Interventional Cardiology

Integrative noetic therapies as adjuncts to percutaneous intervention during unstable coronary syndromes: Monitoring and Actualization of Noetic Training (MANTRA) feasibility pilot

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Background Patients undergoing percutaneous coronary intervention (PCI) for unstable coronary syndromes have substantial emotional and spiritual distress that may promote procedural complications. Noetic (nonpharmacologic) therapies may reduce anxiety, pain and distress, enhance the efficacy of pharmacologic agents, or affect short- and long-term procedural outcomes.

Methods The Monitoring and Actualization of Noetic Training (MANTRA) pilot study examined the feasibility of applying 4 noetic therapies—stress relaxation, imagery, touch therapy, and prayer—to patients in the setting of acute coronary interventions. Eligible patients had acute coronary syndromes and invasive angiography or PCI. Patients were randomized across 5 treatment groups: the 4 noetic and standard therapies. Questionnaires completed before PCI reflected patients' religious beliefs and anxiety. Index hospitalization end points included post-PCI ischemia, death, myocardial infarction, heart failure, and urgent revascularization. Mortality was followed up for 6 months after hospitalization.

Results Of eligible patients, 88% gave informed consent. Of 150 patients enrolled, 120 were assigned to noetic therapy; 118 (98%) completed their therapeutic assignments. All clinical end points were available for 100% of patients. Results were not statistically significant for any outcomes comparisons. There was a 25% to 30% absolute reduction in adverse periprocedural outcomes in patients treated with any noetic therapy compared with standard therapy. The lowest absolute complication rates were observed in patients assigned to off-site prayer. All mortality by 6-month follow-up was in the noetic therapies group. In patients with questionnaire scores indicating a high level of spiritual belief, a high level of personal spiritual activity, a low level of community-based religious involvement, or a high level of anxiety, noetic therapies appeared to show greater reduction in absolute in-hospital complication rates compared with standard therapy.

Conclusions Acceptance of noetic adjuncts to invasive therapy for acute coronary syndromes was excellent, and logistics were feasible. No outcomes differences were significant; however, index hospitalization data consistently suggested a therapeutic benefit with noetic therapy. Of all noetic therapies, off-site intercessory prayer had the lowest short- and long-term absolute complication rates. Definitive demonstration of treatment effects of this magnitude would be feasible in a patient population about 4 times that of this pilot study. Absolute mortality differences make safety considerations a mandatory feature of future clinical trials in this area. (Am Heart J 2001;142:760-7.)

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Clinical investigations in patients undergoing percutaneous coronary intervention (PCI) for acute coronary syndromes have focused on plaque manipulation and anticoagulant or antiplatelet medications.[1,2] These procedures are performed in the awake patient. Risks and discomforts associated with invasive procedures and pharmacologic manipulations in the context of a life-threatening clinical syndrome may result in substantial distress. "Conscious sedation" is widely applied by using parenteral sedative-narcotic regimens, with the risk of compromising homeostatic mechanisms such as respira-

tory drive, airway protection, and resistance vessel vasoconstriction.[3] The safety and efficacy of "noetic" methods, including stress relaxation, imagery, touch therapy, and prayer in this setting have never been studied.

Mental arousal and anxiety can cause ischemia at rest in patients with stable coronary disease.[4-7] Administration of placebo has been reported to provide relief from anginal symptoms,[8] and relaxation training has been reported to reduce ventricular ectopy.[9] Stress-response physiologic mechanisms include profound stimulation of sympathetic tone, with resultant catecholamine cascade.[10,11] In the setting of unstable coronary syndromes and PCI, catecholamine-stimulated tachycardia, inotropy, vasoconstriction, arrhythmogenicity and platelet aggregation are all potential sources of adverse events. Sedatives, narcotics, and antiplatelet, anticoagulant, and anti-ischemic agents are combined in current practice as adjuncts to PCI to reduce such events. We hypothesized that adjunctive noetic therapies might provide further benefit by promoting mind-body-spirit equilibrium. In addition to potentially improving outcomes, this might also result in a more cost-effective and compassionate healing environment for the patient.

Clinical applications of noetic therapies purporting to enhance mind-body-spirit equilibrium have been reported, including studies in cardiac patients.[12-23] The logistic feasibility, safety, and efficacy of such techniques in patients undergoing PCI for acute coronary syndromes, however, has never been investigated. Phase I of the Monitoring and Actualization of Noetic Trainings (MANTRA) Study Project was a prospective, randomized pilot study of noetic interventions in this setting.

