

CLINICAL INVESTIGATIONS

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Do Shorter-acting Neuromuscular Blocking Drugs or Opioids Associate with Reduced Intensive Care Unit or Hospital Lengths of Stay after Coronary Artery Bypass Grafting?

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Background: The authors hypothesized that shorter-acting opioid and neuromuscular blocking drugs would be associated with reductions in duration of intubation, length of stay (LOS) in the intensive care unit (ICU) after tracheal extubation, or postoperative (exclusive of ICU) LOS, and that shorter durations of intubation would be associated with reduced ICU LOS after extubation and postoperative (exclusive of ICU) LOS.

Methods: One-thousand ninety-four patients undergoing primary coronary artery bypass graft surgery at 40 academic health centers were studied. Multiple patient-related factors were included in multivariate models for hypothesis testing.

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|| A full listing is provided in Appendix 1.

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Cardiology Preeminence Roundtable. Reducing Bypass Surgery Cost, vol. I. Aggressive Bypass Surgery Recovery: Decreasing Post-Operative Length of Stay. Washington, Advisory Board Company, 1993.

Results: The duration of tracheal intubation, ICU LOS after extubation, and postoperative (exclusive of ICU) LOS all varied significantly by site. There was no difference between vecuronium and pancuronium in duration of intubation, ICU LOS after extubation, or postoperative (exclusive of ICU) LOS. Use of sufentanil rather than fentanyl was associated with a significant ($P = 0.045$) reduction of 1.9 h (95% CI, 0.04 to 4.1 h) in duration of tracheal intubation but had no significant effect on ICU LOS after extubation, total ICU LOS, postoperative (exclusive of ICU) LOS, or total postoperative LOS. The authors' best model predicts a complex association between increasing duration of intubation and both ICU LOS after tracheal extubation and postoperative (exclusive of ICU) LOS, which was associated with an increase in those measures when duration of intubation exceeded 7.3 or 3 h, respectively.

Conclusions: The LOS measures varied considerably among the institutions. Use of shorter-acting opioid and neuromuscular blocking drugs had no association with ICU LOS after tracheal extubation or with postoperative (exclusive of ICU) LOS. Only when the duration of intubation exceeded threshold values was it associated with increased LOS measures. (Key words: Fentanyl; pancuronium; resource utilization; sufentanil; vecuronium.)

INSURANCE reimbursement for coronary artery bypass grafting (CABG), a resource-intensive procedure, has become increasingly limited. In response, hospitals and physicians have developed a myriad of strategies to reduce costs while maintaining or improving outcomes. An institution's ability to predict and control resource utilization and length of stay (LOS) can allow it to bid a competitive price to insurers. This may require reduced variation in patient management. Unnecessary variations in patient management may result in greater resource consumption but only rarely results in greater financial compensation or improved quality of care or outcomes.

Since the introduction of the intermediate-duration neuromuscular blocking drugs (NMBs) and the short-duration opioid sufentanil, many studies have docu-

mented the pharmacokinetic differences (*i.e.*, shorter context-sensitive half-lives) between these agents and older, longer-lasting agents.¹⁻⁴ Nevertheless, it remained unclear whether use of these newer agents in normal practice outside of a clinical trial would be associated with shorter durations of tracheal intubation or shorter postoperative LOSs. Similarly, although there has been considerable debate about the issue, it remains unsettled whether earlier extubation on the day of CABG surgery would consistently be associated with shorter subsequent postoperative LOS intervals.^{5,6}

For the past 4 yr, the University HealthSystem Consortium (UHC) has organized a benchmarking project to help its participating teaching hospitals remain competitive by identifying and reducing unnecessary variations in their processes of care for patients undergoing CABG.^{**††} (Benchmarking is a process that allows the UHC member institutions to assess their clinical performance in comparison with other, similar institutions on a year-to-year basis.) Using the most recent benchmarking data, we specifically tested two hypotheses related to perioperative management of patients undergoing CABG: That use of the intermediate-acting NMB vecuronium rather than the longer-acting pancuronium would be associated with earlier tracheal extubation and shorter LOS after CABG, and that use of the short-acting opioid sufentanil rather than the longer-acting fentanyl would be associated with earlier extubation and shorter LOS.

In a related analysis, we determined whether earlier tracheal extubation would be associated with shorter intensive care unit (ICU) LOS of extubated patients and shorter postoperative LOS outside the ICU. These latter analyses are important because they determine in a general way whether any strategy designed to reduce the duration of tracheal intubation will alter subsequent LOS intervals. To test these several hypotheses, we developed a model in which we could adjust for the demographic, historical, site-related, and other patient-related factors that predicted duration of tracheal intubation, ICU LOS after extubation, total ICU LOS, postoperative

(exclusive of ICU) LOS, and total postoperative LOS for CABG.

Methods

In November 1995, 40 of 44 participating academic health centers collected data for the CABG benchmarking project (see appendix 1 for a listing of academic health centers that contributed data). This project was initiated in 1993 by the Clinical Practice Advancement Center (Dr. David A. Burnett, Vice President of UHC, served as Director) to identify best practice features and to reduce practice variations in academic health centers.^{**††} Each institution was to gather data in an standardized manner using a common data collection form for 30 consecutive patients, aged 20 yr or older, who were undergoing their first CABG. Patients undergoing emergency surgery, "re-do" surgery, and those who died perioperatively were excluded. Although data were collected for the benefit of the member institutions and condensed versions were available for their use, our study represents an ancillary analysis that was conducted retrospectively after the overall and hospital-specific raw (with no adjustment for comorbid factors) results were reported to the members.

