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The effectiveness of progressive muscle relaxation and interactive guided imagery as a pain-reducing intervention in advanced cancer patients: A multicentre randomised controlled non-pharmacological trial

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ABSTRACT

Background and purpose: Interactive guided imagery (IGI) and progressive muscle relaxation (PMR) are complementary therapies with a recognised positive effect on cancer pain relief. This multicentre randomised controlled trial was designed to assess the adjuvant effect of PMR − IGI in alleviating pain in a sample of hospice patients with terminal cancer.

Materials and methods: A total of 104 patients were randomised to two groups. Group A patients (n = 53) were administered the Revised Edmonton Symptom Assessment Scale (ESAS-r) and the numerical rating scale (NRS) for pain immediately prior to (T1) and 2 h following an individual PMR − IGI session (T3). Group B patients (n = 51) received usual care and were assessed using the same tools. Acute pain episodes and rescue analgesics over the following 24 h were recorded.

Results: The Pain Intensity Difference (NRS at T3-NRS at T1) was 1.83 in group A and 0.55 in group B and was significant in both groups ($p < 0.0001$). The mean Total Symptom Distress Score declined by **8.83** in group A and by **1.84** in group B.The average difference in the emotional symptoms ESAS-r subscore (anxiety and depression) was 2.93 in group A ($p < 0.0001$) and 0.07 in group B ($p > 0.05$).

Conclusion: The results of this trial suggest that PMR − IGI may be considered as an effective adjuvant in alleviating pain-related distress in terminal cancer patients. Further studies should be performed to assess the effectiveness of repeated interventions.

1. Introduction

The use of complementary therapies to relieve the pain experienced by terminal cancer patients is attracting increasing interest, since approximately one third of these patients suffer from moderate to severe cancer pain [1–4].

Especially in patients with advanced cancer, the multidimensionality of pain involves an extension from the physical to the psychological, cognitive, affective, emotional, social, and spiritual domains [5–10], and a poor survival prognosis leads to a situation characterised by fear and anxiety [11–13]. For these reasons, physical symptoms such as weakness, nausea, drowsiness, lack of appetite, and shortness of breath and psychological symptoms such as anxiety, depressed mood and anguish, can alter the subjective perception of pain. Patients' subjective experience and the assessment of their own ability to manage and overcome pain complicate pain evaluation and management by the treatment team [14–16]. Moreover, patients' preoccupation with their impending death and catastrophic thoughts have the potential to amplify pain perception [17–19].

These considerations have suggested the adoption of psychological strategies as adjuncts to pharmacological pain management. Distraction techniques, hypnosis, imagery, and muscle relaxation are complementary therapies that act by taking the mind off pain and the thoughts of deterioration of the body, enhancing pain control and self-efficacy [20–24].

Guided imagery (GI) is a cognitive, behavioural mind − body

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evidence-based technique that is employed to manage pain, including cancer pain, which affects and/or modifies the psychophysiological state of patients [10,22–29]. The frail state of hospice patients at the end of their life prompted the use, in the present study, of GI with a facilitator – integrated or interactive guided imagery (IGISM) – since according to earlier work the relationship with the facilitator has the potential to enhance the imaginative process and induce a stronger effect [30–32]. During an IGI session, patients are helped to visualise positive and pleasant images and to imagine them in the greatest possible detail, with the involvement of multiple senses. It has been reported that GI has profound physiological consequences, since the body tends to respond to imagery as it would to a real external experience [33]. GI has been shown to affect a variety of systems, including the respiratory, cardiovascular, metabolic, and gastrointestinal apparatuses and immune responsiveness [34].

According to some studies, the brain stimulation exerted by GI has the potential to induce the release of excitatory neurotransmitters, such as serotonin, and endogenous opioid peptides, which are known to modulate pain [35,36]. Moreover, its effect can be further primed by the induction of physical relaxation (progressive muscle relaxation, PMR) during a short (5 min) session held immediately before IGI, where patients are invited to relax progressively the main muscle groups [37,38].