Methods

Study design

The MANTRA feasibility pilot study was conducted as a single-center prospective randomized clinical investigation. The study was reviewed by the hospital ethics committee, and informed consent was obtained from all patients. The study was designed around the traditional stress test paradigm in which serial baseline, induced stress, and recovery evaluations provide prognostic information. For this study, the baseline period was defined as the period from when the patient signed the consent form to the time the patient entered the catheterization laboratory. The physiologic stress period was defined as the period beginning with the arteriotomy in the catheterization laboratory until 30 minutes after the last contrast injection. The recovery period was defined as the period from 30 minutes after the last contrast injection through the time of hospital discharge. Long-term follow-up was defined as 6 months from the day of the PCI.

Definitions and noetic therapies

For this study, "noetic" was defined as a "treatment discipline whose influence purports to enable, release, channel, or connect an intellectual, intuitive, or spiritual healing influence without the use of a drug, device or surgical procedure."[24] A noetic "training" was defined as "a technique or discipline whose methods can be systematically described, studied, and taught in a manner commensurate with medical education, clinical or research applications."

The 4 noetic treatment assignments examined in this study were selected on the basis of access to experienced practitioners. Three treatments were conducted at the bedside (imagery, touch therapy, and stress relaxation). Intercessory prayer was conducted off-site as a double-blind component of the study. Details of each noetic treatment can be found on the Web site in Appendix A.

Standard therapy. Standard therapy was defined exclusively by the absence of any noetic treatment assignment by MANTRA protocol. The presence of family, clergy, or chaplain prior to the PCI, as well as whether the patients were aware of anyone specifically praying for their health was systematically documented.

The MANTRA volunteer practitioners group

Nineteen volunteers maintained a 7 days per week, 24 hours per day on-call rotation. All practitioners had previous experience with at least one noetic technique. All completed a day of training in the specific scripts and methods for this pilot, conducted by 2 of the coauthors (S. W. C., J. E. S.).

Randomization and treatment assignments

Patients were randomly assigned equally across 5 treatment groups. On-site envelopes were used for randomization. For patients assigned to any of the 3 hands-on noetic trainings, the practitioner on call worked with the patient before PCI according to the scripted technique. Prayer and standard therapy assignments remained double-blinded to patients, family, and staff. Prayer groups and prayer methods are listed in Table I.

Patient selection

Patients were eligible for the MANTRA pilot study if they had chest pain at rest, with or without acute electrocardiographic changes, and were scheduled for invasive diagnostic angiography or PCI procedures on the basis of the judgment of the attending cardiologist. All patients were managed in the coronary care unit before and after the PCI procedure.

Baseline descriptors and instruments

In addition to classic cardiac descriptors (eg, age, sex, cardiac risk factors), visits from family, hospital chaplains, and clergy before PCI were documented. Patients were also asked whether they knew of anyone who was specifically praying for their recovery. On enrollment, 2 previously developed questionnaires were completed: the Duke University Religion (DUREL) Index,[25,26] and the Spielberger State-Trait Anxiety Inventory.[27]

Duke University Religion Index. The DUREL Index consists of 5 questions that represent 3 discrete areas of assessment[25,26]: community-based social religious activity, personal or private religious activity, and personal belief in the importance of spirituality in life. For this pilot study, each of the 3 sections was prospectively dichotomized. Specifically, social

Table I. Off-site prayer group methods

Affiliation	Location	No. praying	Prayer, frequency and duration	Information provided
Unity School of Christianity	Unity Village, Mo	NA	24-h vigil, 30 d in lighted chapel	Patient name, ailment
Buddhist	Nalanda Monastery, France	18	Medicine Buddha tantra; evenings, 1 h	Patient name, ailment
Buddhist	Kopan Monastery, Nepal	150 monks	Medicine Buddha tantra, mantra of the deity that wears a leaf robe	Patient name, ailment
Catholic	Carmelite Monastery, Towson, Md	17	Daily mindfulness and vespers	Patient name, ailment
Jewish	Virtual Jerusalem, Israel	NA	Printed prayer placed in Western Wall	Patient name, ailment
Fundamentalist Christian	Abundant Life Christian Center, Sanford, NC	Congregation	Daily prayers and motivation by Holy Spirit	Patient name, ailment
Baptist	Elkin, NC	3 congregations	Daily prayers and altar prayer	Patient name, ailment
Moravian	Raleigh, NC	8	Daily prayer service	Patient name, ailment

NA, Not available.

religious activity was defined as "high" for patients indicating community meeting attendance once a week or more versus "low" for less-frequent activity. Private religious activity was defined as "high" for patients indicating personal prayer activity once per day or more versus "low" for other. For the final 3 questions, with potential continuous scores ranging from 3 (high) to 15 (low), personal religious belief was defined as "high" for a score of 3.

