Experience and Attitudes of Surgeons Toward Palliation in Cancer

Joseph M. Galante, MD; Tawnya L. Bowles, MD; Vijay P. Khatri, MD; Philip D. Schneider, MD, PhD; James E. Goodnight, Jr, MD, PhD; Richard J. Bold, MD

Background: Surgery can effectively palliate symptoms in patients with advanced malignancy and thereby maintain quality of life. However, the goal of surgical palliation should be balanced with the associated risks, and the decision to operate can be challenging for even the most experienced surgeon.

Hypothesis: There are significant deficiencies in training during residency and in continuing medical education in palliative surgical care leading to a lack of agreement for treatment recommendations.

Design and Setting: A survey of general surgeons involving 4 clinical vignettes of patients with advanced malignancies and varying degrees of symptoms. Respondents were asked to select the best treatment option for each patient from a list of 6 alternatives. Furthermore, respondents identified the clinical factors that most influenced the decision, as well as the major goal of the palliative intervention.

Subjects: Surgeons in a midsized urban setting and its surrounding region.

Results: Of 124 surveys sent out, 70 (56%) were completed. Significant deficiencies in education were identified; 59 (84%) of the respondents did not receive any education in palliative surgical care during residency and 28 (44%) lacked continuing medical education. A consensus treatment recommendation was not selected in 3 of the 4 clinical vignettes, but the respondents used similar clinical factors and goals of treatment for selection of the specific recommendation.

Conclusions: Palliative care is a major deficiency of postgraduate surgical training. A more focused effort in training surgeons in palliative care may allow for the more uniform and standard provision of palliative surgical care to patients with advanced cancer.

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The decision for surgical intervention in patients with cancer involves numerous factors that both the surgeon and patient weigh carefully before proceeding to an operation. Each surgical intervention has associated risks and benefits; determining an acceptable balance of these factors can be challenging for even the most experienced surgeon. The decision-making process is even more complicated in patients presenting with advanced malignancies when there is little hope of cure. In these patients, the benefit of surgery may not be curative but focused on the treatment or prevention of disease-related symptoms. The relief of symptoms from palliative surgery can lead to an improvement in the quality of life without having a direct effect on the length of survival.

Surgeons, however, receive little training in palliative care and the evaluation of surgical options in patients with incurable malignancies. Lee et al reported that half of surgeons have received no training in medical school and that almost 25% of surgical oncologists have had no continuing medical education (CME) in palliative care. McCahill and colleagues further point out that limited attention is paid to surgical palliative care, even in the field of palliative medicine. In the Oxford Textbook of Palliative Medicine, only 16 (1%) of its 1283 pages focus on the role of surgery in palliation. This lack of education may cause surgeons to fail to offer all valid treatment options to patients with end-stage malignancies. Furthermore, with the variation in surgical subspecialties, the treatment options offered by one group of surgeons may be dramatically different from those offered by another group.

We sought to determine the educational background of a diverse group of surgeons, as well as their opinions and attitudes toward palliative surgical treatment in patients with advanced malignan-
nancy harboring various symptomatic disease processes. Our goal was the identification of potential areas of deficiency in education that may serve as the focus of CME. Furthermore, we wished to determine whether there are consensus treatment recommendations for palliative intervention in patients with advanced malignancy and a variety of common symptomatic presentations.

We surveyed surgeons in Sacramento, Calif, and the surrounding region after approval from the institutional review board of the University of California, Davis, Medical Center, Sacramento. Surgeons were identified through their membership in the Sacramento Surgical Society or the physician rosters at 8 hospitals in the Sacramento region. Attending surgical staff and surgical trainees in their last year of residency or fellowship at the University of California, Davis, were included in the study group. The survey was performed between August 1, 2004, and November 30, 2004. Each participant was sent the survey with a cover letter explaining the purpose of the study. The survey was conducted in an anonymous fashion so that individual responses could not be linked to a specific surgeon. To improve the response rate, a second mailing of the survey was sent to each participant 2 months after the first. The cover letter in the second mailing instructed only those who had not completed the survey the first time to complete it.

