preparation, including prophylactic coronary revascularization strategies (1,2,26). One randomized study indicates that preoperative revascularization does not significantly improve immediate or long-term survival (3). Another study suggested that cardiac testing could safely be omitted in intermediate-risk patients, provided that β-blockers aiming at tight heart rate control are prescribed (4). Furthermore, a recent study found that a negative dobutamine stress echocardiography does not eliminate occurrence of postoperative myocardial necrosis, as detected by routine surveillance by cTnI up to the third postoperative day (6). Therefore, improved detection of MI with better surveillance may identify patients who would benefit from further management or improved perioperative management. The traditional biochemical marker for myocardial ischemic events, CPK-MB, is associated with high false positive rates in patients undergoing vascular surgery (44). In practical terms, the type of troponin that is used for surveillance, cTnI or cTnT is of little concern, as both have similar diagnostic and risk stratification capabilities (45,46).

Using a standard threshold value for cost-effectiveness ratio, i.e., $50,000/QALY gained, our analysis indicated that routine surveillance on Days 0, 1, 2, and 3 is cost-effective in patients aged 65 yr and older with intermediate cardiac risk and who are undergoing abdominal aortic surgery. The cost value of $50,000 is comparable to the annual cost of renal dialysis and commonly funded interventions are based on that threshold value. The same standard threshold value is also applicable in decision analytic cost-effectiveness models related to cardiovascular medicine (36,42). In addition, the current analysis indicated that probability of PMI and efficacy of interventions after cTnI surveillance are the key factors determining the cost-effectiveness of cTnI surveillance. We believe that identification of such key factors could help us in planning future research on the subject.

The role of prolonged, stress-induced, ST-depression-type ischemia in the pathogenesis PMI after vascular surgery is well established (8). In the terminology of "early" PMI and "delayed" PMI (11), the latter constitutes about 60% of PMIs. The delayed type is linked to prolonged ischemia and is more amenable to control with β-blocker therapy. The delayed pattern of PMI is consistent with previous findings that discovered a clear association between postoperative myocardial ischemia and PMI (47). As observed in this study, the relative effectiveness of interventions represents the "driver" for cost-effectiveness (48). We used the data from Raby et al.'s study (16) for efficacy because their study closely matches the scenario of the present model, i.e., intervention after ischemia is detected in the postoperative period. Nevertheless, the difference between the two is important. Whereas Raby et al. monitored ischemia by Holter monitoring of ST-segment depression, the present model relied on cTnI surveillance. Raby et al. used esmolol infusion for 48 h with an aim to restore heart rate to 20% below the ischemic threshold or absolute minimum of 60 bpm. To offer more protection, as suggested by recent data (4,5), the present model attempted to model tight control of heart rate on Days 3 and 4 in the ICU and usual doses of β-blocker until the patient is discharged from the hospital. It may be noted that the use of the efficacy value of 0.55 obtained from Raby et al.'s study as opposed to higher efficacy value of 0.755 obtained from Polderman et al.'s study of "tight heart rate control " strategy (5) makes our model conservative, and biases against the cost-effectiveness of the cTnI surveillance strategy. A related study that used continuous Holter monitoring showed a 50% reduction (i.e., efficacy of 0.5) of myocardial ischemia in atenolol-treated group during the first 48 h after surgery (49). That study, however, did not exclusively include patients undergoing vascular surgery.

The results of this model must be interpreted in the light of recent data indicating lack of encouraging results with regard to β-blockers in preventing cardiac events after vascular surgery (50,51). The new definition of MI requires the increase and decrease of biochemical markers of myocardial necrosis, together with one of the after clinical and electrocardiogram (ECG) criteria: ischemic symptoms, development of pathologic Q waves, ischemic ECG changes, or a coronary intervention (52,53). It may be noted that cTnI cutoff values for diagnosis of myocardial injury are highly variable depending upon the type of assay (53). The present study attempted to evaluate a scenario of intervention at cTnI level >1.5 ng/mL (Dade-Behring Stratus, Paris, France) independent of development of the other criteria. In other words, interventions are intended to limit progression to definite MI. Such a scenario is obviously different from studies that used conventional doses of β-blockers routinely starting from the preoperative period and continued to the postoperative period with a primary aim of prevention of adverse cardiac outcomes (50,51,54).

The need and duration of ICU management with coronary care must be noted. In the present context, coronary care implies continuous heart rate monitoring with ECG, frequent arterial blood pressure monitoring, administration of antianginal medications when required, and related coronary care. Administration of β-blockers alone might not be sufficient for postoperative risk reduction (5). The postoperative state after abdominal aortic surgery is associated with rapid changes in intravascular volume status and

therefore requires constant monitoring of heart rate and arterial blood pressure to maximize the benefits and minimize the side effects of therapy intended for tight heart rate control. Beta-blocker therapy in the presence of hypovolemia results in a catastrophic decrease in arterial blood pressure. To maximize the benefits of therapy for both early and delayed PMI, the 5-day duration period of monitoring and therapy was used in the present model. A recent study found the incremental duration of ICU stay for those suffering perioperative ischemic events to be 3.7 days (38). Given the aggressive treatment with tight control of heart rate in the present model, our assumption of longer duration of ICU stay may not be unreasonable.