Spielberger State-Trait Anxiety Inventory. For this pilot study, the 20 questions from this survey reflecting subjective awareness of anxiety were scored over quartiles including "not at all," "somewhat," "moderately so," and "very much so." Scoring of this survey spans a continuous range from 20 (low anxiety) to 80 (high anxiety). The median score across our population (median 33) was taken as the cut point between low and high baseline anxiety.

Noninvasive monitoring

After informed consent was obtained, all patients were connected to a uniquely constructed noninvasive monitoring array designed for this study by the General Electric–Marquette Electronics Corporation (Milwaukee, Wis). Ten press-on radiolucent electrocardiographic electrodes were placed in torso and precordial positions used in standard 12-lead electrocardiographic monitoring[28] and connected to a bedside Tramscope monitor. Signals from these sources were archived in a central Unity-MUSE information system combined with a continuous 3-lead digital Holter monitor and the ST-Guard continuous 12-lead digital electrocardiographic workstation (General Electric–Marquette Electronics). This configuration allowed uninterrupted patient monitoring of all parameters. ST-Guard acquires and stores a standard digital 12-lead electrocardiogram (ECG) every 60 seconds, recorded at fidelity equivalent of American Heart Association specifications for standard electrocardiographic carts[29] and suitable for quantitative evaluation of ischemia evidenced through ST-segment deviation. The MARS 3-digital Holter playback provides 3-lead beat–beat morphology editing with heart rate variability analyses.

Medical and invasive therapy

All patients were treated medically and underwent invasive procedures in the routine standard of the Durham Veterans Administration Medical Center at the discretion of the attending cardiologist. Routine treatment included the use of aspirin, heparin, nitrates, β-blockers, abciximab, intra-aortic balloon pumps, balloon angioplasty, rotational atherectomy, and stenting.