The demographics section of the survey asked for age, sex, surgical specialty, fellowship training, years since training, practice setting, and number of cases per year. Respondents were also asked to list the percentage of their practice spent in surgical specialty, fellowship training, years since training, practice setting, and number of cases per year. Respondents were also asked to list the percentage of their practice spent in surgical specialty, fellowship training, years since training, practice setting, and number of cases per year.

The remainder of the survey consisted of 4 clinical vignettes. These involved patients with advanced malignancies and various symptoms. The vignettes were based on published case scenarios and clinical experiences. Additional information, such as comorbid illness, living wills, or antecedent patient wishes, were specifically omitted to allow identification of the preferred treatment selection in the absence of variables that may have confounded surgical recommendations. These 4 clinical vignettes are summarized as follows:

- **Case 1.** A healthy 55-year-old man with a history of poorly differentiated adenocarcinoma of the appendix who presents to the emergency department with a complete bowel obstruction and an elevated white blood cell count of 15,000 cells/mL.
- **Case 2.** A 70-year-old man, recently diagnosed as having an adenocarcinoma of the lung, who presents with recurrent gastrointestinal tract bleeding localized to the proximal jejunum. During the current hospitalization, he has been transfused 6 U of blood.
- **Case 3.** A 55-year-old woman undergoing chemotherapy for stage IV breast cancer (liver metastasis) who has sustained multiple injuries from a high-speed motor vehicle crash. Five days after the injury, she remains intubated in the intensive care unit with evidence of entrapment of her left lung.
- **Case 4.** An active 65-year-old man with a history of metastatic prostate cancer who is found to have a symptomatic, non-incarcerated inguinal hernia. His prostate cancer is asymptomatic and has required no therapy.

For each scenario, respondents were asked to select the single best treatment option from a list of preset choices that ranged from major surgical intervention to hospice/withdrawal of care. Major surgical intervention consisted of options such as bowel resection (case 1) or thoracotomy (case 3), whereas minor surgical intervention consisted of options such as gastrostomy tube (case 1) or thoracostomy tube (case 3). Surgeons were also asked to identify the goals of the intervention chosen and then to rank the 3 most important factors that influenced their decision for the selection of preferred treatment (Table 1). Responses were collected and stored in a database. Results were tabulated and analyzed using the unpaired, 2-tailed t test, χ² analysis, and the 2-tailed Fisher exact test.

Of the 124 surveys sent, 70 were returned after 2 mailings for a response rate of 56%. Of these 70, 17 respondents (24%) added comments to their survey response. These comments generally reflected that important issues in clinical decision making that may affect the treatment selection were not included in the vignettes; the presence of comorbid illnesses and patient wishes were the most frequently cited pieces of additional informa-

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<th>Table 1. Questions Asked in Response to Each of the Clinical Vignettes*</th>
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<td><strong>For Each Scenario</strong></td>
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<td>Nonsurgical management with surgical intervention if patient does not improve</td>
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*Respondents were asked to select a single best treatment option, identify the 3 most important factors influencing the selection decision, and select the major goal of the intervention.
tion indicated as being essential for selecting optimal palliative surgical care. Most of the respondents (87%) were male; the average age was 50 years (Table 2). Thirty-three of the respondents (47%) had completed fellowship training in various specialties; of these advanced surgical specialties, the most common were critical care (11 [33%] of 33 respondents), vascular surgery (5 [15%]), and surgical oncology (5 [15%]). When the respondents were asked to characterize their practices, the most common designations were general surgery (30%), surgical oncology (33%), and trauma/critical care (11%). The average length of surgical practice was 18 years, with an average yearly caseload of 290. The practice setting was evenly divided among a university-based setting (30%), private practice (33%), and a community setting with trainees (30%). Seven trainees responded, constituting 10% of the respondents.

