Editorials

Use and Overuse of Angiography and Revascularization for Acute Coronary Syndromes

OVER the past two decades, clinical and pathological studies have examined the pathophysiology of the acute coronary syndromes, unstable angina, and non–Q-wave and Q-wave myocardial infarction. In these conditions, rupture of atherosclerotic plaques leads to varying amounts of platelet adhesion and aggregation, vasoconstriction, and the formation of partially or totally occlusive thrombus. Although the inhibition of platelet aggregation and thrombus formation and the restoration of antegrade flow in occluded coronary arteries improve survival and reduce the incidence of recurrent ischemia and infarction, residual coronary-artery stenosis may cause ischemia, infarction, or even death. As a result, there has been considerable interest in the routine use of coronary angiography and percutaneous revascularization in patients with these syndromes, in the hope of reducing the risk of adverse events.

The publication of the results of the Veterans Affairs Non–Q-Wave Infarction Strategies in Hospital (VANQWISH) Trial in this issue of the *Journal*[1] brings to four the number of large prospective, randomized studies comparing "aggressive" and "conservative" management of acute coronary syndromes. Together, these trials have studied more than 6400 patients with unstable angina,[2,3] non–Q-wave infarction,[1-3] or Q-wave infarction treated with thrombolytic therapy[4-6] who have been assigned to routine aggressive management or to a more conservative strategy, in which angiography and revascularization are performed only in patients with spontaneous or provokable myocardial ischemia (i.e., ischemia-guided therapy). With remarkable clarity and consistency, all four studies show that routine angiography and revascularization do not reduce the incidence of nonfatal reinfarction or death as compared with the more conservative, ischemia-guided approach. In fact, in the VANQWISH study of patients with non–Q-wave infarction,[1] the aggressive strategy (which these investigators call "invasive") was associated with increased mortality during hospitalization, at one month, and at one year.

Although all four trials[1-6] found that the incidence of adverse events was similar (or greater) in patients whose acute coronary syndromes were managed aggressively than in those assigned to conservative management, an aggressive approach continues to be chosen by most physicians in the United States, whereas a conservative strategy is more likely to be followed in Canada and Europe. In the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) trial,[7] which was performed in the United States and abroad, four thrombolytic regimens were compared in patients with Q-wave infarction. After each patient had received one of the four thrombolytic regimens, treatment was determined by his or her own physician.

Although the patients enrolled in the United States were more likely than their Canadian counterparts to undergo coronary angiography (68 percent vs. 35 percent, respectively) and subsequent revascularization (31 percent vs. 12 percent), the incidence of reinfarction and death during more than three years of follow-up was similar.[8] The chief predictors of the decision by U.S. physicians to use coronary angiography were a relatively young age of the patient and the availability of a catheterization facility. Furthermore, there was marked regional variation within the United States in the rates of use of angiography and revascularization,[9] which was not explained by differences in the characteristics of the patients or the incidence of complications of myocardial infarction. A strong relation was noted between the availability of angiography in a geographic area and the likelihood that aggressive management would be chosen. However, the increased use of invasive procedures did not reduce the incidence of recurrent infarction or death.

Why are coronary angiography and revascularization often performed in patients with acute coronary syndromes in the United States, even without an obvious indication? Several factors may be responsible. First, in an era in which invasive cardiac procedures are manifestations of high-technology, resource-intensive medical care, many patients and their family members expect and insist on aggressive management. The term "conservative management" may project the impression (to physicians and patients alike) of obsolescence, inadequacy, and inferiority rather than of thoughtful reflection and the application of scientifically based, ischemia-guided therapy. In the event of an adverse outcome, the patient and his or her family may be more understanding and forgiving if an aggressive approach was pursued (i.e., if "everything possible was done"), even if such an approach contributes, directly or indirectly, to the adverse outcome. In the GUSTO trial,[7] physicians in the United States more often reported that requests by the patient or family members as well as concern about liability influenced them to pursue aggressive management than did their Canadian counterparts.[8]

Second, some physicians in the United States express skepticism about the applicability of the results of the aforementioned trials to their patients. In the three randomized comparisons of aggressive and

conservative management strategies conducted in the United States,[1,2,4] 70 to 80 percent of the patients initially assigned to conservative management nonetheless underwent coronary angiography during or shortly after their index hospitalization[9,10]; in many cases, angiography was recommended without a clear indication. Of the physicians in the United States who participated in the GUSTO trial who were surveyed,[8] 54 percent said they routinely recommended coronary angiography for survivors of uncomplicated myocardial infarction, 71 percent did so for those receiving thrombolytic therapy, and 93 percent did so for survivors of infarction who were less than 45 years old, even though these groups of patients are at low risk for subsequent complications regardless of the manner in which they are treated. In Europe and Canada,[8,11] in contrast, patients who received thrombolytic therapy and were assigned to conservative management underwent angiography and revascularization one third to one half as often as their U.S. counterparts, yet their outcome was similar, and routine aggressive management offered no substantial benefit.