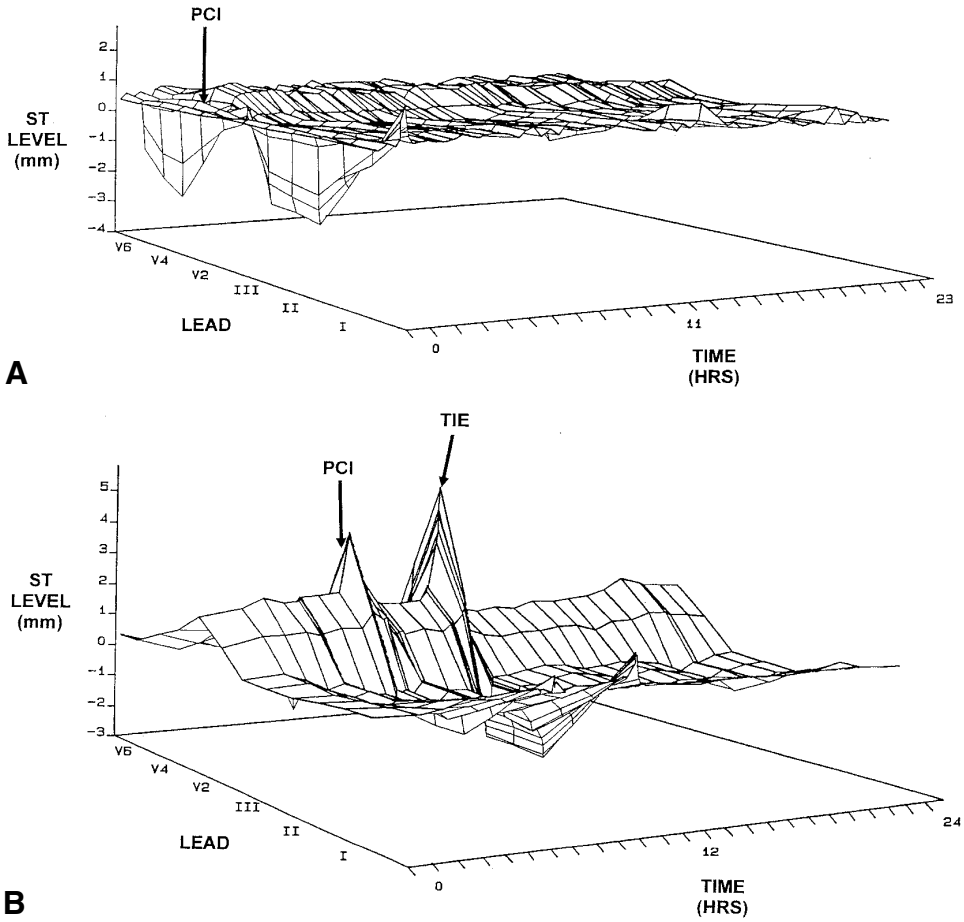
Study end points

End points included risk stratification by "stress test" abnormality as total ischemic burden during PCI; autonomic tone as post-PCI heart rate variability; coronary insufficiency defined as post-PCI ischemia; major adverse cardiovascular end points (MACE), defined as death, myocardial infarction, congestive heart failure, urgent repeat PCI or bypass surgery; and all adverse cardiovascular end points (ACE), defined as either MACE or post-PCI ischemia. The prospectively defined primary end point for this study was the ACE rate in patients treated with any noetic therapy versus patients treated with standard therapy.

Risk stratification—total ischemic burden during catheterization and PCI. Ischemia during the catheterization or PCI "stress test" was determined by continuous 12-lead ST-Guard recordings, beginning with the first contrast injection and continuing to 30 minutes after the final contrast injection. Recordings were archived digitally and forwarded to the Ischemia Monitoring Laboratory, Duke Clinical Research Institute, where they were retrospectively analyzed by an experienced physician blinded to treatment assignment. Episodes of ischemia were defined as >100 μV of new ST deviation from baseline in any of the monitored leads. The total ischemic burden was taken as the total curve area of the 12-lead ST deviation versus time trend, as illustrated in Figure 1, *A*. The greater the value of the total ischemic burden, the more abnormal the "stress test" was considered to be, as has been previously demonstrated in our laboratory.[30]

Heart rate variability (HRV). Holter recordings were edited

Figure 1



Three-dimensional graphic display of continuously monitored ST-segment deviation (*y* axis) over standard 12 leads (*x* axis) over time (*z* axis). **A,** Patient undergoing PCI of circumflex artery stenosis, producing inferolateral ST depression, followed by normal recovery in the cardiac care unit over the subsequent 23 hours. **B,** Patient undergoing PCI of the left anterior descending coronary artery, producing anterolateral ST elevation, followed by transient ischemic episode *(TIE)* of ST re-elevation in the cardiac care unit.

in the Ischemia Monitoring Core Laboratory to identify ectopic beats and artifact by an experienced operator blinded to treatment assignment and clinical findings. HRV variables as previously defined[31,32] include both time domain and frequency spectra indices.

Post-PCI ischemia. Continuous monitoring of 12-lead ECG for 24 hours after PCI was used to document episodes of ischemia (Figure 1, *B*). Recording technique and analysis of new ST-segment deviation described above were applied to the recording period from 30 minutes after the last contrast injection to the end of the monitoring session.

Major adverse cardiovascular end points. MACE end points assessed after PCI and throughout the index hospitalization included the following: death, myocardial infarction (new creatine phosphokinase elevation >2 times normal levels or appearance of new Q waves on ECG), congestive heart failure (auscultatory rales or x-ray evidence of pulmonary edema), and urgent or repeat revascularization.

Adverse clinical end points. ACE was taken as the incidence of patients having either ischemia or post-PCI MACE over the course of the index hospitalization.

Long-term follow-up. Patients were seen in a clinic visit or followed-up with a phone call at 6 weeks and 6 months after PCI. Mortality for all patients was reported at 6 months.

Statistical analysis

All statistical analyses were performed on an intention-to-treat basis. The primary hypothesis was designed to examine outcomes in the combined noetic therapies groups compared with the standard therapy group. Characteristics of each randomized therapy group were summarized in terms of frequen-

cies and percentages for categorical variables and by the median and 25th and 75th percentiles for continuous variables. Mean ± SD was used to describe continuous variables that were normally distributed. The Wilcoxon rank sum test and *t* test procedures were used to examine the relationship between continuous variables and the therapy groups. The χ^2 test, the Cochran-Mantel-Haenszel test, and the Fisher exact test were used to examine correlations between the categorical variables of interest and the therapy groups. A *P* value <.05 was considered statistically significant; 95% CIs were used to evaluate the difference in the incidence of major adverse cardiac events during index hospitalization and at 6 months after randomization for each therapy group.

