Beneficial Effects of Hypnosis and Adverse Effects of Empathic Attention during Percutaneous Tumor Treatment: When Being Nice Does Not Suffice

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PURPOSE: To determine how hypnosis and empathic attention during percutaneous tumor treatments affect pain, anxiety, drug use, and adverse events.

MATERIALS AND METHODS: For their tumor embolization or radiofrequency ablation, 201 patients were randomized to receive standard care, empathic attention with defined behaviors displayed by an additional provider, or self-hypnotic relaxation including the defined empathic attention behaviors. All had local anesthesia and access to intravenous medication. Main outcome measures were pain and anxiety assessed every 15 minutes by patient self-report, medication use (with 50 μg fentanyl or 1 mg midazolam counted as one unit), and adverse events, defined as occurrences requiring extra medical attention, including systolic blood pressure fluctuations (≥50 mm Hg change to >180 mm Hg or <105 mm Hg), vasovagal episodes, cardiac events, and respiratory impairment.

RESULTS: Patients treated with hypnosis experienced significantly less pain and anxiety than those in the standard care and empathy groups at several time intervals and received significantly fewer median drug units (mean, 2.0; interquartile range [IQR], 1–4) than patients in the standard (mean, 3.0; IQR, 1.5–5.0; $P = .0147$) and empathy groups (mean, 3.50; IQR, 2.0–5.9; $P = .0026$). Thirty-one of 65 patients (48%) in the empathy group had adverse events, which was significantly more than in the hypnosis group (eight of 66; 12%; $P = .0001$) and standard care group (18 of 70; 26%; $P = .0118$).

CONCLUSIONS: Procedural hypnosis including empathic attention reduces pain, anxiety, and medication use. Conversely, empathic approaches without hypnosis that provide an external focus of attention and do not enhance patients' self-coping can result in more adverse events. These findings should have major implications in the education of procedural personnel.

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Abbreviations: IQR = interquartile range, RF = radiofrequency

SELF-hypnotic relaxation provided to patients on the procedure table has been shown to decrease pain, anxiety, drug use, and adverse events during peripheral vascular and renal interventions (1). We questioned whether these results would also apply to more invasive procedures, such as percutaneous tumor treatments. We designed a prospective randomized trial to test the effects of procedural hypnosis in patients undergoing transcatheter embolizations and radiofrequency (RF) ablations. In addition, we were interested in the effect of the attention that patients receive in a trial, particularly

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in one that assesses the effects of a communicative mind/body intervention. This is also a response to the increasing emphasis of organizations overseeing medical education on empathy and competency in interpersonal and communication skills (2,3).

In past studies, patients undergoing interventional procedures benefited to various degrees from structured empathy, which was included as an active control condition (1,4). Therefore, we included in our planned trial an empathic attention control condition to assess its effect on patients' perception and well-being. We believed this design could help shed more light on the issue of clinical empathy, which is subject to various interpretations (5–8), and in regard to which few prospective randomized trials correlate behaviors with patient outcomes.

MATERIALS AND METHODS

Patients

The study was conducted in an urban tertiary medical center with approval of its human subjects review board. Adult patients referred for percutaneous tumor treatment by transcatheter embolization or RF ablation who were able and willing to give written informed consent were recruited. Exclusion criteria were body weight less than 55 kg, a score lower than 26 on the Mini-Mental State test (9), indication of psychosis or serious mental disease, severe chronic obstructive pulmonary disease, home use of oxygen, intolerance of midazolam and fentanyl, pregnancy, and inability to hear or understand English.

Interventions Overview and Randomization

Methodology was modeled after published trials that assessed the effect of self-hypnotic relaxation during invasive medical procedures (1,4). Patients were randomly assigned to receive standard care, empathic attention, or self-hypnotic relaxation treatment (consisting of empathic attention plus reading of a hypnosis script) while on the procedure table. After consent for the invasive medical procedure, a research assistant obtained consent for participation in this study, performed mental and psychosis screening, and had patients fill out a Spielberger state-trait anxiety inventory (10). Random numbers in sealed envelopes determined the sequence of group assignment for consecutive patients. The envelopes were opened just before the patient's entry into the procedure room.