Third, studies that substantiate preconceived notions are likely to be embraced and their recommendations followed, whereas those that do not are often ignored. For example, primary angioplasty for acute myocardial infarction is widely used and enthusiastically advocated, yet direct comparisons with thrombolytic therapy in relatively small numbers of patients showed, at best, only a small benefit of angioplasty, and larger studies showed none.[12] Many physicians in the United States, even today, continue to believe that all patients with acute coronary syndromes are best treated with prompt coronary angiography and revascularization, despite the absence of scientific support for such an approach.

Fourth, as compared with Canada and Europe, the United States has an abundance of facilities for prompt angiography and revascularization, physicians trained to perform these procedures, and monetary remuneration to the facilities and physicians. The combination of these factors encourages the use of angiography and revascularization without a clear indication. Physicians who work in hospitals with catheterization facilities are more likely to recommend coronary angiography than those without easy access to such a facility.[9-11] Cardiologists are more likely to recommend angiography than internists, and cardiologists who perform angiography are even more likely than their colleagues who do not perform the procedure to recommend it.[8,10,13]

At present, particularly in the United States, a substantial number of patients with acute coronary syndromes undergo coronary angiography and revascularization without a clear indication. Which patients with unstable angina or myocardial infarction should undergo angiography? First, those who have spontaneous or provokable ischemia despite reasonable medical therapy should undergo invasive evaluation and revascularization. For these patients, angiography and revascularization are clearly indicated and beneficial. Second, symptomatic patients or those with evidence from noninvasive tests of left ventricular systolic dysfunction should undergo angiography, with the goal of identifying those who would be expected to benefit from subsequent surgical revascularization.[14] The treatment of patients whose course is uncomplicated should be guided by the results of the relevant trials,[1-6] such as VANQWISH,[1] rather than physicians' preference or other, nonmedical incentives.

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REFERENCES

1. Boden WE, O'Rourke RA, Crawford MH, et al. Outcomes in patients with acute non–Q-wave myocardial infarction randomly assigned to an invasive as compared with a conservative management strategy. N Engl J Med 1998;338:1785-92.
2. Williams DO, Braunwald E, Thompson B, Sharaf BL, Buller CE, Knatterud GL. Results of percutaneous transluminal coronary angioplasty in unstable angina and non-Q-wave myocardial infarction: observations from the TIMI IIIB Trial. Circulation 1996;94:2749-55.
3. Anderson HV, Cannon CP, Stone PH, et al. One-year results of the Thrombolysis in Myocardial Infarction (TIMI) IIIB clinical trial: a randomized comparison of tissue-type plasminogen activator versus placebo and early invasive versus early conservative strategies in unstable angina and non-Q wave myocardial infarction. J Am Coll Cardiol 1995;26:1643-50.
4. The TIMI Study Group. Comparison of invasive and conservative strategies after treatment with intravenous tissue plasminogen activator in acute myocardial infarction: results of the Thrombolysis in Myocardial Infarction (TIMI) phase II trial. N Engl J Med 1989;320:618-27.
5. Terrin ML, Williams DO, Kleiman NS, et al. Two- and three-year results of the Thrombolysis in Myocardial Infarction (TIMI) Phase II clinical trial. J Am Coll Cardiol 1993;22:1763-72.
6. SWIFT (Should We Intervene Following Thrombolysis?) Trial Study Group. SWIFT trial of delayed elective intervention v conservative treatment after thrombolysis with anistreplase in acute myocardial infarction. BMJ 1991;302:555-60.
7. The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. N Engl J Med 1993;329:673-82.
8. Pilote L, Granger C, Armstrong PW, Mark DB, Hlatky MA. Differences in the treatment of myocardial infarction between the United States and Canada: a survey of physicians in the GUSTO trial. Med Care 1995;33:598-610.
9. Pilote L, Califf RM, Sapp S, et al. Regional variation across the United States in the management of acute myocardial infarction. N Engl J Med 1995;333:565-72.
10. Pilote L, Miller DP, Califf RM, Rao JS, Weaver WD, Topol EJ. Determinants of the use of coronary angiography and revascularization after thrombolysis for acute myocardial infarction. N Engl J Med 1996;335:1198-205.
11. Van de Werf F, Topol EJ, Lee KL, et al. Variations in patient management and outcomes for acute myocardial infarction in the United States and other countries: results from the GUSTO trial. JAMA 1995;273:1586-91.
12. Lange RA, Hillis LD. Should thrombolysis or primary angioplasty be the treatment of choice for acute myocardial infarction? Thrombolysis — the preferred treatment. N Engl J Med 1996;335:1311-2.
13. Every NR, Larson EB, Litwin PE, et al. The association between on-site cardiac catheterization facilities and the use of coronary angiography after acute myocardial infarction. N Engl J Med 1993;329:546-51.
14. Alderman EL, Bourassa MG, Cohen LS, et al. Ten-year follow-up of survival and myocardial infarction in the randomized Coronary Artery Surgery Study. Circulation 1990;82:1629-46.