Results

From April 1997 through April 1998, 170 eligible patients were identified for the pilot study; of those, 150 (88%) gave informed consent and were enrolled. All 150 patients were scheduled for invasive cardiac catheterization. Of the 150, 114 (76%) underwent PCI, 30 (20%) had only diagnostic catheterization, and 6 (4%) did not ultimately go to the cardiac catheterization laboratory. Of the 120 patients assigned to noetic therapy, 118 (98%) completed the therapeutic assignment. Baseline characteristics are shown in Table II.

Baseline survey instruments were completed in 145 patients (97%) for Koenig surveys and in 103 patients (69%) for Spielberger Inventories. Holter recordings were analyzable for HRV end points after PCI in 101 (67%). Continuous 12-lead ST-Guard recordings were analyzable for intraprocedural ischemic burden in 127 (85%) and for post-PCI ischemia in 124 (83%). Clinical end points for the index hospitalization and 6-month mortality data were available for 100% of patients.

Table II. Baseline characteristics

Descriptor/group	Standard therapy (n = 30)	Noetic therapy (n = 120)
Age (y)	61 (53, 66)	65 (54, 69)
Male (%)	100	99.2
Hypertension (%)	53.3	68.1
Diabetes (%)	30.0	25.4
History of smoking (%)	80.0	83.2
Prior myocardial infarction (%)	56.7	62.2
Prior PCI (%)	23.3	42.9
Prior coronary artery bypass grafting (%)	43.3	41.2
Prior congestive heart failure (%)	30.0	14.3
Family history of coronary artery disease (%)	63.3	68.9
Ejection fraction (%)	50 (40, 55)	50 (50, 55)

Data for age and ejection fraction are presented as median (25th, 75th percentiles). All differences are nonsignificant.

Total ischemia during catheterization or PCI

Of the 127 analyzable patients, 101 (79.5%) had PCI procedures, 20 (15.7%) had only diagnostic catheterization, and 6 (4.7%) did not have an invasive procedure. Quantified ischemia from first to last contrast injection is shown in Table III. There were no significant differences in this variable across treatment groups. Highest "risk" by absolute values appeared in the off-site prayer cohort overall and in the imagery cohort who underwent PCI.

Post-PCI heart rate variability

Prospectively defined HRV variables from analyzable patients are shown on the Web site in Table IV (www.mosby.com/ahj). There were no significant or consistent differences across patient subgroups.

Clinical outcomes

Rates of post-PCI ischemia, MACE, and ACE over the index hospitalization and 6-month mortality rates are shown in Tables V and VI. There were no significant differences between treatment arms. There was a 25% to 30% absolute reduction across all adverse outcomes in patients treated with any noetic therapy compared with patients treated with standard therapy. Of the individual noetic arms, the absolute incidence of adverse outcomes during the index hospitalization was lowest overall in patients assigned to off-site prayer.

All mortality occurred in noetic therapy groups. By 6 months, as shown in Table VI, mortality differences suggest a statistical trend favoring the standard therapy group compared with the combined noetic therapies group (*P* = .12). Of the 4 individual noetic treatments, off-site prayer was associated with the lowest absolute mortality in-hospital and at 6 months.

Spirituality by DUREL: community ties, personal spiritual activity, and personal spirituality (data in Tables VII, VIII, and IX on Web site)

Of the 145 patients with completed DUREL index questionnaires, 56 (39%) indicated participation in a community-based spiritual activity at least once weekly (high activity) versus 89 (61%) who did not; 59 (41%) indicated that they performed some personal spiritual activity once or more daily (high activity), whereas 86 (59%) did not; 57 (39%) indicated that they considered spiritual matters meaningful and important in their lives (high spirituality), whereas 88 (61%) did not. There were no significant outcomes differences across these groups or when protocol noetic therapy was administered. Absolute values consistently suggested more favorable outcomes for patients with high community involvement, independent of noetic treatment assignment. Absolute values in patients with low community involvement were consistently more favorable for

Table III. Total ischemia in catheterization laboratory

Variable/group	Standard	All noetic	Prayer	Stress relaxation	Touch	Imagery
Analyzable patients (n = 127)	27	100	24	28	24	24
Total ischemic burden	156 (0, 465)	187 (0, 806)	269 (141, 728)	196 (0, 866)	86 (0, 424)	171 (0, 964)
PCI patients only (n = 101)	24	77	22	21	16	18
Total ischemic burden	159 (0, 476)	204 (59, 833)	188 (105, 441)	244 (81, 833)	136 (0, 695)	494 (0, 1197)

Data are presented as median (25th, 75th) percentiles.

