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Framing for Success: Nocebo Effects in Thoracic Surgery

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Contemporary clinical ethics emphasizes informed consent for medical treatment, which in turn is based on the principles of respect for individual self-determination (respect for autonomy), doing what is best for the patient (beneficence), and minimizing harm (nonmaleficence). Information can be presented to patients in various ways during the informed consent process, each of which has different effects on their attitudes, judgments, and decision making. Surgeons minimize potential harms to their patients in many ways, such as maintaining their own knowledge base and technical skills and ensuring that the surgical team is caring and well-prepared. Surgeons can add another protective strategy: minimizing the nocebo effect.

The inverse of placebo effects are called nocebo effects—psychologically-generated harmful or undesirable outcomes of medical encounters.[1] Such effects have been acknowledged in the medical literature for decades; however, in clinical practice, they have been largely unrecognized and insufficiently controlled. Both placebo and nocebo effects are known to be associated with surgical interventions as well as with medical therapies. Many factors influence the occurrence of psychologically-generated adverse outcomes, some of which can be controlled or managed by physicians. Understanding these factors can help surgeons minimize such outcomes. Perhaps the most important factor surgeons can control is the way they manage the informed consent process, particularly the way they frame the risks of the procedure.

Framing of Information

Prospect theory was developed by Daniel Kahneman and Amos Tversky over the decades following their seminal paper in 1979.[2,3] Their work has been validated and expanded by others, but prospect theory has been so important in the development of behavioral economics that in 2002 Daniel Kahneman won the Nobel Memorial Prize in Economics (Tversky died in 1996 so could not share in the Prize). Appreciation for the importance of their work in medical decision-making and patient counseling has grown recently.[4]

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Prospect theory states that people do not make decisions and judgments on the basis of outcome probabilities, rather, they make them on the basis of the potential value of gains and losses. They weigh gains and losses differently, however—people are much more strongly averse to losses than they are positively disposed to gains.[5] They also overestimate the probability of unlikely events and excessively weigh unlikely events in their judgments. The overweighing results from three aspects of scenario evaluation: 1) focused attention: if an event is likely (e.g., survival without complications after an operation), people tend to focus on the alternatives (i.e., complications); 2) confirmation bias: people tend to retrieve evidence, instances or images related to the focal alternatives that confirm their plausibility; and 3) fluency, or cognitive ease: weighing probabilities is influenced by the ease with which the adverse outcomes are perceived (e.g., complications suffered by a friend or relative after a similar procedure). The role of mathematical probability in weighing outcomes is reduced even more when the mental representation of the outcome is vivid.[5]

Using actual numbers rather than more abstract percentages increases the vividness effect—called denominator neglect. For example, an epidemic that “kills 1,286 people out of every 10,000” is perceived as worse than an epidemic that “kills 24.14% of the population,” even though the latter kills almost twice as many people.[6] Thus, judgment is more biased if actual numbers are used to replace broader representations of the data such as percentages. Prospect theory has important implications for the informed consent process.

Nocebo Effects

A nocebo response occurs when the suggestion of a negative effect of an intervention leads to an actual negative outcome. For example, when clinicians instruct patients that a medical procedure will be extremely painful, they tend to experience more pain than patients who weren’t similarly warned. The nocebo effect has been observed in a variety of clinical trials. Amanzio and colleagues reviewed 73 clinical trials of nonsteroidal anti-inflammatory drugs (NSAIDs), triptans, and anticonvulsant drugs conducted between 1988 and 2007, each comparing anti-migraine medications against placebos. The negative side effects reported by the placebo groups in each study (nocebo effects) were the same as the drug being studied. For example, placebo subjects in NSAID and triptan trials reported no memory problems or tingling, which are side effects of anticonvulsant drugs, but placebo subjects in anticonvulsant trials did report these symptoms. Similarly, placebo recipients in NSAID trials reported NSAID-related side effects such as stomach upset and dry mouth, but these were not reported by subjects in the anticonvulsant placebo groups.[7]

Potential psychological mechanisms for the nocebo effect, as for the placebo effect, appear to be related to factors of subconscious conditioning and conscious expectations. Patients who have had previous experience of adverse effects with an active drug may be conditioned to experience similar adverse effects even when they are only given a placebo. Patients may also anticipate adverse effects if they are influenced by the knowledge of potential adverse effects described by clinicians, and also by the memory of past adverse effects.[8]

Clinicians necessarily frame the information they provide their patients during the informed consent process, and medically accurate information can be presented in different ways.[9] How does the clinician strike a balance between optimizing information while minimizing potential harm? Some have recommended withholding certain information from patients to minimize the nocebo effect,[10] but we believe that withholding information is not necessary. Most procedures surgeons perform or medications we prescribe are susceptible to a host of nonspecific side effects—fatigue, anxiety, difficulty concentrating, drowsiness,

headache, and insomnia.[11] Specific surgery-related nocebo effects have also been observed; fear and distress before an operation may be associated not only with severity of pain, but also with slow postoperative recovery, increased complication rates, and delayed wound healing.[12,13]

Thoracoscopic Lobectomy for Cancer

Consider the case of Iva Krabbe, a 65-year-old retired college history professor who presents with a biopsy-proven 2 cm left upper lobe lung carcinoma. Ms. Krabbe has full capacity to make health care decisions. After pulmonary function testing, her thoracic surgeon, Dr. S.F. Young, determines that the patient is a good surgical candidate and is prepared to offer her video-assisted thoracoscopic surgery (VATS) lobectomy. He also plans to mention the less desirable options of open lobectomy, stereotactic body radiation therapy, radiofrequency ablation or observation (no surgery). Dr. Young wants to provide Ms. Krabbe with as much relevant information as is necessary for her to make a well-considered decision to go forward with the operation. The information should include the nature of the alternative operations and their expected benefits and risks, both short term and long term. Short term issues would include at least description of pertinent procedural details, normal expectations of pain, wound healing, etc., and possible complications. Long term issues would include, at a minimum, likelihood and duration of survival.