Sensitivity analysis is another important issue that needs consideration in decision analytic models. Lower ranges used for MI and the efficacy of the interventions need to be considered in the present context as values below 0.01 and 0.1425, respectively, were found to be critical. Among noncardiac surgical procedures, aortic surgery is a high-risk category and probability of MI <0.01 has not been reported (26). Although institutional factors do play a role, it would be unlikely for interventions evaluated in the model to have an efficacy less than the threshold value in any standard center. Deviation of 50% on each direction from the baseline value of cost data during sensitivity analysis is acceptable (42). Probabilistic sensitivity analysis is an effective means of handling uncertainty in cost-effectiveness models (40). Probabilistic sensitivity analysis involves specifying distributions for model parameters to represent uncertainty in their assumption and using Monte Carlo simulation to select values at random from those distributions. In other words, probabilistic models allow the effects of joint uncertainty across all the parameters of the model. Thus, the standard probabilistic sensitivity analysis is essentially Bayesian in nature (40,48). Hence, representing uncertainty with a cost-effectiveness acceptability curve may seem justified. The curve, which directly addresses the decision-making problem, has advantages over confidence interval estimation for ICERs (25).

Perspective for analysis is an important component in cost-effectiveness analyses (21). This could include the health care system perspective, third-party payer, or societal perspective, i.e., regardless of who pays. In the present model, where available, we used Medicare reimbursement costs to reflect cost to society. Ideally, when the analysis is performed with societal perspective, the costs should also include indirect cost such as cost of loss of income (lost productivity) due to illness or death. Since the target population belongs to the age group of 65 yr with peripheral vascular disease, failure to include such indirect costs are unlikely to affect the overall model output. Even if one incorporates such data in the present model, the cTnI surveillance strategy is likely to be more cost effective, as early management helps in decreasing the long-term cardiac events that would result in lost productivity. Indirectly, the perspective for analysis could be inferred as "social perspective."

Limitations

cTnI surveillance has the additional advantage of having quantitative prognostic value both for short-term and long-term events (17,18). However, this model does not consider differential morbidity and mortality rates both in the short-term and long-term as a function of different levels of troponin. Such modeling was beyond the scope of this study. Among patients undergoing abdominal aortic aneurysm repair, major correlates of in-hospital costs are the number of days spent in ICU and the total number of days spent in the hospital (55), which in turn could be influenced by patient comorbid conditions (56). Gender can also influence outcome after abdominal aortic aneurysm repair (57). Furthermore, there could be a confounding effect of conditions other than acute coronary syndromes in the interpretation of cTnI results. Conditions such as sepsis, hypovolemia, atrial fibrillation, CHF, pulmonary embolism, myocarditis, myocardial contusion, and renal failure can be associated with an increase in troponin level (58). Of those conditions, CHF and renal failure are of particular interest in patients undergoing abdominal aortic vascular surgery. This analysis is limited by lack of subgroup analysis to determine the role of gender or patient comorbid conditions in the cost-effectiveness of the strategy in question. When modeling the future surgical coronary revascularization, this analysis did not differentiate between conventional on-pump CABG and that of off-pump beating heart surgery. However, a meta-analysis suggests that the results of both surgical techniques are comparable with regard to short-term and midterm outcomes (59,60). The ultimate limitation of our study is that the results are based on outcomes and evidence from "other" studies, as is the case with any decision analytic models that use published data.

Finally, statins have shown to be beneficial in prevention of perioperative cardiovascular complications after vascular surgery (61). Specifically, their effects include stabilization of vulnerable plaques and improvement in endothelial function that are independent of lipid-decreasing effects. Ideally, the statin therapy is initiated at least 3 wk before surgery and continued postoperatively. The exact role and necessary timing of statin therapy being initiated in the setting of increasing cTnI levels in the postoperative setting is not clearly known. Therefore, the effects of statin therapy were not incorporated in the present model.

In summary, our decision analysis model suggests that, in patients presenting for elective open abdominal aortic surgery, intensive surveillance with cTnI and early institution of treatment is cost-effective when interpreted by comparing with published ICERs for commonly funded interventions. We believe that the results of our study could be used to plan future

research on the subject in a prospective design. In particular, the key factors that have cost-effectiveness of cardiac troponin surveillance identified in this study, i.e., probability of PMI and efficacy of interventions after surveillance, could be helpful in that regard.

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