Trained abstractors collected preoperative and intraoperative data including age; sex; diagnosis-related group (DRG); weight; height; history (and time) of previous myocardial infarction (MI); history of congestive heart failure; history of cerebrovascular accident, transient ischemic attacks, or of cerebrovascular disease; diabetes mellitus; history of peripheral vascular disease; history of chronic obstructive pulmonary disease; history of hypertension; and preoperative LOS. Strict definitions were provided for each coding field to minimize ambiguity. Every data collection form was scrutinized by UHC personnel for data entry errors and omissions. When nonsensical entries or missing data were encountered, the data collection forms were returned to the member institutions for clarification or correction. These data were analyzed preliminarily by UHC personnel and reported back to the member institutions. In our analyses, duration of tracheal intubation was measured from the end of surgery until extubation. The ICU LOS after extubation included postoperative stays in the postanesthesia care unit (if any) and postoperative stays in the ICU for extubated patients. Postoperative (exclusive of ICU) LOS was measured from the time of transfer from ICU until hospital discharge. These three time in-

** Clinical Process Improvement Program. Clinical process improvement: Coronary artery bypass graft (CABG) clinical benchmarking data base. Report #1. Oakbrook, IL, University Hospital Consortium: Clinical Practice Advancement Center, 1995.

†† Clinical Process Improvement Program. Clinical process improvement: Coronary artery bypass graft (CABG) clinical benchmarking data base. Report #2. Oakbrook, IL, University HealthSystem Consortium Services Corp: Clinical Practice Advancement Center, 1996.

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tervals did not overlap. Total postoperative LOS measured from the end of surgery to hospital discharge was also tested in some analyses, as was total ICU LOS (without excluding duration of intubation). Returns to the ICU after an initial discharge from there were not included in our measures of ICU LOS; these times were included in our postoperative LOS measures.

The initial analysis of the data by UHC demonstrated differences among the member institutions in LOS and also the relative proportions of patients receiving fentanyl, sufentanil, pancuronium, and vecuronium. However, this initial descriptive analysis did not incorporate any adjustment for severity of illness or any other covariates, and therefore it did not directly address any of the three hypotheses tested by our analysis.

The data set was analyzed using the software "Proc Mixed" of SAS, version 6.12 (SAS Institute, Cary, NC). Mixed-effects regression models with hospital as a random effect were used to test for relations between the opioid or muscle relaxant used with the previously described LOS outcomes. Covariates taken from the database were also included in the model, as described subsequently here. Each of the LOS measures was judged to be log-normally distributed based on our inspection of the raw and logarithmically transformed distribution plots, and thus all were logarithmically transformed in the analyses and reported as geometric (rather than arithmetic) means when appropriate. The geometric mean is the anti-log of the mean of the logarithmically transformed data and is an unbiased estimator of the population median value. For geometric means, 95 confidence intervals (CIs) were determined.

A mixed-effects regression model was developed for each measure of resource utilization and was used to test our hypotheses regarding vecuronium *versus* pancuronium and sufentanil *versus* fentanyl and those regarding the effects of duration of intubation. Covariates included in all analyses were age; weight; DRG; sex; history of congestive heart failure, cerebrovascular disease, chronic renal failure, chronic obstructive lung disease, myocardial infarction; peripheral vascular disease; number of distal anastomoses; diabetes; operative urgency; and preoperative LOS. Left-ventricular ejection fraction, which had strong univariate associations with outcome measures in a preliminary analysis, was not included in the multivariate models because of frequent missing values. The mixed-effects models excluded an observation if any of the covariates was missing. Including ejection fraction in the model would have reduced the effective patient pool from 1,094 to 772. The contin-

Table 1. Demographic Characteristics of Patients

Variable	Amount
Total number	1,094
Age (yr) (mean \pm SD)	63 \pm 11
Male/female (N)	775/319
Weight (kg) (mean \pm SD)	83 \pm 17
Cerebrovascular disease (N, %)	104 (10)
Diabetes mellitus (N, %)	352 (32)
History of MI (N, %)	535 (49)
Peripheral vascular disease (N, %)	137 (13)
Left ventricular ejection fraction (mean \pm SD)	50 \pm 14
<30 (N, %)	60 (8)
30–50 (N, %)	278 (36)
>50 (N, %)	434 (56)
Operative status	
Elective (N, %)	757 (69)
Urgent (N, %)	337 (31)

Data are provided as incidences (N) and % of population, or as means \pm SD, as appropriate.

SD = standard deviation; MI = myocardial infarction; EJ = ejection fraction (based upon a sample size of 772 due to missing values).

uous covariates age and weight were modeled as quadratic rather than as linear functions, which allowed for curvilinear relations between the resource utilization measures and age or weight. DRG-covariate interactions were also included. The effect of duration of intubation on ICU LOS after extubation and on postoperative (exclusive of ICU) LOS was tested as both a linear and a quadratic function. Again, quadratic modeling allowed us to approximate curvilinear relations. Schwartz-Bayesian criteria were used to compare statistical models. An alpha level of 0.05 was considered significant. We made no corrections in probability values.