Psychoneuroendocrinoimmunology (PNEI) research has demonstrated that the psychological response to GI can modulate the activity of the hypothalamic – pituitary – adrenal axis, reducing the stress response and increasing the feeling of wellbeing. Central and immune nervous system modulation through the release of enkephalins, endorphins, cholecystokinin, and cortisol may be among the mechanisms mediating these effects [33].

There are encouraging reports of the ability of GI to control pain, depression, and anxiety [25,32] and, via these effects, to improve the quality of life of patients with cancer and/or chronic pain [37–48]. The available data on GI come from a wide range of studies based on a variety of designs and methods, which have stressed the need for further investigations [26,38,42,45,49–53]. In addition, clinical studies [54,55] have found that complementary approaches are well-accepted by more than 60% of hospice patients and improve quality of life at the end-of-life stage [2,4,44–46].

The present study is the first multicentre non-pharmacological randomised controlled trial (RCT) assessing the effectiveness of IGI in controlling pain in hospice patients with terminal cancer. The frail clinical and psychological condition of these patients accounts for the limited number of available studies and their small sample sizes: a review of 103 imagery studies found that only 6 RCTs compared imagery to either a no-treatment control or to another active intervention such as relaxation or hypnosis [42].

2. Study objectives

The primary objective of the present study was to compare the effectiveness of a PMR – IGI intervention to no-intervention (usual care) in reducing the pain experienced by terminal cancer patients. The primary endpoint was a Pain Intensity Difference (PID) score, i.e. a difference in reported pain between before and after the intervention, ≥ 1 [56].

The secondary objectives were the effect of the intervention compared with no-intervention in reducing i) the Total Symptom Distress Score (TSDS) of the Revised Edmonton Symptom Assessment Scale (ESAS-r); ii) the number of acute pain episodes reported in the 24 h period following the PMR – IGI session; and iii) the need for rescue analgesics.

3. Materials and methods

3.1. Patients

The inclusion criteria for the study were: admission to the hospice at least 48 h previously; age > 18 years; a diagnosis of cancer; a baseline pain subscore ≥1 in the 24 h before recruitment, as measured by a numerical rating scale (NRS) included in the ESAS-r; around the clock analgesic therapy; a Karnofsky Performance Scale Index ≥ 20; and written informed consent.

The exclusion criteria were: pathological conditions that prevented participation; a diagnosis of psychiatric or neurological disturbance; total aphasia; and rescue pain treatment received 30 min prior to enrolment or the intervention (to avoid interference with the IGI session).

The size of the sample was calculated to highlight statistically significant differences between patients who had received the intervention and untreated patients. The significance was set at 0.05 (α) for a statistical power of 0.8. It was assumed that the mean difference (δ) between perceived pre- and post-intervention pain reported by patients would not exceed 1 and that its standard deviation would be 1.5. The minimum sample size for each group, calculated on sample size tables for a $\frac{\delta}{\sigma}$ value equal to 0.7, was 53 per arm, i.e. 106 patients.

The inclusion/exclusion criteria and the difficulties related to the fast deterioration of patients' conditions enabled the enrolment of 53 patients for the experimental arm and 51 for the control arm.

Of the 104 patients who were considered eligible, 13 (12.5%) withdrew due to revocation of consent (n = 5), deterioration in their clinical condition (n = 5), and reasons that were independent of the study (n = 3), leaving 91 participants who were randomised to the intervention group (A; 46 patients) or the control group (B; 45 patients). The flow diagram is reported in Fig. 1. The study was promoted by Antea Palliative Care Centre, Rome, Italy. The satellite centres were the Italian Hospital Group Hospice in Guidonia (Rome, Italy) and the Hospice of Larino (Molise Regional Health Service). Each Hospice had a trained practitioner with experience in GI.

The protocol was approved by the Lazio 1 Ethics Board and by the reference Ethics Board of each satellite centre.

3.2. Study protocol

The study involved 4 phases: T0, T1, T2, and T3 (see the flow diagram in Fig. 1).

T0 (patient enrolment): all patients who had been admitted to the hospice at least 48 h previously were screened by a research nurse for inclusion/exclusion criteria.

