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THE ONTOPSYCHOLOGICAL PSYCHOTHERAPY IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION: THE STEP-IN-AMI (SHORT TERM PSYCHOTHERAPY IN ACUTE MYOCARDIAL INFARCTION) TRIAL

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Thematic Axe – Humanist values and technological evolution: parallels and interconnections.

Abstract: This research was aimed to evaluate whether a short-term ontopsychological psychotherapy improves long-term clinical outcomes in patients with an acute myocardial infarction (AMI). Patients ≤70 years old were randomized within 1 week of their AMI to short-term ontopsychological psychotherapy plus routine medical therapy vs routine medical therapy alone. The primary composite outcome was defined as the combined incidence of new cardiovascular events (re-infarction, death, stroke, revascularization, life-threatening ventricular arrhythmias, and the recurrence of clinically significant angina) and clinically significant new comorbidities. Secondary outcome measures were: the rate of re-hospitalization for cardiovascular problems; New York Heart Association functional class; and psychometric tests scores. Ninety-four patients were analyzed. The 2 treatment groups were similar across baseline characteristics. At 5-year follow-up, psychotherapy patients had a lower incidence of primary outcome, relative to controls (77/223 vs 98/202 patient-years, respectively; P = .035; absolute risk reduction = 19%, number needed to treat = 8); this benefit was mainly attributable to the lower incidence of new comorbidities and clinically significant angina in the psychotherapy group. Gains in the primary outcome, relative to controls, among psychotherapy patients occurred in the first year and subsequently remained stable over the following 4 years. A short-term ontopsychological psychotherapy added to routine secondary prevention of myocardial infarction improves clinical outcomes at 1 years, and the results persist up to 5 years post AMI. Other larger studies remain necessary to confirm these results.
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1. INTRODUCTION (CONTEXT AND OBJETIVES)

The research carried out in the last 70 years has clearly demonstrated that psychosocial social risk factors may be critical predisposing to, or precipitating an acute myocardial infarction [1], due to a higher frequency of adverse health behaviors, specific pathophysiological mechanisms involving activation of coagulation factors and platelet aggregation, as well as the neuroendocrine and immune systems [2–4]. On this basis, a variety of randomized behavioral and psychosocial intervention trials have been performed in cardiac patients to assess for possible effects on medical and psychological prognosis. However, across the numerous meta-analyses that have been published on this subject, the results have been controversial [5, 6]. Several psychotherapeutic methods have been tested, chiefly behavioral, cognitive and interpersonal therapy; they have proven to be effective at improving psychological symptoms [5, 6], but there is uncertainty about their efficacy in terms of medical and cardiac prognosis.

In 2004 the assessments of humanistic–existential psychotherapy approaches, and in particular the ontopsychological approach [7, 8], remained missing. In the meantime psychotherapy on selected patients with acute myocardial infarction, the first cause of cardiac morbidity and

mortality, remained unaddressed. To address these shortfalls, we performed, for the first time, a randomized, controlled study to preliminarily assess the efficacy of an original ontopsychological short-term psychotherapy (STP) in a selected population of patients with an acute myocardial infarction treated with an urgent or emergent percutaneous coronary intervention. The ontopsychological approach was delivered by a single operator; the methodology was highly standardized and specifically adapted to the setting of cardiac patients.

The trial was denominated STEP-IN-AMI (Short TErm Psychotherapy IN Acute Myocardial Infarction). The protocol was approved by the ethical committee of San Filippo Neri hospital, Rome- Italy, in 2004, and registered in www.ClinicalTrial.gov NCT00769366.

The research protocol was published in 2009 [9], and the1 year and five year follow-up results were published in 2013 [10] and 2019 [11] respectively.

2. METHOD

The STEP-IN-AMI research is a randomized, controlled trial designed to assess: (1) clinical outcomes after an ontopsychological psychotherapy performed in patients who underwent an urgent or emergent interventional treatment for an AMI; (2) any correlation between psychometric variables and cardiological features in the acute phase and in the follow-up, including the quality of life. The study was performed in San Filippo Neri Hospital, Rome, Italy. The participants recruited in this study were patients aged 70 years or less, admitted to San Filippo Neri Hospital for AMI and treated with primary or urgent percutaneous coronary intervention (PCI). Primary percutaneous transluminal coronary angioplasty (PTCA) was performed up to 12 h after the beginning of chest pain in case of STEMI, whereas patients with NSTEMI were enrolled if the urgent PTCA was performed up to 48 h from the beginning of chest pain. Only patients with a complete revascularization were enrolled in the study. Patients had to be recruited during hospitalization and had to sign an informed consent form prior to the enrollment.

