EFFECTIVE CLINICAL PRACTICE

January/February 2001
Volume 4 Number 1

Decision Support and the Appropriate Use of Fibrinolysis in Myocardial Infarction

ORIGINAL ARTICLE

JOHN KELLETT, MD
Nenagh General Hospital
Nenagh, Ireland

Eff Clin Pract. 2001;4:1-9.

CONTEXT. For patients with suspected acute myocardial infarction, decisions about fibrinolytic therapy must account for trade-offs between risks and benefits, which vary according to the clinical characteristics of the patient.

OBJECTIVE. To assess whether use of a decision-support computer program (DSCP) improves the selection of appropriate candidates for fibrinolytic therapy among patients with suspected acute myocardial infarction.

DESIGN. Before-and-after trial at a small rural hospital in Ireland.

INTERVENTION. DSCP based on a previously published decision-analysis model. With input of patient characteristics (e.g., age, sex, duration of symptoms, findings on electrocardiography) at initial evaluation, the DSCP predicts the likelihood of different outcomes (e.g., mortality, stroke) and life expectancy with and without fibrinolysis.

PATIENTS. 894 consecutive patients (262 before DSCP was introduced, 632 after) admitted to the coronary care unit with suspected acute myocardial infarction between January 1993 and July 1999.

OUTCOME MEASURES. Proportion of appropriate candidates (ST-segment elevation > 2 mm on electrocardiogram, symptom duration ≤ 6 hours) receiving fibrinolysis before and after implementation of DSCP.

RESULTS. In general, patients admitted before and after DSCP implementation had similar clinical characteristics. The preintervention group presented somewhat earlier after the onset of symptoms (5.4 hours for preintervention vs. 7.2 hours for postintervention; $P < 0.01$) but had fewer confirmed acute myocardial infarctions (32% vs. 38%; $P = 0.13$). The proportion of appropriate patients receiving fibrinolysis before and after DSCP was nearly identical (66.7% vs. 68.9%; $P > 0.2$). Patients who received fibrinolysis after implementation of DSCP tended to be older (66.7 years vs. 63.8 years; $P = 0.11$) and were more likely to be female (36% vs. 26%; $P > 0.2$) than those who received fibrinolysis before DSCP implementation. The door-to-needle time decreased significantly from 88 minutes to 67 minutes after implementation of DSCP ($P < 0.01$).

CONCLUSION. Although overall rates of fibrinolysis did not change after implementation of DSCP, fibrinolytics may have been more appropriately directed toward higher risk patients who may be more likely to benefit from them.

Edited by John D. Birkmeyer, MD

See related editorial on pages 34-38.

This paper is available at ecp.acponline.org.

There is now clear evidence from clinical trials that fibrinolytic therapy reduces mortality for selected patients with acute myocardial infarction.[1] However, the therapeutic value of fibrinolysis—the difference between its risks and benefits—varies widely across patient subgroups.[2] The benefit of therapy is greatest for patients presenting soon after symptoms develop and in those at highest risk for mortality after acute myocardial infarction, including women and older patients. The risks associated with fibrinolysis—primarily, bleeding and stroke—increase with age and in the presence of hypertension and other medical conditions. Given the numerous variables involved in clinical decision making, identifying which patients are likely to benefit most from fibrinolysis is not straightforward; this may, in part, explain poorer outcomes observed in community-based settings compared with those reported in large clinical trials.[3]

Decision analysis is an explicit, quantitative approach to weighing the risks and benefits of fibrinolysis in different subgroups of patients with acute myocardial infarction.[4] In some ways, decision analysis performs the reverse function of large clinical trials: Instead of pooling the experiences of many individual patients to determine an overall benefit, decision analysis uses overall experience to determine the probable benefit for an individual patient or patient subgroup. Surprisingly few studies have applied decision analysis to determine whether fibrinolytic therapy is appropriate for patients with acute myocardial infarction, and none has described its use in the direct clinical management of patients with suspected acute myocardial infarction.

Since 1994, our rural community hospital has used a decision-support computer program (DSCP) aimed at improving decisions about use of fibrinolytic therapy. Based on a published decision-analysis model developed by the author,[5] this DSCP uses immediately available clinical parameters to estimate the chances, with and without fibrinolytics, for acute myocardial infarction and death from infarction as well as the risks for major stroke and bleeding. This study explores the impact of the DSCP on the use of fibrinolytics in patients admitted to our coronary care unit (CCU).