Venous Thrombosis — The Interaction of Genes and Environment

VENOUS thrombosis is the obstruction of the circulation by clots that have been formed locally in the veins or have been released from a thrombus elsewhere. The usual sites of thrombus formation are the superficial and deep veins of the legs, but it also may occur in veins in the brain, retina, liver, and mesentery.

An important question is why thrombosis develops in a given person at a specific site at a particular age and time. Probably the formation and growth of a thrombus are caused by local activation of the coagulation system, combined with a disturbance in the balance between coagulation and fibrinolytic reactions favoring clot formation. An increased risk of venous thrombosis can last throughout life because of the presence of mutations in genes coding for hemostatic or fibrinolytic proteins, but the increase in risk may also be of limited duration — that is, due to acquired or environmental factors.

The involvement of genetic factors was recognized in earlier reports on familial clustering of venous thrombotic events (familial thrombophilia); 20 to 30 percent of patients with thrombosis report having at least one relative with thrombosis. On the other hand, clinical studies have revealed that acquired conditions such as trauma, surgery, immobilization, pregnancy, the puerperium, and use of oral contraceptives are important risk factors for venous thrombosis. Detailed information on the identity of these risk factors and the extent of their interaction is needed to establish a policy for individualized treatment and prevention.

In this issue of the *Journal*, Martinelli et al.[1] report on the interaction of two recently identified, common prothrombotic mutations and the use of oral contraceptives in a study of the risk of cerebral-vein thrombosis. Because of the high prevalence of these mutations in the general population, only 40 patients were required for the authors to draw meaningful conclusions from the study.

What are these mutations? The first is a mutation in the gene coding for coagulation factor V. A transition (guanine to adenine) at nucleotide 1691 (G1691A) in exon 10 of the factor V gene results in the replacement of arginine at position 506 by glutamine (factor V Q506, factor V Leiden).[2] Factor V circulates in the blood as an inactive procofactor: it can be activated by thrombin, resulting in the formation of a two-chain molecule (factor Va) that serves as a cofactor of factor Xa in the conversion of prothrombin into thrombin. Inactivation of factor Va occurs through selective proteolytic cleavages in its heavy chain at Arg306, Arg506, and Arg679. The responsible enzyme is activated protein C. Activated factor V Leiden, with a glutamine instead of an arginine at position 506, is not cleaved by activated protein C at this position and is therefore inactivated more slowly. This is the molecular basis of the laboratory phenotype of resistance to activated protein C, first reported by Dahlbäck et al.[3]

The proportion of carriers of factor V Leiden in the white population varies from 2 percent to 15 percent. The mutation is extremely rare in nonwhites, and there is strong evidence that all factor V Leiden alleles originate from a common ancestor.[4] Heterozygous carriers have a risk of deep-vein thrombosis that is 7 times as high as that in the general population; for homozygous carriers, the risk is 80 times as high.[5]

The second prothrombotic mutation involves a guanine-to-adenine transition at nucleotide 20210 of the gene encoding prothrombin, the inactive precursor of thrombin, which is the end product of the coagulation cascade.[6] The importance of this transition is not yet known, but several investigators have reported that heterozygous carriers have 30 percent higher plasma prothrombin levels than noncarriers. Heterozygous carriers are known to have a risk of deep-vein thrombosis that is three to six times that in the general population. Again the abnormality is rare in nonwhite populations. In whites the reported prevalence of carrier status varies from 0.7 percent to 4 percent.[7]

The finding that the G1691A mutation in the factor V gene and the G20210A mutation in the prothrombin gene are common, strong risk factors for venous thrombosis in the legs raised the possibility that these mutations might also be associated with other forms of venous thrombosis.[8] It also raised the question whether there may be an interaction between genetic and environmental risk factors for venous thrombosis.[9] Furthermore, the role of thrombin formation in other complex diseases, such as myocardial infarction, stroke, eclampsia and preeclampsia, and diabetes, became a focus of research interest.

It is in this context that we have to consider the data reported by Martinelli et al.[1] from their study of the roles of prothrombotic mutations and the use of oral contraceptives in the development of idiopathic cerebral-vein thrombosis, a rare form of venous thrombosis. They compared the frequency of the mutations G1691A and G20210A and the use of oral contraceptives among 40 unrelated patients who had a confirmed diagnosis of cerebral-vein thrombosis with that among 120 healthy controls. They made two important observations. First, the prothrombin-gene mutation G20210A is an important risk factor for cerebral-vein thrombosis. This supports previous findings by the same authors and others regarding factor V Leiden as a risk factor for

cerebral-vein thrombosis.[10-12] Interestingly, the frequency of the two mutations was very similar among patients with cerebral-vein thrombosis and among young patients with deep-vein thrombosis in the legs, pointing to a similar role of these mutations in the development of two different presentations of the same disease.