Patients with disability, cognitive impairments, or other life-threatening conditions were excluded from the study.

The randomization scheme was described in a previous publication [9].

Follow-up was planned at 6 months, 1 year, and 5 years with a fully comprehensive medical visit, routine blood tests, echocardiography and stress test, or stress myocardial perfusion scintigraphy. Psychometric assessment was performed at the enrollment and at the 1-year follow-up visit.

The following psychometric tests were selected to obtain a comprehensive picture of psychologic conditions: (1) Self-Evaluation test: to assess the global level of psychological distress [12]; (2) Modified Maastricht Questionnaire, adapted from the Maastricht Questionnaire of Apples and Mulder [13,14], specifically designed to assess levels of vital exhaustion; (3) Social Support Questionnaire: to evaluate each individual's perception of his/her social network, as it explores the presence and importance of three elements in the patient's life (i.e. a particularly important persons, family and friends) [15]; (4) Recent Life Change Questionnaire: designed to evaluate the presence and importance of occasional major life events and chronically recurring aggravations in daily life [16]; (5) Beck Depression Inventory (BDI): to evaluate the presence of major or minor depression (in accordance with the modified Diagnostic and statistical manual of mental disorders, 4th ed., diagnostic criteria) [17, 18]; (6) The MacNew Heart Disease Health-Related Quality of Life Questionnaire: It evaluates the quality of life related to three specific domains – emotional, physical, and social – with a score for each domain and a global score [19].

Medical drug therapy in the acute and chronic phase was left to the treating physician's discretion and carefully recorded in the case-report form. Pharmacological psychiatric treatments, wherever needed, were not part of this protocol and therefore were left to the caring psychiatrist's independent decision and were also recorded in the case-report forms. All patients were informed about the im-

portance of modifying their diet, stopping smoking, and engaging in moderate daily exercise.

To minimize the possibly etherogenous effects of different psychotherapists, psychotherapy was performed by one skilled and graduated psychotherapist, expert in onto psychological psychotherapy, with the help of clinical staff – both psychologists and nurses.

As written elsewhere, we may describe [10] *"The ontopsychological method as a complex and original synthesis in part derived from psychoanalysis, analytical psychology, and the humanistic-existential approach as was initially elaborated by Abraham Maslow [20]. With the ontopsychological approach, the human being is considered a complex system that consists of the union of psyche and body, where anything happening in the body may influence the psyche and vice versa, as demonstrated by several studies in the field of psychoneuroendocrinoimmunology [21, 22]. With this view, a psychotherapeutic intervention must improve not only psychological symptoms, quality of life and cardiac prognosis (the main endpoints considered in previous psychological interventions in patients with ischemic heart disease), but also global health to be considered effective in cardiac patients.".*

The psychotherapy was carried out in individual and group meetings during a 6-month period after the incident AMI. The intervention was tailored to the specific needs and problems of every patient.

For an overview of the method, the original report, published in the International Journal of Cardiology, is displayed here [9]. *"The number of individual meetings was tailored to the specific needs and problems of each patient, ranging from 3 to 11 meetings over a 3-month period. The shortest cycle, which was 3 single sessions, involved a 31-year old man, who exhibited great resistance to the analysis; whereas the longest cycle of 11 sessions occurred with a 56-year old man with clinically-relevant depression and two suicide attempts. Over the duration of this brief course of treatment, the psychotherapist helps the patient to gain insights and elaborate on conflicts that need to be resolved, as well as on dysfunctional behaviors and interpersonal relationships. After the initial interviews, aimed at focusing on and overcoming main conflicts in the patient's life, the psychotherapist helps the patient to gain insights into his/her body sensations. Generally, cardiac patients report a distorted and partial perception of their body, their body often perceived as foreign. The psychotherapist guides the patient to acquire full contact with his/her body, starting from the visceral zone, with the help of abdominal breathing and relaxation techniques. In the final phase of the individual meetings and whenever possible, the psychotherapist guides the patient into deeper insights through dream analysis. Generally, patients who have suffered a recent myocardial infarction report having experienced nightmares, often starting several months or even years before the acute event; or, alternatively, finding it impossible to remember dreams (often, patients only recall a few dreams from their childhood and/or adolescence). As the psychotherapist helps the patients to contact the central positive nucleus of their unconscious (the "In Se"), their nightmares cease and/or the patients resume remembering dreams related to their real-life problems. This reflects inner changes orchestrated by the patient.*