Methods

Practice Setting and Patients

Nenagh Hospital is a small rural hospital in Ireland with 35 acute medical beds that admits 2500 patients per year and serves a widely dispersed rural population of 70,000. During this study, the medical unit was staffed by a general internist, a geriatrician, and six physicians in training.

The study included 894 consecutive patients with suspected acute myocardial infarction admitted to the hospital's 4-bed CCU from January 25, 1993, to July 3, 1999. We excluded patients with absolute contraindications to fibrinolysis (e.g., stroke or gastrointestinal bleeding in the past 3 months or trauma or surgery within the previous 2 weeks). The decision to admit patients to the CCU was made by either the physician or nursing supervisor on duty on the basis of a cursory examination of the patient, findings on electrocardiography performed at admission, or information obtained by ambulance paramedics en route to the hospital. Although the criteria for CCU admission were not precisely defined, a 20-year ongoing audit has shown that approximately one third of patients admitted to the Nenagh General Hospital CCU has had a confirmed diagnosis of acute myocardial infarction.

Study Design

Figure 1 illustrates the study design. Once admitted to the CCU, patients were examined immediately by the physician and/or nurse on duty (depending on availability). During this examination, data were collected to predict the chances for acute myocardial infarction and acute myocardial infarction–related stroke and mortality.[6–10] Before implementation of the DSCP (on October 18, 1994), clinical data were entered into a computer database under the direction of the supervising CCU nurse on duty; the computer was merely a data-collection instrument—it produced no output. The clinical decision to give or withhold fibrinolysis, therefore, was made in the traditional manner by the physician on duty. The treatment administered to the patient and the subsequent patient outcome were recorded in the database.

After the computer program was introduced, data were entered directly into the DSCP by either the nurse or physician on duty (depending on availability). Figure 2 shows a sample DSCP-generated patient profile. Such printouts—which show the estimated chances with and without fibrinolysis for acute myocardial infarction, death within 30 days from myocardial infarction, and stroke—typically were reviewed immediately by the physician on duty, who would then determine how best to manage the patient.

All patients had serial electrocardiography and creatine kinase levels recorded at least daily for a minimum of 3 days. Acute myocardial infarctions were diagnosed by using World Health Organization criteria—chest pain, changes shown on electrocardiography, and levels of cardiac enzymes (i.e., creatine kinase) that were at least twice the reference limit.[11] Statistical comparisons were made by using a Student *t*-test and chi-square analysis.