The second observation concerns the contribution of oral-contraceptive use to the risk of cerebral-vein thrombosis. The use of oral contraceptives appeared to be a strong risk factor for cerebral-vein thrombosis (odds ratio, 22.1; 95 percent confidence interval, 5.9 to 84.2), which is in agreement with the results of an earlier study in which a relative risk of approximately 13 (95 percent confidence interval, 5 to 37) was reported for oral-contraceptive users.[13] What is particularly interesting is that for women who were both carriers of the G20210A prothrombin-gene allele and current users of oral contraceptives, the risk of cerebral-vein thrombosis (odds ratio, 149.3) far exceeded the sum of the separate risks associated with these two factors. This again points to an interaction between a prothrombotic mutation and the use of oral contraceptives and extends the findings of previous studies that have documented an interaction between factor V Leiden and oral-contraceptive use in causing deep-vein thrombosis in the legs and cerebral-vein thrombosis.[13,14] At a molecular level, this interaction is not well understood. Oral-contraceptive use results in changes in the concentrations of many hemostatic and fibrinolytic components of the blood and may add in multiple ways to the disturbance in the hemostatic balance that is introduced by a prothrombotic mutation.

Martinelli et al. further report that 78 percent of all their patients with cerebral-vein thrombosis were women and that, after the exclusion of women who were pregnant or postmenopausal at the time of the event, 96 percent used oral contraceptives; 37 percent were both carriers of a prothrombotic mutation and users of oral contraceptives. These figures clearly differ from those in patients with deep-vein thrombosis in the legs: about 60 percent of these patients are women, of whom 40 percent use oral contraceptives, and 10 percent are both carriers of a prothrombotic mutation and current users of oral contraceptives.[14] So we have to consider seriously the possibility, previously discussed by de Bruijn et al.,[13] that the introduction of oral contraceptives has contributed to the incidence of cerebral-vein thrombosis. This may have occurred particularly in women from families with thrombophilia.

Finally, we still do not know why venous thrombosis develops in the brain in some patients and in the leg in others. The very young age of the patients with cerebral-vein thrombosis at the time of the event (median, 31 years) indicates that in these patients, there must be additional risk factors that are still unknown.[15]

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REFERENCES

1. Martinelli I, Sacchi E, Landi G, Taioli E, Duca F, Mannucci PM. High risk of cerebral-vein thrombosis in carriers of a prothrombin-gene mutation and in users of oral contraceptives. N Engl J Med 1998;338:1793-7.
2. Bertina RM, Koeleman BPC, Koster T, et al. Mutation in blood coagulation factor V associated with resistance to activated protein C. Nature 1994;369:64-7.
3. Dahlbäck B, Carlsson M, Svensson PJ. Familial thrombophilia due to a previously unrecognized mechanism characterized by poor anticoagulant response to activated protein C: prediction of a cofactor to activated protein C. Proc Natl Acad Sci U S A 1993;90:1004-8.
4. Zivelin A, Griffin JH, Xu X, et al. A single genetic origin for a common Caucasian risk factor for venous thrombosis. Blood 1997;89:397-402.
5. Rosendaal FR, Koster T, Vandenbroucke JP, Reitsma PH. High risk of thrombosis in patients homozygous for factor V Leiden (activated protein C resistance). Blood 1995;85:1504-8.
6. Poort SR, Rosendaal FR, Reitsma PH, Bertina RM. A common genetic variation in the 3′-untranslated region of the prothrombin gene is associated with elevated plasma prothrombin levels and an increase in venous thrombosis. Blood 1996;88:3698-703.
7. Rosendaal FR, Doggen CJM, Zivelin A, et al. Geographic distribution of the 20210 G to A prothrombin variant. Thromb Haemost 1998;79:706-8.
8. Desmarais S, de Moerloose P, Reber G, Minazio P, Perrier A, Bounameaux H. Resistance to activated protein C in an unselected population of patients with pulmonary embolism. Lancet 1996;347:1374-5.
9. Rosendaal FR. Risk factors for venous thrombosis: prevalence, risk, and interaction. Semin Hematol 1997;34:171-87.
10. Martinelli I, Landi G, Merati G, Cella R, Tosetto A, Mannucci PM. Factor V gene mutation is a risk factor for cerebral venous thrombosis. Thromb Haemost 1996;75:393-4.
11. Deschiens MA, Conard J, Horellou MH, et al. Coagulation studies, factor V Leiden, and anticardiolipin antibodies in 40 cases of cerebral venous thrombosis. Stroke 1996;27:1724-30.
12. Zuber M, Toulon P, Marnet L, Mas JL. Factor V Leiden mutation in cerebral venous thrombosis. Stroke 1996;27:1721-3.
13. de Bruijn SF, Stam J, Koopman MM, Vandenbroucke JP. Case-control study of risk of cerebral sinus thrombosis in oral contraceptive users who are carriers of hereditary prothrombotic conditions. BMJ 1998;316:589-92.
14. Vandenbroucke JP, Koster T, Briët E, Reitsma PH, Bertina RM, Rosendaal FR. Increased risk of venous thrombosis in oral-contraceptive users who are carriers of factor V Leiden mutation. Lancet 1994;344:1453-7.
15. Lensen RP, Rosendaal FR, Koster T, et al. Apparent different thrombotic tendency in patients with factor V Leiden and protein C deficiency due to selection of patients. Blood 1996;88:4205-8.