Results

A total of 1,164 CABG patients were enrolled, 70 of these were excluded from our analyses for missing covariates or perioperative death, yielding 1,094 usable data sets. Further reductions of 30–287 data sets occurred, depending on the analyses, because of missing drug or resource indicator information. The actual number of patients used in each analysis is provided in the tables. Cardiac catheterization was performed during the same admission as CABG surgery in 574 patients (DRG 106), whereas 520 patients underwent CABG surgery after having cardiac catheterization before the current hospital admission (DRG 107). Table 1 shows the

Table 2. Durations of Intubation and Lengths of Intensive Care Unit and Postoperative Hospital Length of Stay for Coronary Artery Bypass Surgery*

Measurement	Number of Patients	Geometric Mean	95% CI of Geometric Mean	Median	10th %ile	25th %ile	75th %ile	90th %ile
Duration of intubation (h)	1,045	14.4	(13.8, 15.1)	15.2	6.3	9.8	20.0	29.7
ICU LOS after extubation (h)	953	20.3	(19.1, 21.6)	19.7	6.3	10.6	36.4	67.5
Total ICU LOS (h)	1,023	37.4	(36.3, 39.6)	31.5	19.4	23.2	51.7	94.7
Postoperative (exclusive of ICU) LOS (days)	964	4.8	(4.7, 5.0)	4.6	3.1	3.7	5.9	8.1
Total postoperative LOS (days)	1,092	6.1	(5.9, 6.2)	5	4	5	7	11

ICU = intensive care unit; LOS = length of stay; CI = confidence interval.

* The differing number of patients resulted from missing data.

demographic characteristics of the patients. Table 2 shows the LOS characteristics (without covariate adjustments) of this patient population as a whole.

Duration of intubation ($P < 0.00001$), ICU LOS after extubation ($P < 0.00001$), and postoperative (exclusive of ICU) LOS ($P = 0.026$) varied significantly by site, as shown in figure 1 and confirmed by Schwartz-Bayesian criteria (comparing statistical models either adjusted or not adjusted for hospital site in both cases, including all other covariates).

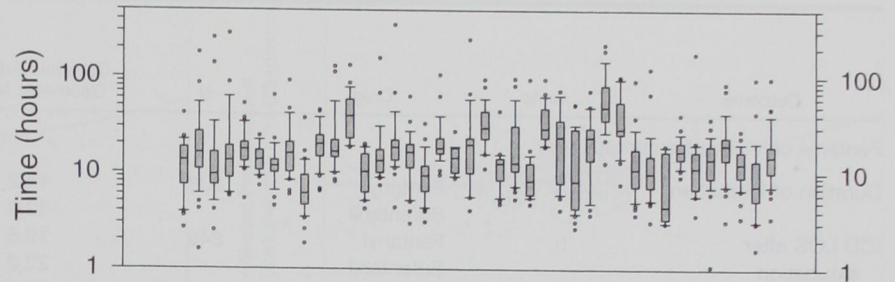
Patients who received sufentanil almost never received fentanyl, and vice versa; however, many patients received both vecuronium and pancuronium (table 3). Therefore, we compared patients receiving only vecuronium ($n = 130$) with patients receiving only pancuronium ($n = 732$); we also compared patients who did not receive vecuronium (*i.e.*, those receiving only pancuronium) ($n = 732$) with all those who received vecuronium (some of whom also received pancuronium; $n = 242$). No significant differences were evident in any of the LOS measurements between patients receiving vecuronium or pancuronium. One hundred ninety-six patients received sufentanil but not fentanyl. The 19 patients who received both fentanyl and sufentanil were not included in the analysis. Eight hundred twenty-four patients received only fentanyl. The probability values for these comparisons were made using our covariate-adjusted mixed-effects models (table 3). Patients who received sufentanil had significantly shorter ($P = 0.04$) durations of tracheal intubation than did those who received fentanyl. The geometric means (12.2 and 14.2 h using our full covariate-adjusted model for sufentanil and fentanyl, respectively) differed by 1.9 h (95% CI, 0.04 to 4.1 h). On the other hand, there were no other significant differences in resource utilization between patients receiving either sufentanil or fentanyl.

We tested for an association between duration of intubation and ICU LOS after extubation and postoperative (exclusive of ICU) LOS using our full statistical model, adjusting for covariates and covariate-DRG interactions, as described in Methods. The outcome measures we illustrate in this section reflect these adjustments. Figures 2 and 3 show an association between intubation duration and ICU LOS after tracheal extubation and postoperative (exclusive of ICU) LOS. A quadratic curve best approximates the relation between the full range of intubation times ($n = 952$) and the adjusted (for covariates) ICU LOS after extubation (table 4). The quadratic relation predicts that only when duration of tracheal intubation exceeds 7.3 h will increasing duration of intubation be associated with increasing ICU LOS after extubation (fig. 2). Similarly, the association between intubation duration and the adjusted postoperative (exclusive of ICU) LOS were best described by a quadratic model when using all the data (table 5 and fig. 3, $n = 963$). The quadratic model predicted a threshold value of 3 h, above which increasing duration of tracheal intubation was associated with increasing postoperative (exclusive of ICU) LOS. In short, our data suggest that there are limits below which further reductions in intubation time will have an effect on subsequent LOS intervals.