Table IV. HRV and treatment groups

	Standard (n = 21)	All noetic (n = 80)	Prayer (n = 23)	Stress relaxation (n = 21)	Touch (n = 17)	Imagery (n = 19)
Average LVF	26.4 (10.7)	23.2 (10.2)	24.5 (11.3)	20.3 (8.9)	23.7 (8.8)	24.6 (11.6)
Average LF	17.2 (8.5)	14.4 (8.0)	15.7 (10.5)	13.1 (6.2)	14.7 (6.6)	14.2 (7.8)
Average HF	11.4 (5.7)	10.7 (6.1)	10.4 (6.2)	10.2 (5.4)	12.5 (7.5)	10.1 (5.2)
Mean NN	953 (114)	956 (124)	962 (149)	958 (136)	931 (86)	971 (108)
SDNN	90.3 (29.4)	79.0 (29.9)	82.7 (25.9)	75.8 (35.4)	82.9 (26.7)	74.6 (32.1)
SDANN	73.7 (24.9)	63.9 (27.4)	65.7 (22.4)	64.0 (34.2)	68.0 (25.7)	57.9 (27.1)
PNN50	7.4 (8.5)	5.9 (7.8)	5.2 (7.6)	5.1 (5.9)	7.4 (9.5)	6.4 (8.4)
RMSSD	28.8 (3.2)	26.3 (13.5)	25.1 (13.2)	25.9 (13.4)	28.7 (15.7)	26.1 (12.4)

Data are presented as mean (SD).

Table V. Clinical outcomes: all index hospitalization and 6-month mortality rates

End point/group	Standard therapy (n = 30)	All noetic patients (n = 120)
In-hospital death (%)	0	2.5
Myocardial infarction (%)	6.7	0.8
Congestive heart failure (%)	0	0.8
Repeat PCI (%)	0	0
Urgent coronary artery bypass grafting (%)	0	0.8
MACE (%)	6.7	4.2
Post-PCI ischemia (%)	25.9	18.6
ACE (%)	25.9	20.4
6-Month mortality (% [95% CI])	0	9.2 (5.0-15.0)

Data are presented as median (25th, 75th) percentiles.

those assigned to a noetic intervention than for those in the standard therapy arm. The absolute incidence of adverse outcomes during the index hospitalization in patients with high personal spiritual activity were consistently (40%) more favorable for those assigned to a noetic intervention than for those in the standard therapy arm. The absolute incidence of all adverse outcome end points during index hospitalization in patients with high personal spirituality was consistently (30%) more favorable for those assigned to a noetic intervention than for those in the standard therapy arm.

Anxiety (Table X on Web site)

Of the 103 patients who completed the Spielberger anxiety questionnaires, the median score across our population was 33. As prospectively defined, the 52 patients with a score of ≥33 were taken as having high anxiety on study entry. No differences across these groups reached significance. High-anxiety patients with noetic therapy had a 33% to 100% lower absolute incidence of all adverse outcome end points during than index hospitalization than did high-anxiety patients assigned to standard therapy.

Discussion

On the basis of our pilot results, the scientific study of noetic phenomena in patients with coronary artery disease undergoing PCI appears feasible. Feasibility contained at least 5 features: patient acceptance, staff acceptance, logistical feasibility, technical feasibility, and statistical feasibility for studies conducted in this area.

Whether patients with acute ischemic symptoms necessitating catheterization or PCI would be willing to be touched, taught abdominal breathing and imagery, use relaxation techniques, or have multidenominational prayers assigned to them was unknown. With 88% of eligible patients giving informed consent, patient acceptance of similar studies in the future appears feasible.