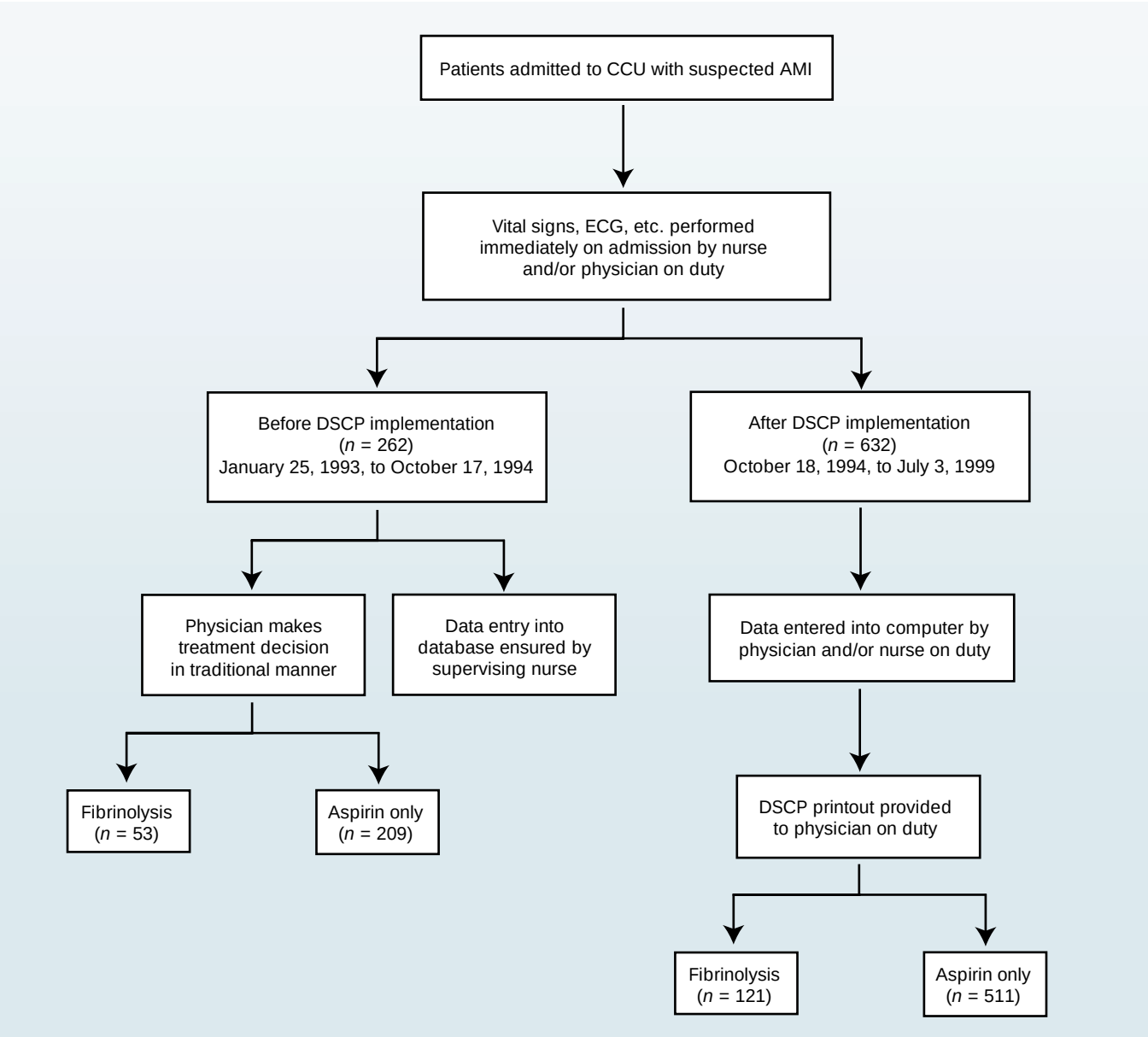

FIGURE 1. Study design. AMI = acute myocardial infarction; CCU = coronary care unit; DSCP = decision-support computer program; ECG = electrocardiography.

Description of the DSCP

The DSCP was based on a previously published decision-analysis model that estimated the risks and gains in life expectancy from fibrinolytic therapy.[5] The chances for acute myocardial infarction, death from acute myocardial infarction within 30 days, and stroke were estimated by using predictive instruments that incorporated data available at the bedside. Based on the results of electrocardiography performed at admission, patients were assigned to one of seven categories previously shown to be associated with different probabilities of acute myocardial infarction.[7] The probability of dying from acute myocardial infarction was determined by a predictive instrument developed by Selker and colleagues.[8] Predictions for mortality from acute myocardial infarction were adjusted to reflect the reduction in mortality produced by fibrinolytic therapy, according to a linear regression model that was based on the Fibrinolytic Therapy Trialist's (FTT) Collaborative Group report.[12] These estimates were further adjusted to reflect the added benefit of tissue plasminogen activator (t-PA) over streptokinase as shown in the Global Utilization of Streptokinase and t-PA for Occluded coronary arteries (GUSTO) trial.[13] Validation of these adjustments to the predictive instrument to estimate

NENAGH HOSPITAL THROMBOLYSIS BY DECISION ANALYSIS

HOSPITAL NUMBER: 5598 TIME: 19:00:55 DATE: 09-05-1998

PATIENT NAME: ******** FIRST NAME: ********

SEX: MALE AGE: 80 years BP: 160 / 70 PULSE RATE = 55 per minute

TIME SINCE ONSET OF SYMPTOMS = 8 hours

NO CHEST/ARM PAIN PRESENT NO P.A.T. PRESENT

PEAKED HYPERACUTE T WAVES INVERTED T WAVES

ANTERIOR–SEPTAL Q WAVES ST ELEVATION & DEPRESSION

MAXIMUM ST DEVIATION = 3 mm NUMBER OF LEADS WITH ST DEVIATION = 2 LEADS
PROBABILITY OF ACUTE MI = 95.3% PROBABILITY OF DYING IF ACUTE MI = 42.9%