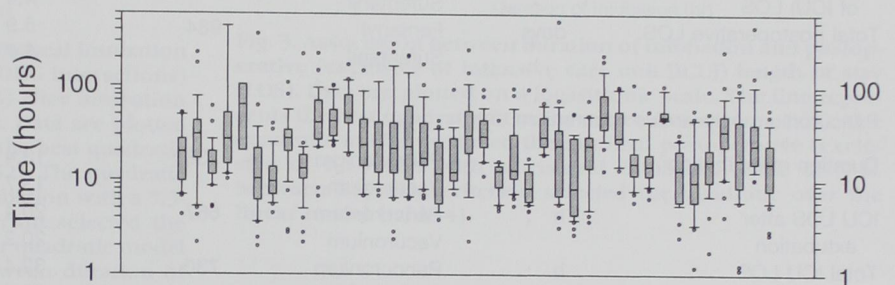
Discussion

Ideally, clinical process improvement provides a systematic method to identify, benchmark, and integrate optimal care by linking defined patient characteristics and clinical processes with measurable quality and efficiency outcomes.***†† Because the UHC CABG benchmarking project is a relatively new effort and care of

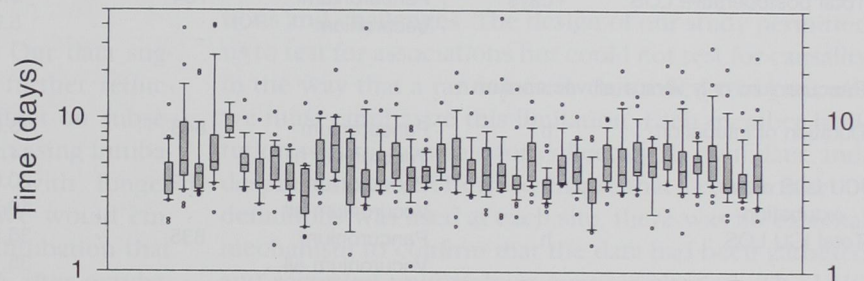
Duration of Intubation



ICU LOS after Extubation



Postoperative (exclusive of ICU) LOS



Individual Hospitals

Fig. 1. Effect of medical center on duration of tracheal intubation, intensive care unit (ICU) length of stay (LOS) after extubation, and postoperative (exclusive of ICU) LOS. Box plots were constructed from the data submitted by each participating center. The boxes denote the range from the 25th to 75th percentiles. The bars denote the median values. The "whiskers" include the 10th to 90th percentiles. Data points falling outside the 10th to 90th percentile range are plotted individually. The effect of center was significant with $P < 0.00001$ for the duration of intubation, $P < 0.00001$ for the ICU LOS after extubation, and $P = 0.026$ for the postoperative (exclusive of ICU) LOS.

the patient undergoing CABG surgery is continuously evolving, we were not surprised to find considerable variation among the institutions in the outcome variables that we studied. Even after we controlled for the degree of patient illness and other covariates, we could not account for much of this variation by center. Therefore, we attribute most of the variation that we observed to differing clinical practice styles.

We found no evidence for outcome benefit from using the considerably more expensive shorter-acting vecuronium compared with the less expensive, longer-acting pancuronium.^{#4} We identified a statistically significant 1.9-h reduction in covariate-adjusted duration of intuba-

tion when patients received sufentanil rather than fentanyl, consistent with differences in the two drug's pharmacokinetic properties.¹⁻³ This difference may not be clinically important in the context of covariate-adjusted geometric mean tracheal intubation times of 12-14 h and the lack of significant differences in ICU LOS after extubation or postoperative (exclusive of ICU) LOS. The limited benefit of the shorter-acting drugs strongly supports the idea that institutional preferences and peculiarities of physician practice patterns have greater influence than drug choice on resource utilization.^{#7}

Increasing duration of tracheal intubation had a com-

Table 3. Effects of Opioid and Neuromuscular Blocking Drug Choice on Duration of Intubation and Length of Stay