We hypothesized that adjunct self-hypnotic relaxation provided on the procedure table would (i) reduce patients' pain, anxiety, and medication use; and (ii) reduce the frequency of adverse events.

Tumor Treatment

Tumor embolizations employed standard angiographic technique via a transfemoral approach and superselective catheterization with 3–5-F catheters (11,12). Benign tumors (mostly uterine leiomyomas) were embolized with 300–700-μm polyvinyl alcohol (Boston Scientific, Natick, Massachusetts) or tris-acryl gelatin particles (BioSphere Medical, Rockland, Massachusetts). Hepatic malignancies were embolized with doxorubicin (for primary tumors) or mitomycin (for metastases) in ethiodized oil followed by Gelfoam slurry (Pharmacia & Upjohn, Kalamazoo, Michigan). RF ablation was performed according to published technique (13) with use of computed tomographic (CT) guidance,17-gauge RF electrodes, and a 500-KHz monopolar generator (Radionics, Burlington, Massachusetts) capable of producing 200 W.

All patients received local anesthesia, intravenous hydration, and antimicrobial prophylaxis. Pretreatment for chemoembolization included allopurinol, hydroxyzine, granisetron, and famotidine perorally and 2 mg hydromorphone subcutaneously; patients with carcinoid tumor also received periprocedural intravenous octreotide. All 89 women with uterine leiomyomas received 30 mg intravenous ketorolac just before particle delivery; the last 43 treated also received preprocedural scopolamine hydrobromide patches.

Interventions

All patients were treated by one or two procedure nurses and technologists, an interventional radiologist, and a fellow and/or radiology resident. In the empathy and hypnosis groups, an additional research assistant sat at the patient's head protected by a mobile transparent lead glass shield hidden behind the radiation tower (or CT gantry) while the operators worked at the opposite end of the patient's body.

In both treatment conditions, the assistant displayed eight standardized empathic attentive behaviors specified in the treatment manual and published in abbreviated form (14): matching the patient's verbal preferences, adapting to the patient's nonverbal communication pattern, listening attentively, providing the perception of control (eg, "let us know at any time what we can do for you"), swiftly responding to the patient's requests, encouraging the patient, avoiding negatively valued language (eg, "you will feel a burn and a sting"), and using emotionally neutral descriptors instead (eg, "this is the local anesthetic"). In the hypnosis group, the assistant also read a hypnosis script (4), which invites patients to roll their eyes upward, close their eyes, breathe deeply, focus on a sensation of floating, and experience a pleasant setting of their choice with all their senses. The text suggested transforming potential discomfort into a sensation of warmth, coolness, or tingling. If needed, a provision in the script guided patients to project their worries and fears onto the left side of an imaginary split screen and find solutions on the right side of the screen. The research assistants coached the patients according to the script and the treatment manual in developing their own imagery and solutions.

The empathic and hypnosis conditions were provided by six research assistants (one male and two female physicians, two female medical students, and one premedical student with a psychology background) who had been trained and tested to reliably execute all key behaviors. To enhance fidelity of treatment administration (15), all procedures were videotaped. Fifty-seven tapes (28%) were randomly selected and analyzed by two other researchers not involved in the cases who had been trained to assess execution of prescribed and proscribed behaviors; the interrater reliability was 0.88. Adherence to the protocol was high. There was no difference in the frequency of and ex-

tent to which the research assistants displayed the structured empathic behaviors in the empathy and hypnosis groups.

Hemodynamic and Respiratory Measures

Heart rate, electrocardiography, respiratory rate, and oxygen saturation were monitored continuously, and blood pressure was monitored every 5 minutes by automated clinical equipment and recorded by nursing staff.