Fatal Impact — Concussion of the Heart

WHEN he died on a winter evening in 1995, Matthew Messing was only 16 years old. It happened while he was playing in a high-school ice-hockey game in Quincy, Massachusetts. The referee said the boy was hit squarely in the chest by an opponent during a routine body-checking maneuver. The spectators noticed nothing unusual about the

check; hockey players are hit like this all the time in competition. The boy was thrown to the ice, and he made a feeble effort to get up but fell back, his young body lifeless. It was over in an instant, as though he had been struck by lightning, and attempts to resuscitate him were fruitless. The town was shocked, and nearly 2000 people attended the funeral a few days later.[1]

Sudden death following a sharp but seemingly inconsequential blow to the chest is a frightening occurrence known as "commotio cordis" or "concussion of the heart." Although commotio cordis is considered rare, other cases similar to that of Matthew Messing have been described.[2] A 15-year-old New Hampshire boy died during a hockey game after he was hit in the chest by a puck at close range. A six-year-old boy died after being struck in the chest by a baseball thrown to him in a high arc by his mother. A 14-year-old lacrosse goalie was hit on the left side of his chest by a shot on goal and instantly collapsed. A year ago, a high-school football player in Virginia collapsed and died after what seemed to be routine body contact at the line of scrimmage. And just last month, a 14-year-old boy who was a junior black belt in karate collapsed and died after receiving a light contact blow to the chest during a match.[3]

These tragic stories are typical of commotio cordis: The victims are usually young people who die unexpectedly after a blow to the chest that does not appear to be unusually forceful. Death is immediate, and with few exceptions,[4] resuscitation is not possible. Three years ago in the *Journal,* Maron et al.[2] reported on 25 such cases. Since then, the authors' registry has grown to 69 cases, mostly young people who were struck in the chest while playing baseball, softball, or hockey (Maron BJ: personal communication). This tabulation is probably an underestimate, since the diagnosis of commotio cordis is sometimes missed and not all cases are reported. Consequently, death from commotio cordis — albeit unusual — may not be as rare as was once thought.

Although death in such cases appears to be a chance event, in several cases of commotio cordis criminal charges were brought against the person causing the fatal impact. In one instance, a 19-year-old Italian hockey player died suddenly after he was hit in the chest with the blade of a hockey stick while he and an opponent were jostling for position in front of the goal. The player who hit him, already devastated by the death and suffering from recurring nightmares, was charged with unintentional manslaughter, which in Italy carries a mandatory sentence of 10 to 18 years.[5] He later agreed to plead guilty to a reduced manslaughter charge and pay a fine. In another poignant case, last year in Washington, D.C., an 11-year-old boy died after his father struck him twice in the chest when the boy gave the wrong answer to the question, "Where is the big hand?" The father, who was trying to teach the boy to tell time, said he was only trying to discipline his son and did not mean to kill him; he was nevertheless charged with second-degree murder. Like the hockey player, the father pleaded guilty to a lesser charge of involuntary manslaughter.[6] He was sentenced to 6 to 18 years in prison.[7]

These controversial cases raise challenging questions: Given that the deaths were unintentional and could not have been foreseen, was it appropriate to bring criminal charges of that severity? In view of what we now know about commotio cordis — that death results from a peculiar accident of normal cardiac physiology — were the convictions and sentences justifiable? These provocative questions demand careful consideration by our justice system so that rational decisions can be reached in such cases in the future.

What is the mechanism of these catastrophes? It is known that blunt trauma to the chest can cause various types of injury to the heart. The most common is myocardial contusion, which can result from direct injury to the heart, compression of the heart between the sternum and vertebral column, or injury from rapid acceleration or deceleration of the heart in the thoracic cavity.[8] Contusions consist of areas of myocardial necrosis and hemorrhage that may cause ventricular dysfunction and generate ventricular arrhythmias. Nonpenetrating trauma to the chest may also cause the laceration or rupture of a cardiac chamber, usually the anteriorly located right ventricle, resulting in cardiac tamponade.[8] A coronary artery may be lacerated, causing myocardial infarction and associated ventricular arrhythmia.[8] In cases of commotio cordis, however, which result from relatively low-energy blows to the chest, no cardiac injuries have been identified at autopsy, nor has there been evidence of preexisting cardiac disorders that occasionally cause sudden death in athletes, such as hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia, myocarditis, or congenital anomalies of the coronary arteries.[2] Illicit drugs also have not been found to be involved. On the basis of a few instances in which the cardiac rhythm was recorded, the mechanism of death has been suspected to be ventricular fibrillation.[4]

In this issue of the *Journal,* Link et al.[9] provide direct evidence that ventricular fibrillation is the cause of most fatal cases of commotio cordis. The investigators developed an experimental model of commotio cordis in anesthetized juvenile pigs. Although animal studies are not often published in the *Journal,* this study contains unique, clinically relevant information that could not have been obtained in human subjects. The authors constructed a device that delivered controlled impacts to the chest, simulating the impact of a baseball thrown at moderate velocity.