Forty-three (61%) of the 70 respondents reported having received some form of education in palliative care, although the overall amount was extremely limited. The median number of hours of such education during surgical residency was 0; 59 (84%) of the 70 received no palliative care education during residency (Table 3). Among the 11 respondents who reported having received some form of palliative care education, the mean length of educational training was 6 hours. The median number of hours during a specialty fellowship was 0; 29 (85%) of the 34 respondents who acquired fellowship training received no further education in palliative care during that training. Among the 5 respondents who reported some form of palliative care education during a specialty fellowship, the mean length of training was 9 hours.

Excluding the 7 trainees, only 35 (56%) of the 63 respondents reported having received additional education in palliative care medicine through various CME sources (Table 3). The median length of career experience of CME education in palliative care was only 4 hours; the mean length was 9 hours over a career, which translated to only 30 min/y for the average 18-year practice. The primary format of CME in palliative care medicine was lectures or courses (25 of the 35 respondents [71%]), followed by journal articles (16 [46%]). The American College of Surgeons has taken a leading role in promoting palliative care education by publishing a series on palliative care issues in their Journal of the American College of Surgeons. Thirty-three (47%) of the 70 respondents reported having read any of the articles within the series. Of those, 9 (27%) reported no other sources of education in palliative care.

Among the 4 clinical vignettes, only for the fourth scenario (the patient with the symptomatic inguinal hernia) was a treatment option selected by a majority of respondents (Figure 1). For that scenario, 67 (96%) of the 70 respondents selected the major surgical intervention of inguinal herniorrhaphy. Although surgical intervention was selected to some degree in the other 3 vignettes, no single treatment option was selected by a majority of the respondents for those scenarios. Surgical palliation remained a viable option, however; in the first 2 clinical vignettes 29 respondents (41%) and 25 (36%), respectively, indicated that they would proceed to surgery if no improvement was observed after conservative medical therapy. The nonsurgical treatment was rarely selected and never constituted more than 10% of the responses.

When asked what factors influenced the treatment decision, functional status of the patient, expected survival time, and potential for pain or symptom relief were consistently chosen from among the 10 options in all 4 scenarios (Figure 2). In addition, functional status of the patient and potential for pain or symptom relief were consistently among the most important factors for recommending the specific treatment option in all 4 clinical scenarios (Table 4). The least common factors were
age of the patient and aggressiveness of the tumor (data not shown). Therefore, despite the lack of a consensus treatment recommendation in 3 of the 4 clinical vignettes, most of the surgeons were using similar criteria to select a treatment option. When the broad goals of the intervention were examined, the respondents recognized the importance of relief of symptoms and cure of the acute disease as the ultimate purposes of palliative care medicine (Figure 3).

Given our observation that a significant fraction of the respondents lacked prior CME education in palliative care, we sought to determine whether the presence or absence of CME influenced the selection of a treatment option (Figure 4). We found that the respondents lacking prior CME experience in palliative care were more likely to recommend a major surgical intervention for the patients in the first 3 clinical scenarios, although the difference reached statistical significance only in case 2 ($P = .02$). Furthermore, the respondents lacking prior CME experience were statistically less likely to recommend surgical intervention for the patient with the symptomatic hernia in case 4 ($P = .02$). These data suggest that prior CME experience in palliative care alters the selection of treatment recommendations for patients with advanced malignancy and symptomatic clinical diseases.

**COMMENT**

Palliation of symptoms is a significant goal of surgical interventions, and palliative procedures may account for up to 20% of a surgeon's practice. Palliative care requires a multidisciplinary approach focused on the improvement of a patient's quality of life, not the cure of the underlying disease or prolongation of survival. Palliative care encompasses chemotherapy, radiotherapy, hospice care, and surgical intervention. Surgical palliation requires a surgeon to consider the risks and benefits of the operation in light of the patient's ultimate prognosis. Although surgeons are most often accustomed to operating for the cure of an acute disease, surgical palliation requires a modification of this goal. Surgical palliation has been defined by Osoba as “surgery aimed at the alleviation of symptoms and improvement in quality of life, with minimal impact on survival.” Involvement in surgical palliation is not limited to surgical oncologists; any surgeon may be called on to evaluate a patient with an advanced malignancy.