Adverse Events and Complications

Adverse events were defined as all occurrences that would attract extra medical attention to restore hemodynamic and cardiorespiratory stability. Patients' vital signs reflect their cardiovascular reactivity and can change based on anxiety levels, pain, sympathetic arousal, vagal stimulation, effects of sedative and analgesic agents, and in response to liberation of the content of hormone-active tumors. When blood pressure and heart rate change during a procedure, the operator often does not immediately know the cause of the change and the extent to which the change will progress. We therefore chose changes that, in our practice, would cause the operator or nursing staff to take notice and consider treatment, or at least divert attention from the ongoing procedure. Inclusion required presence of at least one of the following: systolic blood pressure fluctuations of more than 50 mm Hg with one measurement greater than 180 mm Hg or less than 105 mm Hg unless the trend was toward a more normal value from initial hypertension, vasovagal episodes, de novo diastolic hypertension greater than 95 mm, cardiac arrhythmia, chest pain, tachycardia (>100 beats/min), and respiratory disturbances. We used elements of the modified Aldrete score (16) as guidance, but rather than using percentages of preprocedural values or absolute limits alone, we chose the 50–mm Hg systolic changes only if they produced hypertensive values in a normotensive person or if they resulted in relative hypotension in a patient with hypertension. For example, a 50% increase in systolic blood pressure from 100 mm Hg to 150 mm Hg would not be as worrisome as the same rate of increase in a patient with a baseline measurement of 130 mm Hg whose systolic blood pressure reached 185 mm Hg; a 33% decrease in systolic blood pressure from 180 mm Hg to 120 mm Hg would be comforting, as opposed to a decrease from 150 mm Hg to less than 100 mm Hg.

Complications were reported according to the reporting standards of the Society of Interventional Radiology (17).

Pain, Anxiety, and Medication

Pain and anxiety were assessed by self-reporting on verbal scales that were previously validated and found reliable for use in this setting (18,19). Every 15 minutes, the researcher asked the patients to rate their comfort on a scale between 0 ("no pain at all") and 10 ("worst pain possible") and their anxiety on a scale between 0 ("no anxiety at all") and 10 ("terrified"). When patients indicated discomfort outside the queries, another rating was obtained and the worst score was used as representative for the 15-minute interval.

Patients' intraprocedural use of sedative and analgesic agents (beyond the premedication and intraprocedural ketorolac) was assessed in a modified patient-controlled analgesia model that had been found applicable in this setting (1). Patients were given a button to press to alert the attending nurse to administer one intravenous drug unit. Patients had access to a combination of sedative and analgesic agents. Drug units were based on the customary standard in the procedure suite and represented 0.5 mg midazolam plus 25 μg fentanyl per dose a maximum of four times with a lockout time of 5 minutes, followed by a lockout time of 15 minutes. Medication was withheld when the systolic blood pressure decreased to less than 89 mm Hg, oxygen saturation decreased to less than 93% despite nasal oxygen, or the patient developed slurred speech or was difficult to rouse. Patients received additional medication when they verbally asked for it or developed hypertension or tachycardia (except during a carcinoid crisis), or when distress and movements might have interfered with procedural progress. Rules for overriding the patients' choice of drug use in the patient-controlled analgesia model were agreed on by the procedure personnel before the study and were reviewed on an ongoing basis.

Procedure Time

Procedure time was recorded as the entire time the patient occupied the procedure room.

Blinding

Adverse events were based on recordings from standard hospital electronic equipment and entries on standard hospital procedure flow sheets by the nursing staff within their routine duties. Occurrence of adverse events was based on the nursing notes without knowledge of group attribution and according to the objective parameters outlined earlier. Although the operator was separated by the research assistant through the imaging tower or CT gantry and therefore not in easy auditory range of the interactions between research assistant and patient, complete blinding was not possible.

Statistical Analysis

Sample size analyses for the present study relied on estimates of the time courses of pain and anxiety ratings from an earlier study with the same design and measures (1). For a linear mixed model with smoothed correlations for eight successive bands in a within-subjects correlation matrix, calculations with the RMASS2 program (20), a compound symmetry ρ of 0.70, one-sided α of 0.05, power of 0.80, attrition data estimates from the previous study, and an effect size of 0.71, 94 subjects were required within a treatment condition (282 overall). When a high adverse event rate in the empathy group became evident at the semiannual data safety monitoring board meeting, the study was halted after enrollment of 201 patients.