Staff acceptance of a protocol assigning nontraditional therapies in the midst of short-term “high tech”

Table VI. Clinical outcomes: all index hospitalization and 6-month mortality rates (each group)

Group/end point	Standard therapy (n = 30)	Prayer (n = 30)	Stress relaxation (n = 30)	Touch (n = 30)	Imagery (n = 30)
Post-PCI ischemia (%)	25.9	12.5	23.1	20.8	17.4
MACE (%)	6.7	0	3.3	6.7	6.7
ACE (%)	25.9	12.5	23.1	20.8	25.0
6-Month mortality (% [95% CI])	0	3.3 (0-17.0)	13.3 (4.0-29.5)	6.7 (0.5-21.5)	13.3 (4.0-29.5)

Table VII. Community, spirituality, and noetic therapy

End point/group	High activity overall (n = 56)	Low activity overall (n= 89)	High + standard activity (n = 13)	High + noetic therapy (n = 43)	Low + standard therapy (n = 16)	Low + noetic therapy (n = 73)
Post-PCI ischemia (%)	14.3	22.2	16.7	13.5	35.7	19.0
MACE (%)	0	6.6	0	0	12.5	5.5
ACE (%)	14.3	24.7	16.7	13.5	35.7	22.0
6-Month mortality rate (%)	5.4	6.7	0	7.0	0	8.2

Table VIII. Personal spiritual activity and noetic therapy

End point/group	High activity overall (n = 59)	Low activity overall (n = 86)	High + standard therapy (n = 14)	High + noetic therapy (n = 45)	Low + standard therapy (n = 15)	Low + noetic therapy (n = 71)
Ischemia post PCI (%)	18.0	19.7	38.5	10.8	15.4	20.7
MACE (%)	3.4	4.6	7.1	2.2	6.7	4.2
ACE (%)	20.0	20.8	38.5	13.5	15.4	22.0
6-Month mortality rate (%)	1.7	9.3	0	2.2	0	11.3

Table IX. Personal spirituality and noetic therapy

End point/group	High spirituality overall (n = 57)	Low spirituality overall (n = 88)	High + standard therapy (n = 15)	High + noetic therapy (n = 42)	Low + standard therapy (n = 14)	Low + noetic therapy (n = 74)
Post-PCI ischemia (%)	16.3	20.8	21.4	14.3	33.3	18.3
MACE (%)	1.8	5.7	6.7	0	71.	5.4
ACE (%)	16.3	23.3	21.4	14.3	33.3	21.3
6-Month mortality rate (%)	3.5	8.0	0	4.8	0	9.5

care was a concern. The relatively high enrollment rate across eligible patients is reflective of staff support in identifying patients and allowing them to participate in this study. Although staff acceptance was not systematically quantified, our informal impression was that from the beginning of patient enrollment the staff was enthusiastic about the study.

Logistic feasibility centered around the ability to deliver the treatment assigned without disrupting the flow of care. Because 97% of noetic treatment assignments were completed in this pilot, finding a 30-minute period for a noetic application appears feasible, even in patients needing urgent catheterization.

Technical issues were 2-fold: the ability to gather continuous physiologic data despite physical transfer of the patient from the coronary care unit to the catheterization laboratory and the ability of volunteer noetic practitioners to provide therapy. Seamless MUSE-centered monitor-

Table X. Anxiety states and noetic therapy

End point/group	High anxiety overall (n = 52)	Low anxiety overall (n = 51)	High + standard therapy (n = 9)	High + noetic therapy (n = 43)	Low + standard therapy (n = 12)	Low + noetic therapy (n = 39)
Ischemia after PCI (%)	24.4	14.6	37.5	21.6	20.0	12.9
MACE (%)	3.8	5.9	11.1	2.3	8.3	5.1
ACE (%)	26.1	14.6	37.5	23.7	20.0	12.9
6-Month mortality rate (%)	3.8	9.8	0	4.6	0	12.8

Table XI. Total sample size required to compare 2 therapy groups

Reduction (%)	Event rate 26%	Event rate 35%
20	2084	1384
30	890	596
50	290	198

$\alpha = .05$ and $1 - \beta = .80$.

ing across different patient locations was feasible for most ECG-based information. Volunteer practitioners provided necessary staffing and therapeutic resources.

Statistical feasibility constitutes the most essential feature of the pilot data set, producing a data set supporting power calculations for a more definitive study. In the absence of statistical significance, we used internal consistency across adverse outcome end points as the basis for directing such power calculations. In this regard, the index hospitalization pilot data consistently suggest a potential therapeutic benefit of noetic interventions, reducing absolute combined adverse clinical outcomes by about 30% overall. Despite the higher apparent risk status of the group randomly assigned to the off-site prayer treatment, the greatest absolute reduction in adverse outcomes was observed in this treatment subset.

Power calculations based on our pilot findings are illustrated in Table XI. If our findings were applied to a prospective, independent population, assuming a 35% event rate for the control group, to achieve an 80% likelihood that a 30% treatment effect would be detectable with a 95% certainty that the effect results from the therapy would require about 600 patients randomly assigned to test and control groups.