The impacts were gated to the electrocardiogram so they could be precisely timed to particular phases of the cardiac cycle. When the impacts were delivered within a narrow temporal window between 30 and 15 msec before the peak of the T wave, ventricular fibrillation was reproducibly induced. The vulnerable period of the cardiac cycle amounted to just over 1/100 of a second. Remarkably, ventricular fibrillation was immediate, occurring on the very next heartbeat. The arrhythmia was not produced by impacts at any other time during the cardiac cycle, although transient complete heart block was sometimes observed with impacts during the QRS complex. Occasionally, with impacts delivered just outside the 15-msec period of vulnerability, unsustained polymorphic ventricular tachycardia was seen.

The observation that transient rhythm disturbances may occur with chest impact raises the possibility that there may be "near-miss" cases of commotio cordis. This may have happened last month to St. Louis Blues hockey captain Chris Pronger when he collapsed briefly, then spontaneously regained consciousness, after being struck on the left side of his chest by a puck during a playoff game.[10] Since the episode was captured on videotape, it could be seen that it was most likely an aborted case of commotio cordis. It is possible that other near-miss cases have gone undetected because the arrhythmias were too brief to cause loss of consciousness.

In another part of their study, Link et al.[9] examined whether the use of safety baseballs, which are softer than regulation balls, could reduce the risk of arrhythmia in the animal model. They found that the risk was proportional to the hardness of the ball. This finding has implications for the prevention of commotio cordis in young baseball players, since properly designed safety baseballs are feasible for use in recreational baseball and Little League. They are already being increasingly used. Another approach to prevention is the use of chest protectors specifically designed to cushion the precordium. The shoulder pads worn by hockey and lacrosse players are inadequate to protect the chest, particularly when the arms are raised,[2] and baseball players generally wear no chest protectors at all while batting. The animal model developed by Link et al.[9] will be useful in testing these and other new approaches to the prevention of commotio cordis. Since not all cases will be preventable, it is important to emphasize that rapid cardiopulmonary resuscitation, including a precordial "thump" and immediate defibrillation when possible, may be lifesaving.[4]

It is sobering that a seemingly minor chest impact at an instant when the heart is suspended in diastole can have such devastating consequences. Fortunately, deaths due to commotio cordis are uncommon, since both the timing and the location of the impact must be very precise to trigger ventricular fibrillation. When it happens, however, the life lost is usually that of a healthy, young person. Perhaps the greatest value of the article by Link et al.[9] will be to raise awareness about commotio cordis, demystify its cause, and educate us about the recognition and prevention of this tragic phenomenon.

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REFERENCES

1. Negri G. Community crowds funeral of hockey player; Quincy youth remembered by friends, family. Boston Globe. January 24, 1995:22.
2. Maron BJ, Poliac LC, Kaplan JA, Mueller FO. Blunt impact to the chest leading to sudden death from cardiac arrest during sports activities. N Engl J Med 1995;333:337-42.
3. Hoiles R. Like a neighborhood son. Akron Beacon Journal. May 5, 1998:B1.
4. Maron BJ, Strasburger JF, Kugler JD, Bell BM, Brodkey FD, Poliac LC. Survival following blunt chest impact-induced cardiac arrest during sports activities in young athletes. Am J Cardiol 1997;79:840-1.
5. Swift EM. A cruel blow. Sports Illustrated. December 6, 1993:66-79.
6. Miller B. Man pleads guilty to lesser charge in death of son, 11. Washington Post. January 14, 1998:B7.
7. Slevin P. D.C. man is sentenced in son's death. Washington Post. May 30, 1998:B8.
8. Tenzer ML. The spectrum of myocardial contusion: a review. J Trauma 1985;25:620-7.
9. Link MS, Wang PJ, Pandian NG, et al. An experimental model of sudden death due to low-energy chest-wall impact (commotio cordis). N Engl J Med 1998;338:1805-11.
10. Luecking D. Pronger relives a scary incident. St. Louis Post-Dispatch. May 12, 1998:C1.

Occasional Notes

Bitter Pills to Swallow

I LEARNED more about comprehensive cancer care when I became a patient in 1996 than I had during a residency in medicine or in practice as an internist and palliative care physician in a teaching hospital. When I was given a diagnosis of aggressive inflammatory carcinoma, I found myself transformed from one who orders and administers medication to a terrified recipient. Until then, I had felt that I was a particularly empathetic doctor who listened to and, I thought, heard the stories of my patients. It was a shock, then, to undergo the foreign and surreal experience of becoming a patient.

I had given countless seminars on the topic of "breaking bad news." The second half of each seminar was about "patient responses and how to be most helpful." I knew patients often reacted to their diagnosis with shock, horror, denial, and disbelief, but I was unprepared for the emotional roller-coaster ride precipitated by my discussions with the hospital staff after the diagnosis. I soon realized the number of bitter pills I had unwittingly delivered to patients during my 15 years of practice. Statements are made routinely by doctors who are oblivious to their catastrophic effect on patients. I became aware of this fact only when it was my turn to be on the receiving end of such statements as the following.