With reduced patient numbers and the inability to convert pain and anxiety ratings into normally distributed data sets, nonparametric Mann-Whitney rank-sum tests were used. Data were analyzed on an intent-to-treat bases. Whereas measurements at different time points can be considered interdependent, comparisons among

Table 1
Patient Characteristics

Characteristic	Standard (n = 70)	Empathy (n = 65)	Hypnosis (n = 66)
Median (range) age (y)	50.5 (29–79)	51 (27–88)	48 (33–75)
Median (range) weight (kg)	68 (48–140)	69 (45–112)	69 (42–143)
Sex			
Male	31 (44.3)	22 (33.8)	21 (31.8)
Female	39 (55.7)	43 (66.2)	45 (68.2)
Ethnicity			
Non–Hispanic/Latino	66 (94.3)	62 (95.4)	64 (97.0)
Hispanic/Latino	4 (5.7)	2 (3.1)	2 (3.0)
Unknown	0	1 (1.5)	0
Race			
White	51 (72.9)	48 (73.9)	49 (74.2)
Black	16 (22.9)	14 (21.5)	13 (19.7)
Asian	3 (43)	3 (4.6)	2 (3.0)
Multiple	0	0	1 (1.5)
Unknown	0	0	1 (1.5)
Marital status			
Single	22 (31.4)	15 (23.1)	13 (19.7)
Married	37 (52.9)	41 (63.1)	38 (57.6)
Widowed	3 (4.3)	5 (7.7)	3 (4.5)
Divorced	5 (7.1)	2 (3.1)	7 (10.6)
Other	2 (2.9)	1 (1.5)	3 (4.5)
Unknown	1 (1.4)	1 (1.5)	2 (3.0)
Mean (range) Spielberger state anxiety score*	21.5 (0–61)	23 (10–65)	21.5 (10–62)
Previous angiographic procedure			
No	60 (85.7)	57 (87.7)	59 (89.4)
Yes	10 (14.3)	8 (12.3)	7 (10.6)
Tumor type/treatment			
Hepatic malignancy, total	38 (54.3)	33 (50.8)	33 (50)
Chemoembolization			
Non–hormone-active tumors	23 (32.9)	18 (27.7)	18 (27.3)
Neuroendocrine tumors	10 (14.3)	7 (10.8)	12 (18.2)
RF ablation†	5 (7.1)	8 (12.3)	3 (4.5)
Uterine artery embolization	28 (40)	30 (46.2)	32 (48.5)
Other tumor embolization	4 (5.7)	2 (3.1)	1 (1.5)

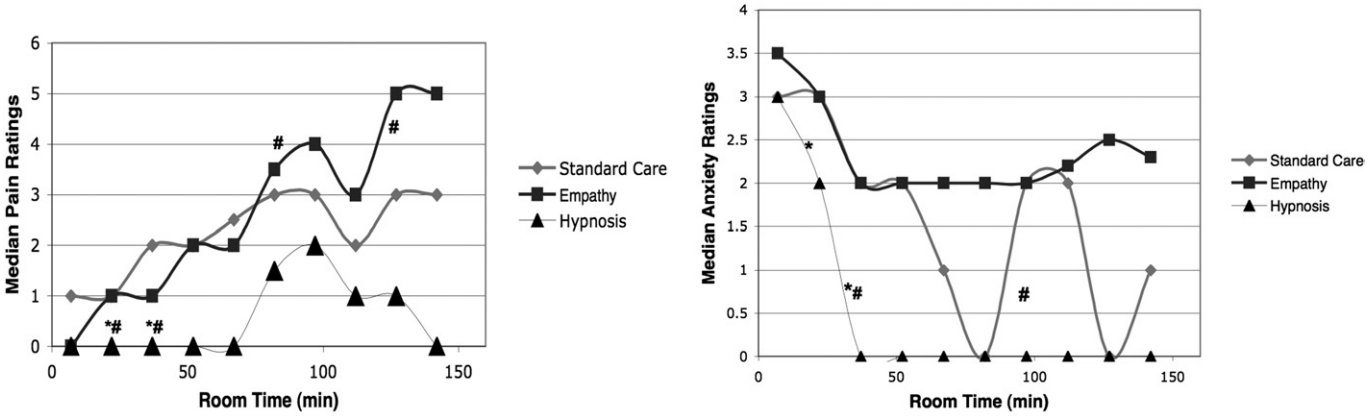
Note.—Values in parentheses are percentages unless specified otherwise.
* The Spielberger state anxiety questionnaire assesses anxiety and apprehension with 20 questions rated individually on a Likert-type scale from 0 to 4 and results in a summary score between 0 and 80.
† All RF ablations were for liver tumors with exception of one treatment for a pulmonary mass in the empathy group.