T1 (within 24 h of T0): the GI practitioner interviewed the eligible patients, informed them of the aims of the study, and described its methods. The following baseline information was collected and entered in the Case Report Form (CRF): demographic data, history data, social data of interest to the intervention (family composition, education, job, leisure activities), Karnofsky Performance Scale Index; tumour type, pain characteristics, and pain treatment. Patients were also administered the ESAS-r. Eligible patients were assigned to the intervention or the control group using a stratified randomisation procedure based on their baseline pain score, which was associated with a randomisation list placed in a sealed envelope that was opened by the research nurse. The results were communicated to the GI practitioner at the end of the interview (T1), after patient data had been recorded in the CRF. Group A patients were scheduled for an individual PMR – IGI session. Group B received usual care. Further, to avoid depriving control patients (group B) of a potentially beneficial intervention, they were also offered an individual PMR – IGI session at the end of the study.

T2 (within 1 h of T1): each PMR – IGI session had a duration of 20 min, due to the frail state of patients and their difficulty in concentrating for a longer period of time. In the first 4 min, a state of

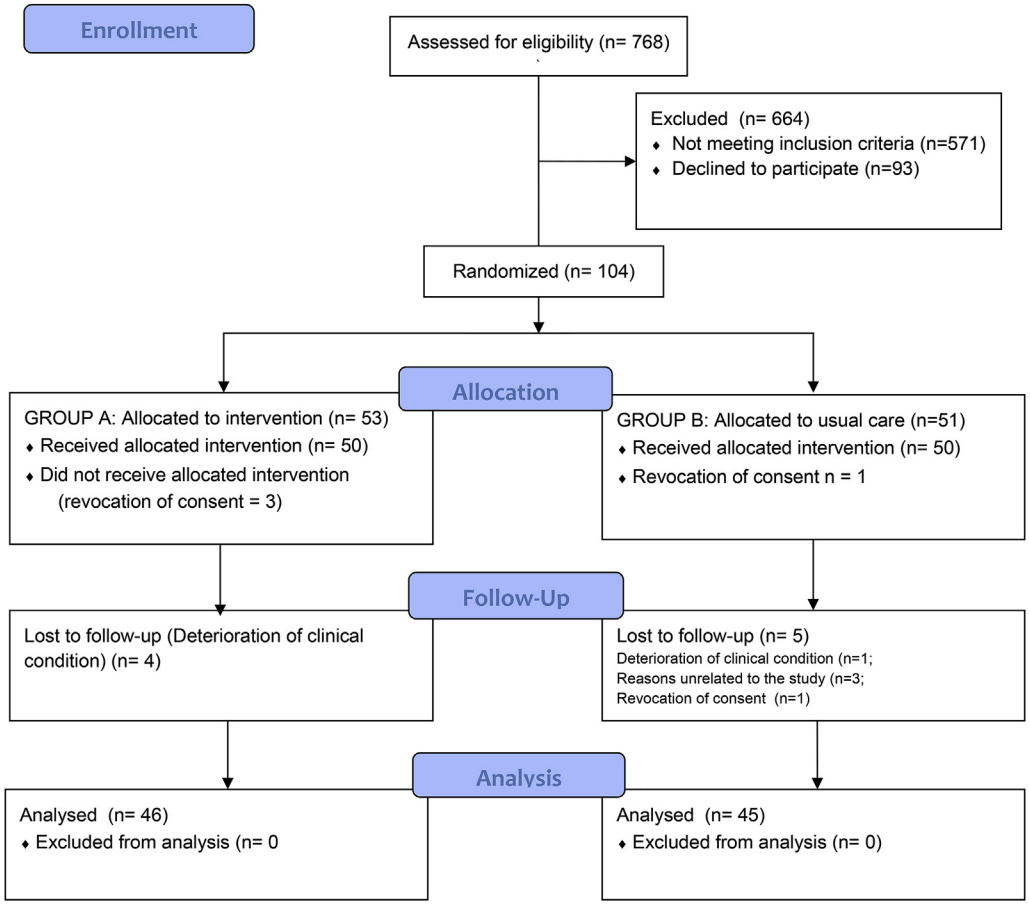

Fig. 1. CONSORT Flow Diagram of the study participants.