We received responses from surgeons comprising 9 surgical subspecialties in various practice environments, from the university to managed care and the rural setting. The overall response rate of 56% is an expected rate for a mailed survey of physicians and is an acceptable sample size for analysis. Our finding that more than 80% of respondents had received no education in palliative care medicine during their training was striking when compared with that of McCahill et al, in which that rate was only 30%. Furthermore, we found that 44% of our respondents had received no CME in palliative care; McCahill et al reported that rate as only 24%. These differences likely relate to the sample of surgeons examined. McCahill et al surveyed members of a specialty organization (Society of Surgical Oncology); furthermore, only 6% of the respondents practiced in a managed care environment and nearly half were affiliated with a university.
Our survey did not rely on membership in a specialty organization and had a broader distribution of practice environments. Therefore, our data are more likely to be representative of the community of general surgeons and are of significant concern given the dramatic educational deficiency in palliative care medicine during surgical residency.

This study has an obvious flaw of recall bias. Respondents were required to report on training that they had received years before, during residency. The actual amounts of training may vary more than the responses indicated. A second flaw is that respondents may have viewed either the information presented in each case or the options for surgical treatment to be too limited. This fact was illustrated by some respondents' writing in answers instead of choosing from those provided or by adding "if-then" statements to the clinical vignettes. For example, in the patient who was involved in the motor vehicle crash (case 3), a respondent did not answer the question because the neurologic function was unknown. Despite these flaws, we still believe that our data set was derived from a representative sample of community surgeons.

The survey did not demonstrate a consensus among the surgeons as to what treatment for symptomatic disease processes should or should not be offered to patients with advanced malignancy. Among the variables we examined (age of respondent, practice setting, specialty training, and CME training), the only variable that was significantly related to treatment selection was CME training. The surgeons with CME training in palliative care were less likely to select surgical palliation for the first 3 scenarios but more likely to select surgical treatment in the last scenario. The implications are that the acquisition of education in palliative care alters the perception of the benefits and risks of surgery in patients with advanced malignancy. Furthermore, the surgeons with CME training in palliative care were less likely to recommend surgical intervention in the first 3 scenarios; this would imply that these surgeons perceived either greater risks or less benefit to surgical palliation than did surgeons without CME training. We would have anticipated the opposite; namely, that further education in palliative care emphasizes the importance of intervention to maintain quality of life. Finally, the selection of surgery was independent of whether the symptoms were attributable to the underlying malignancy (cases 1 and 2) or unrelated (cases 3 and 4).

These data are superficial in the description of palliative surgical care as determined by a survey of regional surgeons. However, little information exists about practice patterns and outcomes of palliative surgical care and, therefore, this work represents the beginnings of the identification of a major effort in the understanding and implementation of palliative surgical care. Therefore, no standard response or accepted recommendations exist for the 4 clinical vignettes used in this study. Part of the lack of a standard approach to palliative surgical care in patients we identified may be based on the fact that phy-
Physicians receive their training and experience in palliative care from diverse sources at various stages in their careers. The American College of Surgeons and the National Residency End-of-Life Education Project are implementing programs designed to better train residents and surgeons. There are also many other programs, such as the End of Life Physician Education Resource Center, Palliative Leadership Centers, and the Education for Physicians on End-of-Life Care project. These programs have begun to develop standardized formats for education during medical school and are being expanded to postgraduate education. It is anticipated that these standardized educational programs will increase the provision of palliative surgical care and allow a standardized approach.

In conclusion, although most surgeons have similar goals in providing palliative care, treatments recommended may vary significantly. Furthermore, prior education clearly affects the recommended treatment option to achieve palliation of disease-related symptoms in patients with advanced malignancies. Thus, we advocate a continued effort to train surgeons in palliation and recommend that the training be part of a nationwide program to standardize palliative surgical care.

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Previous Presentation: This paper was presented at the 76th Annual Session of the Pacific Coast Surgical Association; February 21, 2005; Dana Point, Calif, and is published after peer review and revision. The discussions that follow this article are based on the originally submitted manuscript and not the revised manuscript.