standard versus empathy, standard versus hypnosis, and empathy versus hypnosis treatment groups were considered to be independent of each other, and we therefore used Bonferroni corrections to place the significance level at $P = 0.0167$ (ie, 0.05/3) in two-tailed tests. The same testing was applied to the analysis of medication use and procedure time. Medians and interquartile ranges (IQRs), defining values between the 25th and 75th percentiles, were given to illustrate central tendencies for these variables. Frequency of adverse procedural events was compared between standard versus empathy, standard versus hypnosis, and empathy versus hypnosis treatment by two-tailed Fisher exact test at a significance level of $P = .0167$.

RESULTS

Between September 2004 and June 2006, 232 consecutive patients were assessed for eligibility. Ten were unable to understand English. Twenty refused to participate in this randomized study and one failed psychosis testing. The remaining 201 patients were randomized: 70 were allocated to and received standard-of-care intervention; 65 were allocated to and received empathic attention; and 66 were allocated to and received guidance in self-hypnotic relaxation. **Table 1** summarizes the patient characteristics, which were relatively homogenous among groups.

The **Figure** depicts the time course of the median pain and anxiety ratings. **Table 2** provides the data spread, P values, and patients remaining for each procedure interval. Anxiety decreased significantly in the hypnosis group compared with the standard group in the first 15–30 minutes. By 30–45 minutes, anxiety in the hypnosis group was significantly decreased compared with the standard and empathy groups. Pain measurements were significantly lower for the hypnosis group than the standard and empathy groups in the 15–30- and 30–45-minute intervals. In the 75–



a. b.

Figure. Median pain **(a)** and anxiety **(b)** ratings. Source data are from **Table 2**, which contains the IQRs and patients remaining at each interval. Asterisk indicates a significant difference between hypnosis and standard treatment, and the cross-hashes (ie, number signs) indicate a significant difference between empathy and hypnosis treatment. The significance level is $P = .0167$. Ischemic changes are anticipated at approximately 50 minutes of room time.

Table 2
Descriptive Statistics for Ratings of Anxiety and Pain as a Function of Room Time

	Standard			Empathy			Hypnosis			*P* values of Mann-Whitney rank-sums		
Time (min)	Median	IQR	No. of Pts.	Median	IQR	No. of Pts.	Median	IQR	No. of Pts.	Standard vs Empathy	Standard vs Hypnosis	Empathy vs Hypnosis
Ratings of anxiety												
0–15	3.0	0–6	70	3.5	2–6	63	3.0	0–5	65	.550	.331	.131
15–30	3.0	0–5	68	3.0	1–5	63	2.0	0–4	66	.985	.016*	.019
30–45	2.0	0–4	69	2.0	0–4	64	0.0	0–3	65	.825	.015*	.006*
45–60	2.0	0–4	63	2.0	0–3	61	0.0	0–2	60	.466	.036	.125
60–75	1.0	0–4	59	2.0	0–3	54	0.0	0–3	54	.873	.103	.129
75–90	0.0	0–3.5	45	2.0	0–4	49	0.0	0–2	40	.265	.276	.012*
90–105	2.0	0–4	34	2.0	0–4	37	0.0	0–2.6	34	.697	.142	.050
105–120	2.0	0–3.5	25	2.2	0–4	28	0.0	0–3.5	21	.675	.424	.272
120–135	0.0	0–3	13	2.5	1.1–4	14	0.0	0–3	16	.140	.750	.107
135–150	1.0	0–5.5	9	2.3	0–3.5	10	0.0	0–1.5	9	.834	.145	.055
Ratings of pain												
0–15	1.0	0–3	70	0.0	0–2	65	0.0	0–2.5	65	.223	.056	.530
15–30	1.0	0–3	68	1.0	0–3	65	0.0	0–2	66	.527	.002*	.014*
30–45	2.0	0–4	69	1.0	0–4	64	0.0	0–2	66	.855	.002*	.004*
45–60	2.0	0–4	63	2.0	0–4	62	0.0	0–2.3	61	.957	.073	.057
60–75	2.5	0–5	58	2.0	0–4.1	54	0.0	0–4	55	.988	.079	.088
75–90	3.0	0–5.8	45	3.5	0–5.5	49	1.5	0–4	41	.692	.054	.012*
90–105	3.0	0–6.3	34	4.0	0–6	37	2.0	0–4	34	.877	.237	.137
105–120	2.0	0–7.5	25	3.0	0.5–6	29	1.0	0–4	21	.778	.218	.049
120–135	3.0	0–6.5	13	5.0	2.5–6.5	14	1.0	0–4	17	.161	.370	.004*
135–150	3.0	0–7	9	5.0	0.8–6.4	10	0.0	0–3	9	.589	.118	.019