DECISION ANALYSIS AND SENSITIVITY ANALYSES RESULTS

NEED FOR A BLOOD TRANSFUSION IF THROMBOLYSED = 6.1%

CHANCE OF DEATH FROM INFARCTION
AFTER STREPTOKINASE 32.9% WITHOUT STREPTOKINASE 42.9%

CHANCE OF A MAJOR STROKE
AFTER STREPTOKINASE 3.9% WITHOUT STREPTOKINASE 1.0%

LIFE EXPECTANCY
AFTER STREPTOKINASE 3.64 yrs WITHOUT STREPTOKINASE 3.26 yrs

THROMBOLYSIS IS CONTRAINDCATED IF:
CHANCE OF ACUTE INFARCTION < 36.0% CHANCE OF MAJOR STROKE >21.0%
CHANCE OF DEATH FROM INFARCTION WITHOUT THROMBOLYSIS < 10.1%
CHANCE OF MAJOR BLEED > 20.0% ONSET OF PAIN WAS MORE THAN 22 HRS AGO
UTILITY OF A MAJOR STROKE < 0 CHANCE OF PERICARDITIS >100.0%
CHANCE OF FATAL TAMPONADE >100.0% CHANCE OF AORTIC ANEURYSM >100.0%
UTILITY OF HEART FAILURE < 0

CHANCE OF DEATH FROM INFARCTION
AFTER accelerated TPA 32.9% WITHOUT accelerated TPA 42.9%

CHANCE OF A MAJOR STROKE
AFTER accelerated TPA 5.0% WITHOUT accelerated TPA 1.0%

LIFE EXPECTANCY
AFTER accelerated TPA 3.61 yrs WITHOUT accelerated TPA 3.26 yrs

THROMBOLYSIS IS CONTRAINDICATED IF:
CHANCE OF ACUTE INFARCTION < 42.0% CHANCE OF A MAJOR STROKE > 21.0%
CHANCE OF DEATH FROM INFARCTION WITHOUT THROMBOLYSIS < 13.1%
CHANCE OF MAJOR BLEED > 20.0% ONSET OF PAIN WAS MORE THAN 21 HRS AGO
UTILITY OF A MAJOR STROKE < 0 CHANCE OF PERICARDITIS >100.0%
CHANCE OF FATAL TAMPONADE >100.0% CHANCE OF AORTIC ANEURYSM > 100.0%
UTILITY OF HEART FAILURE < 0

****

TPA OFFERS NO ADVANTAGE OVER STREPTOKINASE

****

FIGURE 2. Example of a printout generated by the decision-support computer program used for all patients with suspected acute myocardial infarction who were admitted to the coronary care unit at Nenagh General Hospital, Ireland, after October 17, 1994.

death from infarction with and without fibrinolysis for patients in the Nenagh General Hospital CCU has already been reported.[14, 15] Until March 17, 1998, a predictive instrument based on the results of a study by Simoons and colleagues[9] was used to estimate the risk for stroke; thereafter, the predictive instrument reported by Gore and colleagues[10] was used.

The probabilities of all other chance events used in the model were derived from literature identified by a MEDLINE search.[5] Life expectancy was calculated by a Markov process[16] from age-specific mortality rates adjusted to account for excess mortality from stroke or congestive heart failure. The DSCP model was constantly updated and revised during the course of the study as new and better information on the risks and benefits of fibrinolysis became available. The original decision tree[5] was expanded to include the probabilities of morbidity and mortality from leaking aortic aneurysm[17–19] and acute pericarditis.[20–24] The DSCP tests the robustness of its own results by performing repeated sensitivity analyses with varying probabilities of all the major chance events and quality-of-life adjustments, thus determining the threshold probabilities and quality adjustments at which the DSCP-recommended treatment option changes. In situations in which accelerated t-PA provides a benefit over streptokinase, the DSCP also performs a cost-effectiveness analysis.[25] All DSCP results are provided to the physician in a printout at the bedside.