"Our newer technologies are so much better"

Perhaps telling patients that medical technology had improved in recent years simply made the discussion easier for me as the doctor bearing bad tidings. I had thought that it would be helpful to patients to learn that we had made tremendous advances in technology and supportive care. I tried to explain to patients requiring a colostomy that the new appliances and adhesives were far superior to the older ones. I had noted that few patients seemed encouraged by this fact, but I felt better having some good things to say about the procedure.

In a similar vein, I often told women about the history of breast surgery. The original Halsted procedures were far more mutilating than the much simpler approach used these days. Now that it was my turn, the term "modified radical mastectomy" seemed a contradiction in terms. I found little comfort in the knowledge that it was merely my breast that was to be removed, and not the pectoral muscles as well.

It was not helpful — and it actually augmented my distress — to be told how quickly the surgery was done. It seemed that since I would have to stay in the hospital for only two or three nights, my despair should be correspondingly less intense. Patients who have received bad news and are dealing with the prospect of upcoming surgery are frightened and angry. Trying to minimize the seriousness of the procedure they are fearing serves only to heighten their anxiety. Patients should be encouraged to express their fears and emotions. Once they have done so, it may then be helpful to speak about the positive and more hopeful aspects of the illness. Warning: Don't be surprised if the patient is still upset during future meetings, or if you have to explain it all again.

"Don't worry — your hair will grow back"

How many times had I reassured patients about to undergo chemotherapy that their hair would grow back? Probably hundreds. In the meantime, fabulous wigs were available. "No one will ever know you're wearing a wig." Occasionally, I would secretly wonder why they were so inconsolable about losing renewable hair when they could potentially lose their lives.

I had absolutely no comprehension of how devastating the physical changes associated with even early-stage cancer can be. There I was, engaged in a battle for my life, and weeping on day 21 of the first cycle of chemotherapy because my hair — which would grow back — was slithering away down the drain. Losing my hair was more upsetting than any of the other physical consequences of cancer therapy.

A bald head always made me feel naked. Yes, there were some very cute cotton hats or scarves. Yes, my wig was a dead ringer for my natural hair. But both hats and wigs felt suffocating. Regular people do not wear hats indoors. Wearing hats inside was almost as humiliating as walking around bald. Out of doors, the first puff of wind struck terror to my heart. I had to choose between walking along with my hand on my head or chasing after a truant wig.

Alopecia comes just at the time when the patient is feeling physically ill, tired, and demoralized. The body in which you are living feels quite foreign. These symptoms combine to cause great anguish. We cannot prevent anticancer drugs from causing alopecia. We can, however, be more attuned to the ways in which our patients express the nightmares they are living. Patients' despair about physical signs like alopecia or skin color often provides an entrée into the more global despair they are feeling. It is therefore not sufficient simply to tell patients that their hair, eyebrows, and lashes will grow back or that their normal skin texture and color will return. Even if patients are not expressing concern about these changes, as practitioners we must recognize that although the primary target of our chemical assault is neoplastic tissue, self-esteem and the quality of life are in-

nocent victims. Recommendations about support groups or counseling are just as important as prescriptions for prochlorperazine in helping our patients live through the experience of cancer.

"YOUR PROCEDURE IS CANCELED TODAY"

Cancellations or postponements are sometimes unavoidable. Discharges are postponed, or treatments may be delayed. This is frustrating for physicians trying to provide good and efficient care. Most of us, however, have little appreciation of the effect that delays have on our patients.

We know that ultrasound examinations, radiology, and computed tomography are painless and relatively simple procedures. Many patients do not know this. All patients awaiting even simple tests are anxious about what the results may show. Considerable mental energy and emotion are required to prepare oneself for these investigations. As a result, the news that there will be a delay is a bombshell for the waiting patient.

I was terrified of radiation treatments. As a medical professional, I was ashamed of my fear and knew it to be irrational. Only with great mental effort was I able to get myself to the clinic for the first two treatments. At the end of the second treatment, the technician told me that the machine would be down the following day for routine maintenance. I was shattered. The following day was Friday. That meant three days without therapy. My fear of radiation changed to terror at the possibility that my tumor would spread in the interim. Yes, I understood why machines needed servicing. The technician was rather detached as he prepared the room for the next patient. He seemed surprised by my reaction, and he obviously had no understanding of how hard it had been to make myself come for the treatments.

We cannot avoid delays in procedures or therapy, but if we had a better understanding of how patients feel while waiting for tests, we could be more empathetic and diminish the impact of delays. The shorter the time that remains before a procedure, the more devastating it is when the procedure is canceled. All health care practitioners must have a better understanding of the psychology of being ill. We are too often nonchalant about procedures or treatments and do not stop to think how it feels to be in the patient's shoes.