REFERENCES


DISCUSSION

Lawrence D. Wagman, MD, Duarte, Calif: I think this is an absolutely critically important area for us to talk about and think about. The hypothesis is nicely planned: to examine deficiencies in training. Given the concepts of lifelong training and the relative newness of palliative surgery as a definable entity, the development of a cadre of trained surgeons is imperative. The implications are that a curriculum can be created and that there can be success in transferring the knowledge and testing it.

Although the authors gleaned some information regarding their hypothesis, it’s clearly inferential and based on respondent self-reporting, ie, there is no documentation of the respondent’s curriculum. There is no interview with the program director and no performance on an objective test that showed that they might have learned something during those 42 minutes. In effect, we are presented with a set of information that we can’t back up with scientific background but that still is critically important. As this is a nascent area of surgical education and surgical focus, it’s exactly what we should anticipate early on. What we get from this is not the pure data points and the P values but the beginning of an exploration.

The 4 scenarios are carefully constructed to include variation in cancer risk: progressive disease after a long latent phase, high risk but curable, incurable with variable progression, and a chronic cancer. The patients are relatively consistent in these scenarios—age 55 to 70 years—and we are given variable levels of surgical exigency: in scenario 1, the sun doesn’t set on a bowel obstruction; in scenario 2, a surgically treatable disease with continuing symptoms; in scenario 3, an indicated operation for trapped lung complicated by variable outcome from a closed head injury; and in scenario 4, a very standard general surgical procedure done to palliate and cure disease.

In scenario 1, there is a common treatment of a cancer and symptoms, so that is a 2-for-1. In scenarios 2 and 3, the clinical nature weighing the surgical morbidity of treating the nonmalignant problem with the life-limiting impact of a malignancy. The palliative outcome might be less time in the hospital receiving transfusions, fewer episodes of hypotension and its associated symptoms, and fewer lifestyle interruptions for the patient with a bleeding jejunal lesion. The woman with the trapped lung will be palliated with less time on a ventilator in the intensive care unit, less discomfort, and, hopefully, the ability to communicate.

Scenario 4 is almost too easy. This is a simple problem: high-yield intervention in a chronic cancer. As such, I think it serves as the control—ie, any surgeon who would not repair a symptomatic hernia in a patient with a chronic cancer is the ulti-
mate surgical minimalist or not a surgeon—but most likely represents not understanding the basic risk-benefit ratio of hernia surgery and the chronicity of prostate cancer.

The responses to the survey are excellent and, for anybody who has done a survey, to get a 50% response rate is superb. Kindly it wasn’t mentioned that Dr McCahill’s study done in the Society of Surgical Oncology had only a 25% response rate. So this is a credit to the survey design. I had an opportunity to look at the survey. It was easy to complete. To the survey process, it got to the individuals and it was easy to return, and also [credit] goes to the community. There is an intellectual quality of the community that supports the advancement of surgical care. All of these are very critical.

I question one thing, and it did bother me a bit. How many trainees received questionnaires, and were they able to complete and return them? Responding to this survey is definitely worth 15 minutes in any 80-hour workweek. I would suggest the results from the analysis, when prepared as a manuscript, should be the basis for an educational session in the 60% of the practice settings that included trainees. Our requirement of trainees would be to answer the questions. Then, while presenting the answers and the interpretations, I would expect a lively and extremely eye-opening session to ensue. I clearly think it would be better than just another tiresome repetition of the etiology of wound infections and incisional hernias that we go through at so many mortality and morbidity conferences.

Although formal education is historically limited, the fact that 47% of respondents reported having read some or all of the palliative care articles in the *Journal of the American College of Surgeons* suggests an interest and an effort to be better educated. The College should be congratulated for meeting the needs of its members in this area. For cases 1 and 2, either immediate or delayed surgery was selected approximately 70% of the time. For these 2 scenarios, these would be minor surgeries: a gastrostomy tube for decompression or a Hickman catheter for many transfusions. The nonsurgical management is medical care for case 1 and transfusion ad infinitum for case 2. About 8% of the respondents selected hospice for these patients. A total of 23% would do virtually nothing for those 2 patient groups. I think that is disturbing: to just walk away from any kind of surgical intervention, as minor as it may be, for those patients.