Results

Patients admitted before and after implementation of DSCP generally had similar clinical characteristics (Table 1). The preintervention group presented somewhat earlier after the onset of symptoms (5.4 compared with 7.2 hours in the postintervention group; $P < 0.01$). However, the proportion of patients who were appropriate for fibrinolysis (presentation within 6 hours of symptom onset and ST-segment elevation > 2 mm) was nearly identical before and after implementation of the DSCP. Overall, the use of fibrinolysis did not change after implementation of the DSCP: Of the patients admitted to the CCU, 20.2% received therapy before the computer intervention was introduced compared with 19.2% after ($P > 0.2$) (Table 2). The proportion of appropriate patients receiving fibrinolysis was also nearly identical before and after implementation of the DSCP (66.7% vs. 68.9%; $P > 0.2$). Conversely, a similarly low proportion of patients not appropriate for fibrinolysis received the therapy before and after the DSCP was implemented (6.4% and 5.6%; $P > 0.2$).

TABLE 1
Characteristics of Patients Admitted before and after Implementation of DSCP*

CHARACTERISTIC	BEFORE DSCP IMPLEMENTATION (*n* = 262)	AFTER DSCP IMPLEMENTATION (*n* = 632)	*P* VALUE
Mean age, *yr*	**63.5**	**64.0**	**>0.2**
Men, *%*	**64.9%**	**64.9%**	**>0.2**
Systolic blood pressure, *mm Hg*	**141**	**139**	**>0.2**
Pulse rate	**81**	**80**	**>0.2**
Delay of presentation after symptom onset, *hr*	**5.4**	**7.2**	**<0.01**
Presenting ≤ 6 hours after symptom onset, *%*	**73.7%**	**64.9%**	**<0.02**
ST-segment elevation > 2 mm, *%*†	**27.9%**	**28.3%**	**>0.2**
Proportion appropriate for fibrinolytics, *%*‡	**22.9%**	**21.5%**	**>0.2**
Acute myocardial infarction confirmed, *%*	**32.1%**	**37.7%**	**0.13**

**DSCP = decision-support computer program*
†*Based on results of electrocardiography taken at admission.*
‡*Patients were considered appropriate candidates if they presented within 6 hours of symptom onset and had ST-segment elevation > 2 mm.*

TABLE 2

Use of Fibrinolytic Therapy before and after Implementation of DSCP*

PATIENT SUBGROUP	PROPORTION RECEIVING FIBRINOLYTICS		
	BEFORE DSCP (n = 262)	AFTER DSCP (n = 632)	P VALUE
All patients	**20.2%**	**19.2%**	**>0.2**
Presenting ≤ 6 hours after symptom onset			
Yes	**23.8%**	**25.2%**	**>0.2**
No	**10.1%**	**8.1%**	**>0.2**
ST-segment elevation > 2 mm†			
Yes	**64.4%**	**60.7%**	**>0.2**
No	**3.2%**	**2.9%**	**>0.2**
Appropriate for fibrinolytics‡			
Yes	**66.7%**	**68.9%**	**>0.2**
No	**6.4%**	**5.6%**	**>0.2**

**DSCP = decision-support computer program.*

†*Based on results of electrocardiography taken at admission.*

‡*Patients were considered appropriate candidates if they presented within 6 hours of symptom onset and had ST-segment elevation > 2 mm.*

Although the overall proportion of patients receiving fibrinolysis did not change, there was a trend toward greater use of fibrinolysis among higher-risk patients (who are potentially more likely to benefit from the therapy) after DSCP implementation. Patients receiving fibrinolysis after the intervention was introduced were somewhat older (63.8 years vs. 66.7 years in the postintervention group; $P = 0.11$) and were more likely to be female (26.4% vs. 36.4% in the postintervention group; $P > 0.2$). The predicted mortality for all patients receiving fibrinolysis was the same during both phases of the study (20.1% vs. 21.2%; $P > 0.2$) (Table 3).