The psychotherapeutic work done during the individual sessions is reiterated during group sessions, where the analysis and goals achieved in the individual sessions can be reinforced via exchanges between group members. Group sessions, to which partners are invited, entail educational cardiological therapy (which includes a broader explanation of myocardial infarction and atherosclerotic processes, while accentuating the importance of cardiac risk factors prevention/reduction and lifestyle changes); music-guided breathing and muscular relaxation; comprehension of body signals; elements of oneiric language; and attention to specific partners/relationships.

The aim of all these processes was to stabilize the pathology and promote global well-being within each patient."

A comprehensive explanation of the ontopsychological method applied to cardiac patients is reported in *"Roncella, A. Short-Term Psychotherapy in Patients with Acute Myocardial Infarction.*

In Psychotherapy for Ischemic Heart Disease; Roncella, A., Pristipino, C., Eds.; Springer: Cham, Switzerland, 2016; Chapter 13; p. 187" [23].

Study endpoints and outcome measures: as psychotherapy may have effects not limited to the cardiovascular system, a broad definition primary composite outcome was adopted, which consisted of the cumulative incidence of new cardiovascular events (i.e. myocardial reinfarction, death, stroke, any revascularization, lifethreatening ventricular arrhythmias, and recurrence of typical angina pectoris) and the occurrence of any clinically-significant new non-cardiovascular co-morbidity at 1 and 5 years in the study arms.

The secondary endpoints were the assessment of: (2) Incidence of new hospital admissions for cardiological and/or medical reasons; (3) Echocardiographic ejection fraction, ventricular volumes and wall motion score index; (4) Prevalence of New York Heart Association (NYHA) class II; (6) Changes in psychometric tests score; (7) Change in quality of life.

3. RESULTS AND DISCUSSION

101 patients aged ≤70 years and admitted to our hospital for AMI were enrolled in the study. Among them, 49 pts were treated with medical therapy plus psychotherapy, and 45 pts were treated with medical therapy alone. The baseline characteristics of the 2 groups of patients were similar for: age (55 ± 9 the psy group; 55 ± 8 0.78 the traditional therapy group); female prevalence; BMI; left ventricular ejection fraction; post-MI cardiological rehabilitation; cardiovascular risk factors (active smoking, hypercholesterolemia, family history of cardiovascular disease, arterial hypertension, diabetes mellitus); number of active medical diseases; characteristics related to AMI presentation, angiographic characteristics, and technical PTCA procedures; drug therapy; psychometric tests scoring.

3.1 OUTCOMES AND FOLLOW-UP AT ONE YEAR

Enrollment was begun in June 2005 and ended in January 2011.

Of the 49 patients enrolled in the psychotherapy group, four patients completed individual sessions but discontinued the STP before group sessions. Average attendance rate of individual sessions was 95% and of group sessions 85%.

Medical outcomes

At one year, patients randomized to STP on top of standard cardiological therapy had a significantly lower incidence of the composite primary endpoint, relative to patients undergoing cardiological therapy only (43% vs. 78%, p = 0.0006), equaling a 35% absolute risk reduction and a number needed to treat (NNT) of three (95%CI: 1.9 to 6.1). However, no deaths or strokes occurred after one year, with the ensuing MACCE similar in the two groups. A benefit observed in the STP group appeared to be attributable to the lower recurrence of typical angina (P= 0.04) and to the lower incidence of newcomorbidities versus controls (p = 0.0001). The following new-onset non-cardiological events were adjucated: major depression, generalized anxiety disorder, acute hepatitis, arterial hypertension, renal failure, type II diabetes mellitus, acute bronchial asthma, severe lumbago, hip arthritis, respiratory failure, cancer, herpes zoster resulting in severe pain, renal colic with and without calculi, a bladder stone with severe hematuria, an inguinal hernia requiring urgent surgical repair, severely hemorrhagic hemorrhoids, intermittent claudication of the lower legs, severe perianal abscess requiring hospitalization, viral pleuro-pericarditis, thorax basalioma, and global transient amnesia with ischemic brain lesions detected on magnetic resonance imaging (MRI).

Of note, although not statistically significant, three episodes of life-threatening arrhythmias occurred in the cardiological therapy only group, while none occurred in those receiving STP.