* Because three tests were performed on each variable, a significance level of $P = .016$ was accepted.

90-minute interval, when effects of tissue ischemia and cell death were expected to begin, and also at 120–135 minutes, patients who received hypnosis experienced significantly less pain and anxiety than those in the empathy group. As best seen in **part b** of the **Figure**, patients in the standard group had varying anxiety and pain experiences that, overall, did not differ significantly from those in the empathy group.

Patients in the hypnosis group received significantly less medication (mean, 2.0 units; IQR, 1–4 units) than those in the standard group (mean, 3.0 units; IQR, 1.5–5.0; $P = .0147$) and empathy group (mean, 3.50 units; IQR,

Table 3
Adverse Events

Event	Standard (n = 70)	Empathy (n = 65)	Hypnosis (n = 66)
Systolic blood pressure fluctuations			
>50 mm Hg with one value ≤105 mm Hg or de novo hypotension <80 mm Hg	3	3	3
>50 mm Hg with one value ≥180 mm Hg	5 (1)	12	3
De novo diastolic hypertension >95 mm Hg	0	2 (1)	0
De novo bradycardia	1	4	1 (1)
Vasovagal reaction	3	3	1
Sustained tachycardia >100 beats/min	1	2 (2)	0
Cardiac arrhythmia	1	2	0
Chest pain	2	0	0
Hypoxia with oxygen saturation <90%	0	1 (1)	0
Shortness of breath	0	2	0
Total	18 (2)	31 (7)	8 (1)

Note.—Unbracketed numbers indicate the main event that led to inclusion of the patient in the adverse event category. Each patient was counted only once for the statistical analysis. For patients with more than one adverse event, the additional events are indicated in parentheses.

2.0–5.9; P = .0026), whose results did not differ from each other (P = .4505).

When the trial was halted, 31 of 65 patients (48%) in the empathy group had experienced adverse events at a significantly higher frequency than those in the hypnosis group (eight of 66; 12%; P = .0001) and standard group (18 of 70; 26%; P = .0118). The difference between standard and hypnosis groups showed a trend but was not significant (P = .0514). In the empathy group, there were not only more patients who had adverse events, but those who had them also tended to experience more than one adverse occurrence (**Table 3**). Delayed complications are shown in **Table 4**. Small event numbers in the individual complication subcategories did not provide sufficient power to enable meaningful comparisons among the groups.

Median procedure durations were 110.0 minutes (IQR, 90–151 min) for the standard group, 120.0 minutes (IQR, 83–140 min) for the empathy group, and 110.0 minutes (IQR, 75–145 min) for the hypnosis group. The differences were not significant (P values between .7728 and .9109).