The door-to-needle time decreased significantly from 88 to 67 minutes ($P < 0.01$) after implementation of DSCP. The observed mortality was not significantly different before and after DSCP was introduced, either overall (7.6% vs. 5.5% in the postintervention group; $P > 0.2$) or for all patients receiving fibrinolysis (7.5% vs. 13.2% in the postintervention group; $P > 0.2$). However, the observed mortality among appropriate patients who did not receive fibrinolysis tended to be higher before DSCP use (40.0% vs. 16.7% in the postintervention group; $P = 0.09$).

Discussion

Surprisingly few attempts have been made to apply decision analysis to any aspect of coronary care, and the technique still remains largely within the domain of medical managers, health economists, and policymakers.[26] This study is the first to describe the use of a decision analysis model in clinical practice to guide decision making on use of fibrinolytic therapy in patients with suspected acute myocardial infarction.

The fact that the DSCP did not change the proportion of appropriate patients receiving fibrinolysis is not unexpected, as it is now standard care to use fibrinolytics in patients with marked ST-segment elevation who present within a few hours of symptom onset. Although pre- and post-DSCP patients were similar superficially, the proportion of predicted and observed deaths of patients who were appropriate candidates for therapy but who did not receive it decreased with DSCP use (predicted mortality, 34.3% in the preintervention group vs. 24.7% in the postintervention group; $P = 0.14$; observed mortality, 40% in the preintervention group vs. 16.7% in the postintervention group; $P = 0.09$). In the pre-DSCP phase, therefore, fibrinolytics may not have been given to some appropriate patients with clear electrocardiographic evidence of acute myocardial infarction, timely presentation, and a high risk for death. It is probable, therefore, that in some pre-DSCP patients, administering fibrinolysis would have been appropriate. With DSCP use, fibrinolytics were probably more appropriately directed toward women and older patients and less likely to be given to those who presented too late for fibrinolysis to be beneficial.

TABLE 3
Characteristics of All Patients Receiving Fibrinolytics*

CHARACTERISTIC	BEFORE DSCP (*n* = 53)	AFTER DSCP (*n* = 121)	*P* VALUE
Mean age, *yr*	**63.8**	**66.7**	**0.11**
Proportion male, *%*	**73.6%**	**63.6%**	**>0.2**
Delay of presentation after symptom onset, *hr*	**3.9**	**4.0**	**>0.2**
Presentation ≤ 6 hours after symptom onset, *%*	**86.8%**	**85.1%**	**>0.2**
ST-segment elevation > 2 mm, *%* †	**88.7%**	**89.3%**	**>0.2**
Proportion appropriate for fibrinolytics, *%*‡	**75.5%**	**76.9%**	**>0.2**
Predicted mortality, *%*	**20.1%**	**21.2%**	**>0.2**
Door-to-needle time, *min*	**88.2**	**67.2**	**<0.01**

**DSCP = decision-support computer program.*
†*Based on results of electrocardiography taken at admission.*
‡*Patients were considered appropriate candidates if they presented within 6 hours of symptom onset and had ST-segment elevation > 2 mm.*

Any improvement in the appropriateness of care for CCU patients with acute myocardial infarction may not be attributable to the DSCP or its printout alone, but may simply result from an increasing awareness of decision analysis by CCU staff, who would in turn give more careful consideration to risks and benefits when making important medical decisions. However, I do not believe this to be the case: Even as the author of the program, I am constantly surprised by the DSCP's printout and often have to think it through to make sure that I understand it.

Because this was a long-term observational study with a before-and-after design, changes in the patient population and case-mix over time may have confounded the results. Although the mean length of hospital stay for all medical admissions decreased from 7.0 to 5.4 days during the course of the study, the average patient age (60 years) and overall mortality rate (5.0%) have remained unchanged for the past 20 years. Nevertheless, it is possible that the trend of a lower mortality rate seen in patients with acute myocardial infarction following the introduction of DSCP may reflect unidentified improvements in CCU care rather than any difference between pre- and post-DSCP patients. Undoubtedly, during the course of this study, the hospital's nursing and medical staffs continued to gain experience in use of fibrinolytics. However, because the hospital had participated in the Second International Study of Infarct Survival (ISIS-2), the nursing staff had been familiar with the use of fibrinolytics for at least 5 years before the current study started.