"I HAVE A REALLY GREAT CASE"

As a teacher of medicine, I have been in pursuit of "great cases" for two decades. A nonmedical friend used to take exception to my use of the term. I always thought that he was being rather stuffy until I found myself "a great case."

The various treatments for my cancer complicated the management of several concurrent medical conditions. One day, discouraged, I sat in an examining room waiting for the return of my physician. I heard him talking to a resident about "a great case" he had. It was a good example of how one thing can seem to make everything else go wrong — the classic domino effect. I began to weep when I realized that *I* was the great case.

We will always require good illustrative cases for educational purposes. We must, however, refine the methods used in clinical teaching in the corridor and at the bedside. Physicians must remember that although patients may be invisible because of curtains or thin clinic walls, they are not out of earshot. The attitudes revealed and the manner in which cases are discussed can be devastating to the listening patient. Worse still is raucous laughter while doctors are discussing your problem. Patients know that the worse their dilemma, the more interesting they are to the doctors who are talking about them.

Before any discussions about a patient take place, the participants must ensure that their words cannot be overheard by anyone, especially the patient. In addition, we must broaden both our approach to and our understanding of our patients. If we fail to acknowledge that they are first and foremost people struggling with an illness, this attitude will be evident to all concerned. Teaching physicians must remember that they are transferring more than knowledge during clinical interactions. Physicians who are callous and insensitive toward their patients will encourage the same characteristics in those whom they teach. As I have learned by bitter experience, anyone can become the next great case overnight.

"YOU ARE NOT ELIGIBLE FOR THIS STUDY"

As an academic physician, I was raised on clinical trials. I believe very strongly in evidence-based medical practice. Studies need to be vigorously designed if the results are to be useful. An important premise, of course, is that the groups of patients receiving different treatments are all similar at the outset. Particularly during my residency, we searched diligently for patients to enroll in clinical trials. Often as the interview with a new prospect proceeded, it became apparent that the patient was not suitable for the study after all. "You are not eligible for this trial" was the explanation we always used. This was not so disturbing to patients considering a trial of new antihypertensive medications. Life would carry on with the old medication. That statement could be shattering, however, when the stakes were much higher and the patient believed that an experimental treatment might make the difference between life and death.

My pathology report indicated that my tumor was relatively drug-resistant. The outlook was grim. Panic-stricken, I immediately thought about bone marrow transplantation. When I learned that I was "not

eligible" for ongoing studies involving transplantation, I was distraught. Was I supposed to die quietly because no researcher had thought to try transplantation at this point in the disease trajectory? At that moment, it felt as if the only life-saving option for me was being denied for arbitrary reasons.

Detailed discussion on a subsequent visit made me realize why transplantation was not a good option at the time. I was considerably comforted by this discussion. I know that my family and I would have felt resentful and bitter had I been denied this treatment only because of the design of the trial.

I am in no way proposing the discontinuation of clinical trials. I do, however, feel that the language of the clinical-trial world should not be used with desperate patients who are considering various treatment protocols. The term "eligible" is commonly used in everyday speech in different contexts. In an emotionally charged medical situation, it carries the connotation that the patient is being denied something desirable. If a patient is found to be ineligible for a clinical trial, this information must not be transmitted in a manner that implies that useful treatment is being withheld.

CONCLUSIONS

It is virtually impossible for one person to know exactly how another is feeling unless he or she has been through a similar situation. It is neither practical nor desirable that physicians experience a serious illness as part of their education. This does not mean that we cannot teach physicians to be more sensitive in their interactions with patients and to communicate better. I do not believe that most physicians intend to be callous or insensitive. I, myself, used all the classic phrases I have quoted here while in practice. I thought that I was being a sensitive physician and had no idea of the effect my words were having on my listeners. I learned to say these things from teachers who worked with me during my formative years. No doubt there are doctors who learned the same phrases from me.

Several suggestions may help. We must increase the time students spend learning the psychology of illness while they are doing clinical work. Many medical colleges now offer courses on this topic during the first years of training. Such courses are much less effective, however, when they are taught in a nonclinical setting. Several minutes could be reserved during bedside and clinical-teaching rounds for patients to describe how they are feeling. This approach would not only expose trainees to patients' emotions, but it would also present patients as real people rather than simply objects of interest for budding physicians. Too often, clinical teachers speak about patients but rarely speak to them as people. Role-playing is an effective method of allowing students some sense of how it feels to receive bad news from a doctor. With the opportunity to play out the scenarios in many different ways, students can experience the difference between good and poor communication.

Finally, our profession ought to be working on effective methods for practitioners to deal with the stress of work. Many physicians prefer to keep a detached attitude toward patients, because it is too difficult emotionally and too time-consuming to encounter the suffering that accompanies human illness. This approach is not advantageous for either patients or doctors. There have been some strides toward improving doctor–patient relationships, but there is still much more work to be done. Perhaps increased attention to this aspect of patient care and the more interdisciplinary approach practiced these days will help doctors to do a better job of communicating with their patients.

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Supported by the Edward Dunlop Foundation and the Geoffrey H. Wood Foundation.