Outcome	Units	Drug	N	Covariate Adjusted Geometric Means	95% Confidence Limits		P Values
					Lower	Upper	
Fentanyl only versus sufentanil only							
Duration of intubation	h	Fentanyl	938	14.2	12.6	16.0	0.04
		Sufentanil		12.2	10.4	14.4	
ICU LOS after extubation	h	Fentanyl	849	19.6	16.5	23.2	0.20
		Sufentanil		22.2	17.6	27.9	
Total ICU LOS	h	Fentanyl	917	36.2	32.1	40.8	0.96
		Sufentanil		36.3	30.9	42.7	
Postoperative (exclusive of ICU) LOS	days	Fentanyl	859	4.7	4.5	5.0	0.13
		Sufentanil		4.4	4.0	4.8	
Total postoperative LOS	days	Fentanyl	984	5.9	5.5	6.2	0.54
		Sufentanil		5.7	5.3	6.2	
Pancuronium only versus vecuronium only							
Duration of intubation	h	Pancuronium	738	13.4	11.8	15.1	0.75
		Vecuronium		13.7	11.5	16.3	
ICU LOS after extubation	h	Pancuronium	667	20.4	17.1	24.3	0.94
		Vecuronium		20.2	15.8	25.8	
Total ICU LOS	h	Pancuronium	730	32.4	32.4	41.7	0.83
		Vecuronium		30.4	30.4	42.9	
Postoperative (exclusive of ICU) LOS	days	Pancuronium	677	4.8	4.5	5.1	0.72
		Vecuronium		4.7	4.2	5.2	
Total postoperative LOS	days	Pancuronium	784	6.0	5.6	6.3	0.85
		Vecuronium		5.9	5.4	6.3	
Pancuronium only versus all vecuronium							
Duration of intubation	h	Pancuronium	848	13.6	12.0	15.4	0.51
		Vecuronium all		14.1	12.2	16.4	
ICU LOS after extubation	h	Pancuronium	769	20.5	17.3	24.3	0.64
		Vecuronium all		19.7	16.1	24.2	
Total ICU LOS	h	Pancuronium	835	36.5	32.2	41.4	0.72
		Vecuronium all		35.7	30.8	41.5	
Postoperative (exclusive of ICU) LOS	days	Pancuronium	780	4.7	4.4	5.0	0.83
		Vecuronium all		4.7	4.4	5.1	
Total postoperative LOS	days	Pancuronium	895	5.9	5.6	6.3	0.84
		Vecuronium all		5.9	5.5	6.3	

LOS = length of stay; Fentanyl only = those receiving fentanyl, but not sufentanil; Sufentanil only = those receiving sufentanil, but not fentanyl; Pancuronium only = those receiving pancuronium, but not vecuronium; Vecuronium only = those receiving vecuronium only, but not pancuronium; Vecuronium all = those receiving vecuronium (who may also have received pancuronium).

plex association with ICU LOS after extubation and with postoperative (exclusive of ICU) LOS. Our data suggest that those associations are not well described using a simple linear model. We found no evidence that decreasing covariate-adjusted intubation time to <7.3 h would decrease ICU LOS after extubation. Our results could indicate that most patients will spend most of the first postoperative day in the ICU, regardless of whether they remain intubated. Those who are extu-

bated earlier in the day will spend a longer time in the ICU after extubation compared with those who are extubated later, but still they are discharged from the ICU by the next morning. Using our covariate-adjusted quadratic model, we also found that when duration of intubation exceeded 7.3 h, ICU LOS after extubation also tended to increase. This could result from an increased incidence of perioperative complications (e.g., stroke or respiratory or renal failure) in patients with

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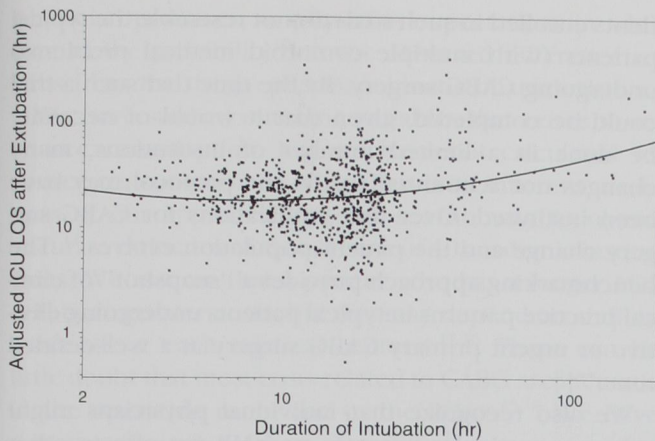


Fig. 2. Association between the duration of tracheal intubation and adjusted (for covariates and covariate-DRG interactions) intensive care unit (ICU) length of stay (LOS) after intubation after adjustment using our statistical model. Data are plotted on a logarithmic scale. The line represents the best quadratic fit to the covariate-adjusted data set (n = 952). The quadratic model predicted minimal ICU LOS after extubation with a 7.3-h intubation time. Schwartz-Bayesian criterion selected the quadratic over the linear model (table 3). Our quadratic model does not predict a positive association between duration of intubation and increasing ICU LOS after extubation when tracheal intubation lasted <7.3 h.

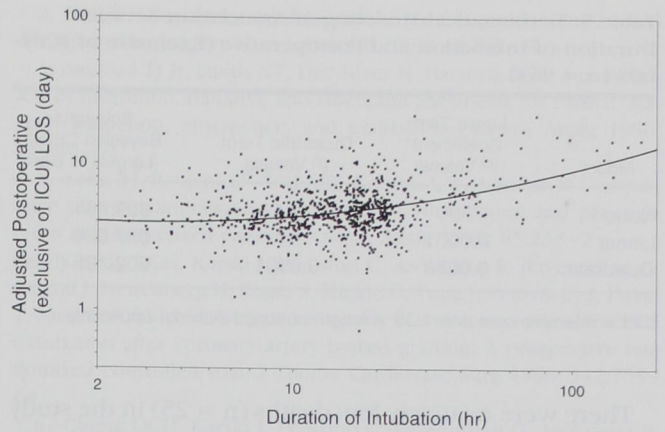


Fig. 3. Association between duration of intubation and postoperative (exclusive of intensive care unit [ICU]) length of stay (LOS). Data are plotted on a logarithmic scale. The line represents the best quadratic fit to the entire data set (n = 963). The quadratic model predicted the minimal postoperative (exclusive of ICU) LOS with a tracheal intubation time of 3 h. Schwartz-Bayesian criterion selected the quadratic over the linear model (table 4).