DISCUSSION

Hypnosis recipients had less pain, anxiety, and medication use than patients who received standard-of-care treatment. This is consistent with previous trials of invasive medical procedures (1,4,21–23), although the procedures in this study were more invasive in that they involved induction of tissue death, and patients were aware of overall greater treatment risks. Surprisingly, findings in the empathy group differed markedly from those in previous studies (1,4). A strikingly high adverse event rate (31 of 65; 48%) significantly exceeded that seen with patients under hypnosis (eight of 66; 12%) or receiving standard care (18 of 70; 26%) and ultimately prompted this trial to be halted. We were able to treat all the occurrences successfully, and small patient numbers in consideration of the low delayed major complication rates do not permit a statistically meaningful conclusion about the long-term impact. However, one should not underestimate the stress such procedural adverse events place on the procedural team and patients. At the time of their occurrence it is not clear whether these events are reversible or portend further untoward sequelae. We therefore chose to err on the side of patients' safety and end the trial.

Hypnosis has been shown to reduce cardiac sympathetic activity and myocardial ischemia during percutaneous transluminal angioplasty (24) and to improve the heart rate variability profile (25,26), a quantitative measure of changes in intervals of heart beats associated with autonomic function and predictive of cardiovascular risk (27). Trance can occur spontaneously without formal induction, particularly under conditions of stress (28). Patients in the hypnosis group—and possibly some in the standard group who might have experienced spontaneous hypnosis—may have benefited from such improved autonomic function and may therefore have escaped excessive adverse events. Conversely, patients in the empathic attention group may have been less able to engage their internal coping skills as a result of the external focus of attention (ie, the sympathizing personnel), resulting in poorer autonomic function and higher rates of adverse events.

The higher medication use in the empathy group, in contrast to a previous study in vascular/renal intervention (1), may be partly explained by the provision in the protocol that patients who develop hypertension or tachycardia could receive nurse-administered medication without patient request. It is also possible that the higher medication use is an expression of the greater reliance on the external provision of comfort. That there was no significant difference in room time among groups is likely a result of the rate-limiting slowness by which embolization agents can be infused and RF necrosis can be induced.

Percutaneous tumor treatments are prone to induce patient distress. Perceiving others in distress produces an affective response, which is oriented to decrease distress to the observer as well as to the suffering person, and elicits a behavioral response, which may be targeted toward providing comfort and reassurance or withdrawal (29). This affective response to the perception of others' pain can be documented on functional magnetic resonance imaging and is greater in intensity the higher the observer scores on empathy scales (30). However, higher scores on empathy scales do not necessarily translate to appropriate clinical behavior. A study in the postoperative acute care setting (31) reported that nurses who scored higher on such empathy scales, but did not have advanced education in

Table 4
Delayed Complications Categorized According to Society of Interventional Radiology Reporting Standards (17)

Complication	Standard (n = 70)	Empathy (n = 65)	Hypnosis (n = 66)
Minor complications			
Class A: no therapy, no consequence	**1**	**1**	**1**
Small hematoma	1	1	1
Class B: nominal therapy, no consequence	**1**	**1**	**2**
New right bundle branch block; telemetry overnight	1		
Transient creatinine increase to 1.5 mg/dL			1
Pain control* (extended observation)			1
Rash		1	
Major complications			
Class C: require therapy, minor hospitalization (<48 h)†	**3**	**3**	**2**
Volume overload, shortness of breath			1
Extended nausea and vomiting* difficult to control	1	1	1
Pain difficult to control*	1	1	
Panic attack, shortness of breath, tachycardia		1	
Chest pain	1		
Class D: require major therapy, unplanned increase in level of care, prolonged hospitalization (>48 h)	**3**	**4**	**1**
Hypertensive crisis, encephalopathy			1
Hypertension, electrocardiographic changes		2	
Flank ecchymosis, hypertension, rigors		1‡	
Ileus; prolonged inability to eat	2	1	
Confusion, encephalopathy	1		
Class E: permanent adverse sequelae	**0**	**1**	**1**
Readmission for gastrointestinal bleeding, syncope, and ascites 8 days later			1
Encephalopathy, renal failure		1	
Class F: death	**1**	**1**	**0**
Hepatorenal failure (day 4)		1	
Exsanguination from ileostomy varices (day 5)	1		

* Nausea, vomiting, pain, or temperature increases within the postembolization syndrome were not considered complications unless they were resistant to ordinary medical therapy and/or necessitated a prolonged hospital stay.
† Because tumor interventions typically include one night postprocedural observation, time 0 for extended hospitalization started 24 hours after the procedure.
‡ Patient died after discharge at day 28 as a result of disseminated metastatic disease.