The proportion of pre- and post-DSCP patients with acute myocardial infarction who received fibrinolysis, which was high by international standards,[27] may already be close to the optimal rate. The impact of the DSCP on overall fibrinolytic use might be more apparent in a CCU with a lower initial rate of fibrinolytic use. The DSCP made no difference to the proportion of patients without acute myocardial infarction who received fibrinolysis. However, it is noteworthy that in all cases in which fibrinolytics were administered after DSCP implementation to patients without acute myocardial infarction, either the electrocardiographic findings had been misinterpreted or the advice of the DSCP had been overruled.

Many physicians in training had great difficulty accepting the concept of their clinical practice being guided by a machine. Also, developing an acceptable format for the DSCP printout took some time. The final form (Figure 2) was deliberately designed not to make explicit recommendations and to leave the physician a role as interpreter and final arbiter. Because there is no simple relationship between risk for stroke and life-expectancy benefit, the decision to use fibrinolytics requires balancing considerations of long-term benefit and up-front risk. From the physician's point of view,

the immediate consequences of a massive stroke may not seem justified by a trivial theoretical benefit to life-expectancy. The example printout in Figure 2 illustrates the point: An 80-year-old patient presented 8 hours after the onset of a near-certain acute myocardial infarction that was estimated to carry a 43% chance of death. Use of streptokinase quadruples the patient's chance for an acute stroke from 1% to 4%. Despite the delayed presentation and increased risk for stroke, the patient could have an increased life expectancy of 0.4 of a year from streptokinase therapy.

Although the DSCP attempts to capture as explicitly as possible all the variables known in the literature to determine the outcome of fibrinolytic therapy, it cannot capture everything. In particular, it cannot accurately assess the patient's values and acceptable risk trade-offs for different outcome states.[4] However, an accurate assessment of these factors is seldom possible by any other means, given the urgency usually associated with acute myocardial infarction. The DSCP printout does at least provide an explicit way of showing the likely impact of the patient's personal values and/or acceptance of risk on the final treatment decision. Provided it is based on the best possible data and assumptions available, decision analysis will always make the best possible decision, with the risks and benefits clearly defined. Regardless of subsequent outcomes, each decision can be repeatedly and reproducibly reviewed, analyzed, criticized, and defended.

Take-Home Points

- **The value of fibrinolytic therapy for patients with suspected acute myocardial infarction depends on trade-offs between its risks and benefits, which vary widely among individuals.**
- **We implemented a decision-support computer program to improve clinical decision making for patients admitted to the coronary care unit at our rural hospital in Ireland.**
- **The overall proportion of patients receiving fibrinolysis (approximately 20%) did not change after implementation of the decision-support tool.**
- **After the intervention was implemented, however, use of fibrinolytics increased slightly among higher-risk patients (women and older patients).**
- **Optimal decision making on whether to use fibrinolytic therapy in patients with suspected myocardial infarction must account for patient preferences, as well as clinical variables.**