longer durations of tracheal intubation. Our data suggest that there are limits below which further reductions in intubation time will have no effect on subsequent LOS intervals. In a similar way, increasing intubation times to >3 h was associated with longer postoperative (exclusive of ICU) LOS. We would emphasize that the threshold durations of intubation that were associated with increased ICU LOS after extubation or increased postoperative (exclusive of ICU) LOS likely vary among institutions.

The UHC Benchmarking data do not supply dosing information or identify possible LOS-extending complications of the surgery. Thus we were could not perform a standard cost-effectiveness study. However, it is unlikely that choice of anesthetic drug could result in relevant cost savings, improved patient prognosis, or a longer life span. Our analysis documented only a minimal difference in utility between the opioids and no difference between the two NMBs. Nevertheless, the costs of these drugs, even when generic (\$14.59 versus \$1.19 per 10-mg vial for vecuronium and pancuronium,

respectively),^{‡‡} are trivial in the context of the overall patient charge for CABG surgery.

Analysis of our database presents inevitable limitations and challenges. The design of our study permitted us to test for associations but could not test for causality in the way that a randomized, controlled trial can, and we must emphasize this limitation. Each member institution was responsible for collecting its own data, and, despite extensive efforts to ensure that a common set of definitions was used at each site, there was no external mechanism to confirm that the data had been gathered and recorded uniformly in every institution. The UHC personnel responsible for collecting and collating data had no vested interest in the outcome of the analysis we report here and were not aware that we would test our three hypotheses using the benchmarking data; thus these personnel would be a remote source of bias.

Table 4. Mathematical Modeling of Association between Duration of Intubation and ICU LOS after Extubation (n = 952)

Model	Linear Term Coefficient (P Values)	Quadratic Term (P Values)	Schwartz-Bayesian Criteria (Largest is Best)
None	NA	NA	-1290.55
Linear	0.0001	NA	-1285.31
Quadratic	0.0001	0.0001	-1265.13 (best)

ICU = intensive care unit; LOS = length of stay; NA = not applicable.

^{‡‡} Personal written communication to Dr. Butterworth from the Pharmacy Department, North Carolina Baptist Hospital, Winston-Salem, North Carolina, May 2, 1997.

Table 5. Mathematical Modeling of Association between Duration of Intubation and Postoperative (Exclusive of ICU) LOS (n = 963)

Model	Linear Term Coefficient (P Values)	Quadratic Term (P Values)	Schwartz-Bayesian Criteria (Largest is Best)
None	NA	NA	-699.464
Linear	0.0001	NA	-627.526
Quadratic	0.0088	0.0001	-602.125 (best)

ICU = intensive care unit; LOS = length of stay; NA = not applicable.

There were relatively few deaths (n = 25) in the study population. Had large numbers of patients died during or immediately after CABG (and had we included these patients in our LOS analyses), our estimates of LOS might have been skewed. We examined the case records of these 25 patients and determined that their use of fentanyl, sufentanil, vecuronium, and pancuronium was in no way different from that of the surviving patients. The data did not identify individual physicians, so we could not draw any conclusions about the role of individual physicians in controlling the outcome variables.^{7,8} Nevertheless, using hospital as a surrogate for the physicians practicing there, we found that the institution in which a patient underwent CABG had a highly significant association with duration of tracheal intubation, ICU LOS after extubation, and postoperative (exclusive of ICU) LOS, even after adjusting for comorbid medical illnesses and other covariates.

It could be argued that the best way to compare relaxants or narcotics during CABG surgery would be to conduct a prospective, blinded clinical trial. In such a trial, randomization could ensure that patients receiving either one of the paired agents would have comparable comorbid factors and would be treated using a similar algorithm by a relatively small number of physicians.⁹ The controlled clinical trial format would also serve to ensure that individual hospital preferences and practices would not influence the pure comparison of the agents. On the other hand, we would argue that the controlled clinical trial would ignore the very factors most important in determining whether one agent is better than another in clinical practice; that is, how the individuals who prefer the agent choose to use it. A clinical trial tries to eliminate variance produced by the physician-drug interaction; however, this variance likely makes major contributions to LOS and cost (for review, see Spilker¹⁰). Controlled clinical trials are typically restrictive, with many exclusion criteria. The pa-

tients enrolled in such trials do not resemble the typical patients (with multiple comorbid medical problems) undergoing CABG surgery. By the time that such a trial could be completed, given that it would of necessity be done in a limited number of institutions, many changes not accounted for by the protocol may have been instituted. Over time, indications for CABG surgery change and the patient population evolves.¹¹ The benchmarking approach provides a "snapshot" of clinical practice patterns in typical patients undergoing elective or urgent primary CABG surgery at a well-defined time.^{**††}