psychophysical relaxation was induced by prolonged deep breathing and relaxation of the main muscle groups (PMR). The patient was invited by the practitioner to focus on his/her voice, its tone, pitch, and volume. Once relaxation had been achieved, the next 16 min were employed as follows:

a) patients were invited to close their eyes and to follow a script that had been selected by the practitioner according to the preferences/suggestions supplied by the patient during the baseline interview (T1). The script was chosen from a pool of scripts taken from the literature that involved a walk along a deserted beach, through fields, through woods, or on a mountain. A script involving the scenery and colours was proposed to those patients who seemed to be unable to produce a vivid imagery or reported significant localised pain and could not shift their attention [48,57];
b) patients were encouraged to focus on the object of the imagery with help from the practitioner's questions and prompts to participate in the scenes, to look at, hear, smell, taste, and touch what they were visualising through imagination;
c) patients were gently invited to reopen their eyes and make contact with their surroundings.

T3 (within 2 h of the intervention): patients were re-administered the ESAS-r by the research nurse and asked if they perceived control over pain (possible answers: yes, no, not sure).

T4: the number of acute pain episodes arising in the 24 h period following the intervention and the administration of rescue analgesics were recorded in the CRF.

Group B patients received the ESAS-r assessment at baseline (T1) and 2 h later (T3).

3.3. Data collection tools

The frailty of participants prompted the use of simple assessment tools. Notably, the existence and experience of symptoms related to global pain can affect the ability to create mental images and to enact the imagery process. Since good symptom control is critical for the effectiveness of palliative care, patients were evaluated with the ESAS-r, which assesses 9 symptoms besides pain [58–66].

The ESAS-r is a multidimensional tool whose total score, the TSDS, is the sum of the scores of 10 NRS that measure the intensity (from 0, no symptom to 10, worst possible symptom intensity) of 10 symptoms [59]. The ESAS-r has proved sensitive in detecting clinical symptoms as well as subtle differences in the clinical status of patients with advanced cancer [63–69]. Recently, it has been subdivided into a 7-item physical subscore (PHS, 0–70 points) encompassing pain, tiredness, drowsiness, nausea, lack of appetite, shortness of breath, and constipation and a 2-item psychological subscore (PSS, 0–20 points) assessing anxiety and depression [68,69]. The TSDS (0–100) combines the PHS, the PSS, and a general wellbeing score which is related to both domains and is therefore assessed separately [69]. Cutoffs of these subscores have recently been calculated to reflect improvement or deterioration in patient status [see the Appendix].

4. Statistical analysis

The structural characteristics of the patient sample are reported in Tables 1 and 2. The descriptive statistics and frequency distribution of the demographic variables are listed in Table 1. Patient symptoms recorded at enrolment (T1) were analysed by ANOVA to establish whether the two groups were comparable, and to confirm the random

Table 1
Demographic data.

	Patients, n = 104	%
Age		
Mean (standard deviation)	71.83 (11.57)	
Range	41–99	
Gender		
Male	50	48.07
Female	54	51.92
Education (years)		
≤5	22	21.15
6–8	39	37.50
8–13	27	25.96
≥13	11	10.57
Not available	5	4.80

Table 2
Disease characteristics and main indices.

	Patients n = 104	%
Primary cancer site		
Breast	7	6.73
Gastrointestinal tract	22	21.15
Genitourinary apparatus	18	17.30
Reproductive organs	5	4.80
Head and neck	6	5.76
Lung	12	11.53
Liver and pancreas	24	23.07
Blood	1	0.96
Other	8	7.69
Karnofsky Performance Scale Index		
20	11	10.57
30	47	45.19
40	42	40.38
50	4	3.69
NRS pain score (± SD)	4.3 (2.2)	
TSDS (± SD)	39.5 (16.3)	
Days To Death	17.7	

*NRS, Numerical Rating Scale; SD, Standard Deviation; TSDS, Total Symptom Distress Score.

assignment of patients. The ESAS-r subscores measured at T3 were also subjected to ANOVA. The difference in the pain scores between before and after the intervention (group A) or between the two ESAS-r assessments (group B) were analysed using a paired *t*-test. Data are reported as mean ± standard deviation (SD). The level of significance was set at 0.05. Data were analysed using STATA software, v. 13 (StataCorp. LP, College Station, TX, USA).