References

1. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Lancet. 1994;343:311-22.
2. Stevenson R, Ranjadayalan K, Wilkinson P, Roberts R, Timmis AD. Short and long term prognosis of acute myocardial infarction since introduction of thrombolysis. BMJ. 1993;307:349-53.
3. Meehan TP, Hennen J, Radford MJ, Petrillo MK, Elstein P, Ballard DJ. Process and outcome of care for acute myocardial infarction among Medicare beneficiaries in Connecticut: a quality improvement demonstration project. Ann Intern Med. 1995;122:928-36.
4. Sox HC, Blatt MA, Higgins MC, Marton KI. Medical Decision Making. Boston: Butterworths; 1988.
5. Kellett J, Clarke J. Comparison of "accelerated" tissue plasminogen activator with streptokinase for treatment of suspected myocardial infarction. Med Decis Making. 1995;15:297-310.
6. Tighe M, Kellett J, Corry R, Reddan E, Ryan B. The early diagnosis of acute myocardial infarction. Comparison of a simple algorithm with a computer program for electrocardiogram interpretation. Ir J Med Sci. 1996;165:159-63.
7. Kellett J. Early diagnosis of acute myocardial infarction by either electrocardiogram or a logistic regression model: portability of a predictive instrument of acute cardiac ischemia to a small rural coronary care unit. Can J Cardiol. 1997;13:1033-8.
8. Selker HP, Griffith JL, D'Agostino RB. A time-insensitive predictive instrument for acute myocardial infarction mortality: a multicenter study. Med Care. 1991;29:1196-211.
9. Simoons ML, Maggioni AP, Knatterud G, Leimberger JD, de Jaegere P, van Domburg R, et al. Individual risk assessment for intracranial haemorrhage during thrombolytic therapy. Lancet. 1993;342:1523-8.
10. Gore JM, Granger CB, Simoons ML, et al. Stroke after thrombolysis. Mortality and functional outcomes in the GUSTO-I trial. Global Use of Strategies to Open Occluded Coronary Arteries. Circulation. 1995;92:2811-8.
11. World Health Organization, Regional Office for Europe. Ischaemic heart disease registers; report of the Fifth Working Group, Copenhagen, 26–29 April 1971. Working Group on Ischaemic Heart Disease Registers. Copenhagen: Regional Office for Europe, World Health Organization; 1971.
12. Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. Lancet. 1996;348:771-5.
13. Newby LK, Rutsch WR, Califf RM, et al. Time from symptom onset to treatment and outcomes after thrombolytic therapy. GUSTO-1 Investigators. J Am Coll Cardiol. 1996;27: 1646-55.
14. Tighe M, Kellett J, Reddan C, Ryan B. Audit of a rural hospital's coronary care unit: comparison of two predictive instruments of acute myocardial infarction mortality. Ir J Med Sci. 1996;165:254-8.
15. Kellett J. Performance of a predictive instrument of acute myocardial infarction mortality. Ir J Med Sci.1998;167:29.
16. Sonnenberg FA, Beck JR. Markov models in medical decision making: a practical guide. Med Decis Making. 1993;13:322-38.
17. Wilcox RG, von der Lippe G, Olsson CG, Jensen G, Skene AM, Hampton JR. Trial of tissue plasminogen activator for mortality reduction in acute myocardial infarction. 17. Anglo-

Scandinavian Study of Early Thrombolysis (ASSET). Lancet. 1988;2:525-30.
18. Very early thrombolytic therapy in suspected acute myocardial infarction. The Thrombolysis Early in Acute Heart Attack Trial Study Group. Am J Cardiol. 1990;65:401-7.
19. Wilcox RG, von der Lippe G, Olsson CG, Jensen G, Skene AM, Hampton JR. Effects of alteplase in acute myocardial infarction: 6-month results from the ASSET study. Anglo-Scandinavian Study of Early Thrombolysis. Lancet. 1990;335: 1175-8.
20. Brush JE Jr, Brand DA, Acampora D, Chalmer B, Wackers FJ. Use of the initial electrocardiogram to predict in-hospital complications of acute myocardial infarction. N Engl J Med. 1985;312:1137-41.
21. Permanyer-Miralda G, Sagrista-Sauleda J, Soler-Soler J. Primary acute pericardial disease: a prospective series of 231 consecutive patients. Am J Cardiol. 1985;56:623-30.
22. Guberman BA, Fowler NO, Engel PJ, Gueron M, Allen JM. Cardiac tamponade in medical patients. Circulation. 1981;64: 633-40.
23. Lew AS, Hod H, Cercek B, Shah PK, Ganz W. Mortality and morbidity rates of patients older and younger than 75 years with acute myocardial infarction treated with intravenous streptokinase. Am J Cardiol. 1987;59:1-5.
24. Barrington WW, Smith JE, Himmelstein SI. Cardiac tamponade following treatment with tissue plasminogen activator: an atypical hemodynamic response to pericardiocentesis. Am Heart J. 1991;121:1227-9.
25. Kellett J. Cost-effectiveness of accelerated tissue plasminogen activator for acute myocardial infarction. Br J Med Econ. 1996;10:341-59.
26. Thornton JG, Lilford RJ. Decision analysis for medical managers. BMJ. 1995;310:791-4.
27. Translation of clinical trials into practice: a European population-based study of the use of thrombolysis for acute myocardial infarction. European Secondary Prevention Study Group. Lancet. 1996;347:1203-7.

Correspondence

John Kellett, MD, Nenagh General Hospital, Nenagh, County Tipperary, Ireland; telephone: 353-67-31491; fax: 353-67-33440; e-mail: kellett@iol.ie.