We also recognize that individual physicians might prefer a particular narcotic or NMB for effects other than to influence the three outcome variables we studied. For example, a clinician might be concerned that an occasional patient may develop sufficient tachycardia after receiving pancuronium to lead to myocardial ischemia.¹² If many patients receiving pancuronium required a β -adrenergic receptor blocker to restore a safe heart rate, pancuronium might represent an overall more expensive choice than vecuronium, despite pancuronium's very small acquisition cost. The data we collected for our benchmarking project do not permit us to address this issue. Because effects on heart rate are sometimes cited as a potential advantage of vecuronium compared with pancuronium for CABG surgery, we note that during fentanyl anesthesia, when pancuronium was compared with vecuronium, or with pipecuronium and doxacurium (which are newer and much more costly long-acting NMBs with almost no tendency to increase heart rate), pancuronium was found uniformly to require fewer drug interventions to control heart rate and blood pressure than the other NMBs.^{13,14}

It is likely that the physicians caring for the patients in this database may not have made equivalent efforts to minimize the duration of tracheal intubation or ICU or hospital LOS. On the other hand, the institutions participating in this project chose to do so to compare their resource utilization with that of other comparable academic medical centers. Compared with the 1994 benchmark study, the average LOS decreased by >1 day in the 1995 data base.^{**††} Thus we are confident that physicians in each unit were making an attempt, some more effectively than others, to reduce LOS and resource utilization, regardless of the narcotic or NMB drug they chose to use. Indeed, the underlying cause of the statistically significant difference in duration of tracheal intubation that we observed between sufentanil and fentanyl could be differences in drug dosing,

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physician practices, or physician expectations in addition to the possibility that the observed difference results from the drugs' pharmacokinetic characteristics.

We have studied outcome variables that relate to resource consumption, but we have not calculated resource consumption or costs. This is an inherent weakness of our approach, but we see no way to obtain accurate estimates of cost at each of 40 academic institutions. We assume that a patient who has a longer LOS will have greater costs, but this may depend on staffing practices at each medical center.^{15,16} There can be little doubt that most costs related to CABG are incurred in the operating room and in the ICU.^{15,16} We have not measured any markers of quality of care or of quality of life, and we recognize that these factors are more important than cost or LOS to most patients, families, and physicians.^{9,10,17,18}

In conclusion, despite articles that promote the value of newer shorter-acting agents to achieve earlier tracheal extubation after CABG surgery, in actual practice, patients receiving the less-expensive, longer-acting pancuronium tended to have durations of tracheal intubation, ICU LOS after extubation, and postoperative (exclusive of ICU) LOS that were comparable to those of patients receiving vecuronium. Use of sufentanil rather than fentanyl was associated with a small but statistically significant reduction in duration of tracheal intubation but had no effect on ICU LOS after extubation, total ICU LOS, postoperative (exclusive of ICU) LOS, or total postoperative LOS. Consistent with the work of Cheng *et al.*,^{5,6} we found an association between longer durations of intubation with longer postoperative (exclusive of ICU) LOSs. On the other hand, with adjusted intubation times <7.3 h, we found only limited or no positive association with other outcome variables. Our analyses and the marked variability among institutions suggest that reductions in LOS and costs could be accomplished through reduction of intubation times to <7.3 h, earlier transfer from the ICU, and more efficient and coordinated scheduling, particularly if this were combined with an aggressive, proactive approach to recovery and hospital discharge. An emphasis on which opioid or NMB is to be used for CABG surgery may be less useful than a coordinated program with full cooperation from patients, families, physicians, nurses, and other allied health professionals.

References

1. Shafer SL, Varvel JR: Pharmacokinetics, pharmacodynamics, and rational opioid selection. *ANESTHESIOLOGY* 1991; 74:53-63

2. Hall R: The pharmacokinetic behaviour of opioids administered during cardiac surgery. *Can J Anaesth* 1991; 38:747-56

3. Sanford TJ Jr, Smith NT, Dec-Silver H, Harrison WK: A comparison of morphine, fentanyl, and sufentanil anesthesia for cardiac surgery: Induction, emergence, and extubation. *Anesth Analg* 1986; 65:259-66

4. Sohn YJ, Bencini AF, Scaf AHJ, Kerslen UW, Agoston S: Comparative pharmacokinetics and dynamics of vecuronium and pancuronium in anesthetized patients. *Anesth Analg* 1986; 65:233-9

5. Cheng DCH, Karski J, Peniston C, Asokumar B, Raveendran G, Carroll J, Neirenberg H, Roger S, Mickle D, Tong J, Zelovitsky J, David T, Sandler A: Morbidity outcome in early versus conventional tracheal extubation after coronary artery bypass grafting: A prospective randomized controlled trial. *J Thorac Cardiovasc Surg* 1996; 112:755-64

6. Cheng DCH, Karski J, Peniston C, Raveendran G, Asokumar B, Carroll J, David T, Sandler A: Early tracheal extubation after coronary artery bypass graft surgery reduces costs and improves resource use. A prospective, randomized, controlled trial. *ANESTHESIOLOGY* 1996; 85:1300-10

7. Zander K: Collaborative care: Two effective strategies, Managing Outcomes through Collaborative Care. The Application of Caremapping and Case Management. Edited by K Zander. Chicago: American Hospital Association, 1995, pp 1-38