So I wondered if the authors could enlighten us as to why so many surgeons might select a nonoperative course for bowel obstruction or resectable bleeding sites.

I was also a bit concerned when I saw the impact of the palliative care CME on decision making. It looked like an inverse time-independent scenarios and the luxury of having every- other in the room at the same time, it’s really hard to push this. I wonder if anybody remembers taking their oral boards and if the author could enlighten us as to why so many surgeons might select a nonoperative course for bowel obstruction or resectable bleeding sites.

I will mention a pretty simple arithmetic calculation of the value of palliative surgery that is a conglomerate of the risk of cancer, the risk of acute and chronic symptoms to be palliated, and the risk of the intervention. This is put forth by Lawrence McCahill, an assistant professor of surgery in Vermont and one of our former fellows at the City of Hope, and he termed it as the *therapeutic index*.

Simply stated, the surgeon can create a ratio of time—maybe days, maybe weeks, maybe months; it’s rarely years. The time required to resolve the symptom is divided by the time the patient is symptom free. If you have a therapeutic index that is under 20%, it was projected that those patients will have good to excellent quality-of-life improvements—both from the patient’s and surgeon’s perspective.

So, if you took Patient 1, the 55-year-old man with the appendiceal carcinomatosis, if he spent 2 weeks in the hospital and 25 weeks postoperatively free of his bowel obstruction, that would give you a therapeutic index of about 4% and you would anticipate the patient would do well.

If the symptom resolution was only 5 weeks after a 2-week hospitalization for the operation, the therapeutic index would then be 40%, and you would predict the patient would have a little satisfaction. I would ask the authors consider requiring or requesting that surgeons and trainees define the therapeutic index at the time they are about to start their operation, a prospective analysis.

Papers such as those presented today will raise our awareness of the scientific approach, the necessary education, the decision-making process, and, potentially, the science of palliative surgery.

I close with congratulations and a charge to the team from UC Davis: the congratulations are for the willingness to pursue the emerging field, and the charge is to keep after it.

William P. Schecter, MD, San Francisco, Calif: I would just like to emphasize one point. It is extremely important to talk with the patient about his or her treatment goals. To me that is the most important question. What is the patient’s goal, what do they expect to achieve, and what cost are they willing to incur in terms of the treatment? In other words, treating advanced cancer is like being a tailor. You have to make the suit fit the customer. If you buy off the rack, it usually doesn’t work out too well.

Laura J. Esserman, MD, San Francisco: I just wanted to make the point that it’s really important to have a family discussion and a discussion with the oncologist in that these scenarios could be very variable. Someone with metastatic breast cancer, for example, could have a life expectancy of 3 months or 5 years, and it really depends because now there are so many different kinds of agents that keep people alive that you have to understand what the projected life expectancy is. I particularly like the idea that Dr Wagman suggested of what the therapeutic index is and trying to bring that into the forum. The best thing about this paper was that it makes people think about it, and it really should emphasize our need as oncologists and encourage our oncology colleagues to make sure that they have patients think about what they want and make plans for how they want to be treated should emergencies arise.

Dr Goodnight: Let me point out that the work of this paper and this study has been predominantly done by Dr Bold and Dr Galante, and I was glad to tag along. Clearly, in this realm of palliative supportive care the paper raises more questions than it answers. That is really like Dr Wagman’s analysis throughout. I think what is going to happen is that we will develop better data surrounding palliative, supportive care, and to wait to introduce this into the patient’s care until essentially we have exhausted all other modalities is simply misplaced. In other words, we expect that there are benefits from hospice-type care and supportive care, and this should be moved...
way back in the patient’s course. The issue is will it be cost-effective, and obviously that is going to require a number of clinical trials to develop appropriate data that would tell us about length of life, expectations. Hopefully, we will develop collectively better measures of quality of life so that we can determine if our interventions actually improved quality of life, and then [collect] data regarding the cost for this improved quality of life. These will be the things that will need to be taught in CME, to be taught to our trainees, and what we would hope, then, to profit from in the development of these studies.