Limitations

The principal limitation of this pilot study was the small denominator of patients. Parallel randomization to 4 different noetic therapies across 5 study arms prohibited assessment of any possible synergy between therapies. Assessments of patient and staff belief systems and personal use of noetic therapies was limited. The noetic practitioners themselves were heterogeneous in their training and experience. Finally, because this study primarily enrolled male patients at a single Veterans Administration Medical Center in the southeastern "Bible belt," it would be difficult to generalize these findings.

Despite the study's limitations, we believe that our initial findings have provided an impetus and a clearer framework for the design of a more definitive study. The intuitive supposition of benefit afforded by a compassionate, hands-on, spiritual healing space for patients undergoing PCI and the presumption of the potential cost-effectiveness in using such non-drug-, non-device-dependent therapies appear worthwhile to explore, with use of traditional clinical trial methods to assess safety and efficacy. A more definitive trial would ideally involve a multicenter study enrolling patients of both sexes from different regions, in sufficient numbers to reach statistical significance, with random assignment of patients to therapeutic and control arms.

Data from questionnaires characterizing anxiety and spirituality are potentially important as descriptors that appear to interact with noetic treatment effects and serve as a potential source of bias. The role of physiologic surrogate end point monitoring in patients with ischemia appears relevant, whereas the role of HRV measures is less evident.

Patient acceptance was similar and excellent across all 4 noetic therapies in our study. In absolute values, off-site intercessory prayer appeared to have the most beneficial treatment effect.

A future study might consist of a factorial design with concomitant randomization to double-blind off-site prayer and subrandomization to a hands-on bedside noetic technique. Such a design would allow some quantification of both the incremental and the synergistic effects of the 2 therapies.

Future considerations

Our 6-month mortality data promote 2 additional design considerations. Because little is known of the mechanisms of noetic therapies, short- and long-term effects may vary, and both warrant study in future trials. Additionally, safety cannot be presumed for these therapies, as indicated by our 6-month mortality data

and previous reports.[33] We believe study of noetic therapies in human subjects mandates a dedicated data safety monitoring and review board.

As adjuncts to modern technology, noetic therapies with potential influence on mind, body, and spirit may promote a more optimal healing environment for patients undergoing PCI. Questions about methods, safety, and efficacy, however, remain largely unaddressed. The MANTRA study project seeks to approach this area with systematic study.

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Appendix: Noetic methods

Imagery:

Fifteen minute sessions were conducted before PCI by a noetic practitioner using a written imagery script. Rapport was established and the patient was taught soft abdominal breathing. The patient was then assisted in focusing on a "preferred" place, defined as a peaceful or relaxing place where the patient would rather be. After the patient was transferred to the cardiac catheterization laboratory, the noetic practitioner repeated the imagery script to reassociate the patient with the preferred place. Patients were encouraged to continue using these practices on their own during the PCI procedure.

Touch therapy

Sessions of 30 minutes were initiated by a noetic practitioner before PCI. Touch therapy for our protocol consisted of the modified "chakra connection" technique.[28] Rapport was established, the touch therapy technique was introduced verbally using a written script, and soft abdominal breathing was taught. The practitioner then gently touched the patient with both hands in the prespecified sequence of positions,[28] pausing for approximately 45 seconds at each of the 22 hand positions. The patient was then taken to the cardiac catheterization laboratory and was verbally reminded of the touch therapy experience.

Stress-relaxation therapy

Sessions of 30 minutes were initiated by a noetic practitioner before PCI. Sessions were conducted according to a written script emphasizing supportive listening and instruction in self-relaxation skills and soft abdominal breathing combined with a personally selected phrase of meaning (such as "easy does it" or "the Lord is my shepherd"). In the catheterization laboratory the practitioner meditated on the patient's personal phrase in the control room for 30 minutes.

Off-site intercessory prayer[32]

Each patient's name, illness, and procedure were supplied by phone, e-mail, or Internet connection to a total of 8 participating prayer groups: the Unity School of Christianity in Missouri, the Moravian Church in North Carolina, a Baptist congregation in North Carolina, the Virtual Jerusalem Web site in Israel (Jewish), the Abundant Life Christian Center in North Carolina, the Nalanda Monastery in France (Buddhist), the Kopan Monastery in Nepal (Buddhist), and the Carmelite Monastery in Maryland (Catholic). Each group prayed in their customary fashion, as summarized in Table I.