8. Butterworth JF IV: Clinical pathways for the high-risk patient. *J Cardiothorac Vasc Anesth* 1997; 11(suppl 1):16-8

9. Friedman LM, Furberg CD, DeMets DL: Fundamentals of Clinical Trials, 3rd edition. St. Louis, Mosby-Year Book, 1996

10. Spilker B: Quality of Life and Pharmacoeconomics in Clinical Trials. Philadelphia, Lippincott-Raven Publishers, 1996

11. Jones EL, Weintraub WS, Craver JM, Guyton RA, Cohen CL: Coronary bypass surgery: Is the operation different today? *J Thorac Cardiovasc Surg* 1991; 101:108-15

12. Thomson IR, Putnins CL: Adverse effects of pancuronium during high-dose fentanyl anesthesia for coronary artery bypass grafting. *ANESTHESIOLOGY* 1985; 62:708-13

13. Gravlee GP, Ramsey FM, Roy RC, Angert KC, Rogers AT, Pauca AL: Rapid administration of a narcotic and neuromuscular blocker: A hemodynamic comparison of fentanyl, sufentanil, pancuronium, and vecuronium. *Anesth Analg* 1988; 67:39-47

14. Rathmell JP, Brooker RF, Prielipp RC, Butterworth JF IV, Gravlee GP: Hemodynamic and pharmacodynamic comparison of doxacurium and pipecuronium with pancuronium during induction of cardiac anesthesia: Does the benefit justify the cost? *Anesth Analg* 1993; 76:513-9

15. Smith LR, Milano CA, Molter BS, Elbeery JR, Sabiston DC Jr, Smith PK: Preoperative determinants of postoperative costs associated with coronary artery bypass graft surgery. *Circulation* 1994; 90(part 2):II-124-8

16. Mauldin PD, Weintraub WS, Becker ER: Predicting hospital costs for first-time coronary artery bypass grafting from preoperative and postoperative variables. *Am J Cardiol* 1994; 74:772-5

17. Dupuis J-Y, Wynands JE: Risk-adjusted mortality to assess quality of care in cardiac surgery [Editorial]. *Can J Anaesth* 1993; 40:91-7

18. Hammermeister KE, Johnson R, Marshall G, Grover FL: Continuous assessment and improvement in quality of care. A model from the Department of Veterans Affairs cardiac surgery. *Ann Surg* 1994; 219:281-90

Appendix 1. Academic Health Centers Contributing to the 1996 CABG Clinical Benchmarking Data Base

- Crawford Long Hospital of Emory University, Atlanta, Georgia
 Emory University Hospital, Atlanta, Georgia
 Froedtert Memorial Lutheran Hospital, Inc., Milwaukee, Wisconsin
 Hermann Hospital at the University of Texas Health Science Center, Houston, Texas
 Indiana University Medical Center, Indianapolis, Indiana
 John Dempsey Hospital, The University of Connecticut Health Center, Farmington, Connecticut
 Louisiana State University Medical Center, New Orleans, Louisiana
 Loyola University Medical Center, Maywood, Illinois
 Medical College of Georgia Hospital & Clinics, Augusta, Georgia
 Medical College of Ohio Hospital, Toledo, Ohio
 Medical College of Virginia Hospital, Virginia Commonwealth University, Richmond, Virginia
 Medical University of South Carolina, Charleston, South Carolina
 New York University Medical Center, New York, New York
 The Ohio State University Medical Center, Columbus, Ohio
 Oregon Health Sciences University Hospital & Clinics, Portland, Oregon
 Pennsylvania State University/Milton S. Hershey Medical Center, Hershey, Pennsylvania
 Robert Wood Johnson University Hospital, Hamilton, New Brunswick, & Trenton, New Jersey
 Stanford University Hospital, Stanford, California
 State University of New York Medical Center of Stony Brook, Stony Brook, New York
 Thomas Jefferson University Hospital, Philadelphia, Pennsylvania
 University Medical Center Corporation, Arizona, Tucson, Arizona
 University of Alabama Hospital, Birmingham, Alabama
 University of California Irvine Medical Center, Irvine, California
 University of California Los Angeles Medical Center, Los Angeles, California
 The University of Chicago Hospital & Health System, Chicago, Illinois
 The University of Illinois at Chicago Medical Center, Chicago, Illinois
 The University of Kansas Hospital, Kansas City, Kansas
 University of Kentucky Hospital, Lexington, Kentucky
 University of Massachusetts Medical Center, Worcester, Massachusetts
 The University of Medicine & Dentistry of New Jersey, University Hospital, Newark, New Jersey
 University of Minnesota Hospital & Clinics, Minneapolis, Minnesota
 University of Missouri Hospital & Clinics, Columbia, Missouri
 University of Nebraska Medical Center, Omaha, Nebraska
 University of North Carolina Hospitals, Chapel Hill, North Carolina
 University of Virginia Health Science Center, Charlottesville, Virginia
 University of Washington Academic Medical Center, Seattle, Washington
 Vanderbilt University Hospital & Clinic, Nashville, Tennessee
 Wake Forest University Baptist Medical Center, Winston-Salem, North Carolina
 West Virginia University Hospitals, Morgantown, West Virginia
 Yale-New Haven Hospital, New Haven, Connecticut