To answer Dr Wagman’s questions, the number of trainees was 23. The cases, Dr Esserman, were intended to be open-ended. You could interpret the case in various ways, and so it does yield a very lively discussion when you get a group of surgeons—whether they are trainees or others—to discuss these. Yes, we have held the discussions and we will continue the effort. Obviously, we will continue to refine these cases. That might be something that would come out of CME. This is an opportunity for an open group of very intelligent and very well-trained surgeons to focus on this particular area and to focus on the type of questions and profit from the discussion.

Why did so many surgeons walk away? One can only speculate. They have a sense of futility, lack of good information, lack of data.

What was the impact of CME? Again, I don’t know, but probably in the realm of permissive pain management; again, better expectations; what’s the framework in which the patient is being treated, context. I agree absolutely with Dr Schecter. All of this has to do with what you take to the bedside, what you offer the patient. Obviously, the patient has an enormous, dominant vote in this, but you are their guide. So the better the information you provide them, the better that it can be.

Accuracy? A lot was said the other day in the simulation session—fascinating ability to ultimately quantify and define very well what we do. But there was a common thread in a number of the excellent discussants who got up and said, “Don’t forget the human element.” There is a whole raft of things that we still will bring to simulation or robotic assistance in doing cases that will define quality. While we want to get at quantifying this—in other words, the effort to bring the question of available data, expectations, cost, and so forth to the bedside—there will still be that wonderful human element of mixing and matching.

So would we want to demand a therapeutic index? Sure. The degree to which we develop a better framework, a better ability to assess these things, and so forth, it would be a way of organizing the data and, of course, it would be entirely appropriate. It would be an excellent focus for a clinical trial. That is what we will see happening progressively in this arena as appropriate questions are posed: data coming in, and then appropriately testing in a clinical trial. Ultimately what will come out of this, I hope, is that collectively we will develop better measures of quality of life, which then we will apply widely throughout our interventions, whether they are palliative or not. In other words, basically, are we doing good?

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**ARCHIVES OF INTERNAL MEDICINE**

**Warfarin-Induced Skin Necrosis and Venous Limb Gangrene in the Setting of Heparin-Induced Thrombocytopenia**

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**Background:** Heparin-induced thrombocytopenia (HIT) is a common, often catastrophic, syndrome that produces the most hypercoagulable states. Emerging therapeutic strategies use alternative anticoagulants; warfarin’s place is being reexamined. Early in the course of warfarin therapy, there may be net procoagulant effects because of the inhibition of protein C. With HIT, it has been suggested that unopposed warfarin can precipitate venous limb gangrene. There are also reports of warfarin-induced skin necrosis. We seek to confirm and increase awareness of the risks of warfarin with HIT.

**Methods:** We describe 6 patients with HIT seen at 3 medical centers in whom frank or impending venous limb gangrene, central skin necrosis, or both were temporally related to warfarin initiation.

**Results:** At warfarin initiation, 5 patients had recognized HIT and 1 had it recognized later. Complications emerged after 2 to 7 days, and consisted of warfarin-induced skin necrosis (n=5) and venous limb gangrene (n=2); 1 patient had both. This emerged with unopposed warfarin in 4 patients and as a direct thrombin inhibitor was being withdrawn in 2. All had supratherapeutic international normalized ratios. One patient required leg and breast amputations, and another one died.

**Conclusions:** Because of the early effects on protein C, warfarin can precipitate venous limb gangrene and/or skin necrosis in the extreme hypercoagulable milieu of HIT. With HIT, unopposed warfarin should be avoided and is needed during transition from a direct thrombin inhibitor. Warfarin should be initiated at modest doses in patients with HIT after platelet recovery. Implications extend to warfarin initiation with other thrombolytic diatheses. (2004;164:66-70)

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