Dr. Young describes how the VATS procedure is done. Complications are relevant to the patient's decision-making process and must be conveyed to her. Dr. Young uses numbers rather than percentages because numbers are more concrete and therefore easier to understand, he believes, so he tells Ms. Krabbe that the likelihood of her surviving the operation without complications is 75%, but also explains that many complications can occur after this operation: the likelihood of air leak requiring chest tube drainage longer than a week is 8 out of 100 patients, cardiac arrhythmia 7 of 100, bleeding requiring transfusion 4 of 100, and pneumonia 3 of 100 patients. He also explains that fewer than 1 of 100 patients have a heart attack, stroke, wound or chest infection, and kidney or bladder infection. Other complications are rare, each occurring in fewer than 1 of 1000 patients. In all, 25 patients of 100 undergoing this procedure have any complication at all. Only 19 patients in 1,000, just 1.9%, die after the operation. Nearly 2/3 of patients have mild or no pain, and only 6 of 100 have severe pain, many fewer than after the open operation. He also describes the likelihood and duration of long term survival and cure after the operation.

Dr. Young has been thorough in discussing the possible results of surgery, so the patient can make a well-informed decision about consenting to surgery, which she does without hesitation. Has the surgeon's thoroughness served the patient well? We suggest that the patient may not have benefited from Dr. Young's carefully thought out, complete explanation. Prospect theory and the nocebo effect can explain why the patient might have been harmed by the disclosure process.

How Can the Informed Consent Process Harm Patients?

Research in prospect theory over several decades tells us that people in general attach greater weight to losses—adverse outcomes—than to gains. This effect is magnified when the positive aspects are dominant and losses are proportionately small. Using actual numbers rather than percentages tends to focus the subject's attention on images of people who are suffering the adverse outcomes. Moreover, large numerators are seen merely as large numbers rather than proportions—so-called denominator neglect—further accentuating the negative images. Any previous experiences the patient might have had with undesirable outcomes, either personally or in friends and relatives, add to the vividness of the images and feelings, resulting in even heavier weighing of adverse outcomes.[5] In this way, the

threat of complications assumes proportions much greater than the actual statistics warrant, which can lead to increased anxiety and stress before the operation.

We can apply these observations to the case of Ms. Krabbe. Dr. Young told his patient that she has a 75% chance of coming through the operation without complications. That's good news, but its magnitude changes her focus to potential losses: complications and death. Her mind's eye visualizes 8 patients in the hospital with an air leak and a chest tube for over a week, 7 patients with abnormal heart beats, 4 patients bleeding from their chests, 3 patients with pneumonia, and 6 patients in severe pain, neglecting the denominator for each bad outcome. Still worse, 19 patients are dead; again, her personal calculus ignores the denominator of 1,000.

Dr. Young presented accurate evidence-based information,[14] but framed it in a way that may have increased the stress and anxiety that ordinarily accompanies imminent surgery. Some degree of postoperative nocebo effect is likely in the form of the nonspecific symptoms mentioned above and increased possibility of surgery-specific complications.

A better approach for Dr. Young would have been to provide the same information, but to frame it differently. He would have kept the 75% survival without complications, and mentioned only the most frequent complications in general terms, perhaps something like, "The most common potential complications are an air leak lasting for a week or more, abnormal heart beats, bleeding, and lung infections, all uncommon, occurring in 1–7% of patients like you. Other problems can occur rarely, less than 1% of the time. Pain accompanies nearly all chest operations, but the vast majority of patients having this operation have only mild pain or no pain at all, far less than the older open operation." He must mention survival outcomes as well, of course, but would not describe them as 19 deaths out of 1,000 patients, rather, he would frame them positively: "You will have a 98–99% chance of coming through the operation and leaving the hospital in good shape." If Ms. Krabbe wants more specific statistical details, Dr. Young can easily provide them.

Framing the discussion of risks in this way emphasizes the positive aspects of VATS lobectomy while informing the patient of the risks in a less threatening manner. Ms. Krabbe can make a well-informed decision without the extra weight of imagined losses that lead to increased fear and distress. Her postoperative course is likely to be smoother, with fewer nonspecific side effects such as fatigue, anxiety, and difficulty concentrating, and with fewer complications specifically associated with surgery, such as slower recovery time and delayed wound healing, among others.[12,13]

Conclusion

Thoracic surgeons may be able to minimize nocebo effects after surgery by presenting a generally optimistic tone preoperatively, in the context of values and preferences of the individual patient. They should present relevant information accurately, according to the best evidence available, including description of plausible alternatives. As surgeons, we should be mindful of the impact of our conversations on surgical outcomes; we should frame preoperative discussions by emphasizing potential gains and discussing losses (complications and death) honestly but in a way that minimizes the negative effect that loss aversion is likely to have on the postoperative course. A thoughtful, fact-based informed consent process may optimize outcomes while honoring the principles that require serving our patients' best interests and respecting their self-determination.

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