Consistent with primary outcome findings, in patients randomized to STP, the re-hospitaliza-

tion rate was significantly lower at one year compared to controls (0.02). Moreover, psychotherapy subjects experienced a better average NYHA (New York Heart Association) functional class than their counterparts, despite similar mean left ventricular ejection fractions and wall motion score echocardiographic indices at follow up in the two groups. The prevalence of patients on therapy with the different classes of drugs was similar between the two groups at one year. However during follow-up, 35/45 (78%) patients of the control group needed an increase in doses of diuretics or betablockers or vasoactive drugs (nitrates and/or calcium-antagonists and/or ace-inhibitors and/or angiotensin-receptor blockers), as compared to 15/49 (31%) in the psychotherapy group (p= 0.001). No patient receiving STP required psychiatric drugs during the first year of follow-up, whereas three controls were administered psychiatric treatment for major depression and generalized anxiety disorder.

Psychological and quality-of-life outcomes

At one year, those who were randomized to STP exhibited a significantly lower BDI depression score than controls, consistent with a marked trend toward a lower prevalence of depression overall. This appeared to be due both to improved BDI scores in the STP group and to worsening BDI scores in controls relative to baseline (P=0.03).

All other psychological test scores were similar in the two groups.

The STP patients experienced statistically better quality of life in the physical domain (P= 0.03), and trended toward enhanced quality of life in the social domain and globally.

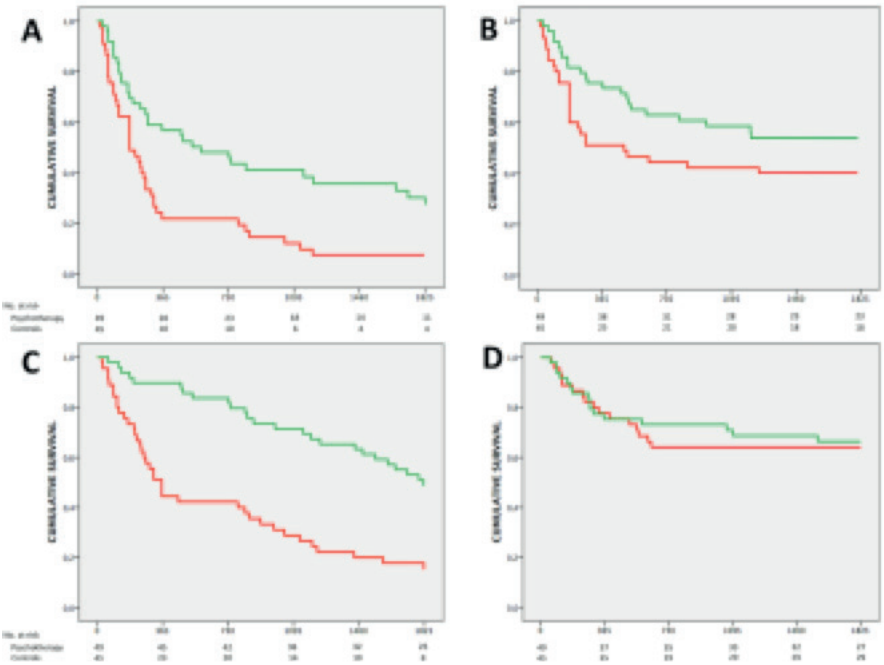
3.2 OUTCOMES AND FOLLOW-UP AT FIVE YEARS

Clinical follow-up was performed every year up to five years after enrolment.

At five year follow up a statistical significant lower incidence of the primary endpoint, angina, new comorbidities persisted in pts who had received an STP, compared to controls.

Figure 2: Plot of cumulative event-free survival from the primary endpoint (A), angina (B), new comorbidities (C) and major adverse cardiac and cerebrovascular events (D), in those receiving short-term psychotherapy (green line) versus controls (red line).

Figure reproduced from "The American Journal of Medicine (2019) 132:639−646"



4. CONCLUSIONS

The STEP-IN-AMI trial is the first randomized research conducted in an Italian hospital, with the application of the ontopsychological method.

As showed in the results, the ontopsychological psychotherapy improved the clinical follow--up at 1 and 5 years of patients with AMI, already treated with the most advanced interventional and medical therapies.

In coherence with what affirmed by the ontopsychological school, it is possible to adjust a personalized medicine, which helps the patients to achieve a global psycho-physic health improvement.

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