patient interactions, did not provide better pain management for their patients. Well-meant sympathizing comments by caregivers can even produce "nocebo" effects if wording is not chosen carefully (32,33). In a setting in which physicians and nurses are aware of the procedural risks and may have witnessed serious complications and even death on the procedure table, one should not underestimate the fears these individuals bring with them into the procedure room. During review of the videotapes, we noted often nervous laughter and attempts at lightening the atmosphere with gentle jokes when patients were first brought into the room. One may speculate that seeing the expression of a patient becoming more relaxed while entering a trance state may potentially also calm the procedure team.

In the standard care condition, nurses left patients mainly on their own after the procedure started and checked on their well-being from time to time, such as when called by the patient or at critical parts of the procedure. In the empathy condition, nurses engaged to a greater extent with the patient and the empathic care provider. There were more frequent interactions of a conversational nature. These conversations followed patterns of social interactions, eg, when patients mentioned topics such as travel, careers, or encounters with the health care system, nurses expressed understanding and sympathy by contributing their own experiences. Rather than being a pleasant distraction, such discussions may have been experienced as disinterest on the part of the caregiver in the patient's distress. It is also possible that the responsive stance activity in the empathy condition served to further focus subjects' attention on their reported distress without giving them a means of controlling that distress, thereby compounding it. Conversely, in the hypnosis group, topics the patient mentioned were used by the researchers to structure desirable imagery, and, if they hinted at distressing emotional content, were further explored and addressed according to the provisions of the script and training manual. The focus was on helping patients help themselves. Therefore, the researcher displaying empathic attention skills did not remain an external focus of coping as in the empathy group, but enabled patients to mobilize their own internal resources and engage in self-hypnosis.

There are various interpretations of

empathy (5–8). In a review, Irving and Dickson (7) showed how the construct of empathy is surrounded by "ambiguity and conceptual confusion" and how this complicates its study and application in the health setting. A patient's experience may be very different from that of the caregiver, and emotional understanding requires careful listening on the part of the observer so the observer's response can match the patient's affective state (34). Although nurses in our study expressed great sympathy, the results seem to support that trying to be "nice" does not suffice. Ideally, positive feedback is developed, based on which the observer can identify the patient's feelings, concerns, or quandaries and reflect that back in an appropriate empathic response. However, this requires considerable interpersonal skill training.

The present study has limitations. We halted the trial because of a high adverse event rate in the empathy group. Analyses of the original planned primary outcomes (pain, anxiety, drug use, and adverse events) could not be performed at the power level planned and statistical analyses were adapted to the lower patient numbers. Total blinding of the operators was not achieved because the voice level in the procedure room and whole atmosphere typically calmed considerably after induction of hypnosis. Pain and anxiety data may have been biased because the individuals structuring empathy and hypnosis obtained them, but these demand characteristics should then have affected patients' ratings in both conditions similarly. Moreover, the main finding of the study—the difference in adverse event rates—was based on objective hemodynamic and respiratory data obtained from automated machines.

This study was able to show beneficial effects of analgesic and anxiolytic hypnotic techniques employing hypnosis in conjunction with empathic attention during invasive tumor treatment and the adverse effects that can be elicited by empathy alone without appropriate behavioral responses. Other treatments with a lower probability of hemodynamic and cardiorespiratory disturbances would have required much larger patient numbers to provide sufficient power for a meaningful comparison among groups. For example, in a trial with 236 women undergoing large core breast biopsy with local anesthesia only, there were one vasovagal episode in the standard care group, two in the empathy group, and none in the hypnosis group (4). Less invasive procedures have lower odds of adverse events overall, but they are performed more commonly, and in the aggregate, a potential adverse effect of an incomplete empathic approach can affect large numbers of patients and caregivers. It is important for caregivers to be aware of the effect of their behavior on patient outcomes not only in psychosocial but also hemodynamic terms. This will require considerable efforts in promoting awareness and training. It would appear that nonspecific support without providing means of managing acute pain and anxiety may do more harm than good.

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