5. Results

Of the 104 patients who were considered eligible, 13 (12.5%) withdrew from the study, leaving 91 participants who were randomised to the intervention group (A; 46 patients) or the control group (B; 45 patients).

The demographic characteristics of the patient sample are reported in Table 1.

The disease characteristics, NRS pain score, and TSDS of each group are reported in Table 2. The NRS pain score at T1 (enrolment) was 4.3 (± 2.2), the TSDS was 39.5 (± 16.3).

Patient distribution in relation to the NRS pain intensity scores (mild, 1–3; moderate, 4–6; severe, 7–10) at T1 is reported in Table 3. Overall, 39.57% of patients (19.78% in group A and 19.78% in group B) had mild pain (NRS score 1–3), whereas 60.43% (30.76% and 39.66%, respectively) had moderate or severe pain (NRS score ≥4).

Patients' pain scores at T1 and T3 are reported in Table 4A and B for group A and B, respectively. Overall, 32.6% of group A patients – 38% of those with mild pain, 27% of those with moderate pain, and 33% of those with severe pain – reported feeling no pain following the intervention.

Table 3
Percent distribution of patients by their NRS pain score at enrolment (T1).

Group	NRS pain score			
	Mild (1–3)	Moderate (4–6)	Severe (7–10)	Total
A	19.78	24.17	6.59	50.56
B	19.78	17.58	12.08	49.44
Total	39.57	41.76	18.67	100.00

*NRS, Numerical Rating Scale.

Table 4A
Percent distribution of group A patients (n = 46) by their NRS pain score at T1 and T3.

	NRS pain score at T3				
Pain score at T1	None (0)	Mild (1–3)	Moderate (4–6)	Severe (7–10)	Total
Mild (1–3)	38.89	44.44	16.67	0.00	100.00
Moderate (4–6)	27.28	36.36	36.36	0.00	100.00
Severe (7–10)	33.33	33.33	16.67	16.67	100.00
Total	32.61	39.13	26.09	2.17	100.00

*NRS, Numerical Rating Scale.

Table 4B
Percent distribution of group B patients (n = 45) by their NRS pain score at T1 and T3.

	NRS pain score at T3				
Pain score at T1	None (0)	Mild (1–3)	Moderate (4–6)	Severe (7–10)	Total
Mild (1–3)	33.33	44.44	16.67	5.56	100.00
Moderate (4–6)	18.75	25.00	43.75	12.50	100.00
Severe (7–10)	0.00	9.09	9.09	81.82	100.00
Total	20.00	28.89	24.44	26.67	100.00

*NRS, Numerical Rating Scale.

At T3, the NRS pain score fell from 4.11 at T1 to 2.28 in group A and from 4.51 to 3.96 in group B patients (primary objective of the study). The PID, i.e. the difference in the pain score between T1 and T3, was 1.83 in group A, involving a 44.5% (± 2.54) reduction, and 0.55 in group B, involving a 25.2% (± 2.14) reduction (primary endpoint). Both differences were significant (*t*-test, $p < 0.0001$).

Patients' NRS pain scores at T1 and T3 and their PID scores are reported in Table 5A.

Approximately 65% of group A patients reported an improvement in pain following the intervention, and 39.13% of these achieved a reduction in the pain level ≥ 3, which is usually considered clinically significant [24]. In group B, approximately 45% of patients reported pain relief from T1 to T3, and 20% of these achieved a reduction in the pain level ≥3. Some patients experienced a worse level of pain following the intervention. This proportion was twice as high in group B than in group A.

The ESAS-r score and subscores are reported in Table 6. The PSS (anxiety and depression) of the two groups showed no significant differences; nonetheless, at T3 the mean score of the patients in the intervention group was lower than that of control patients. In group A, all subscores decreased from T1 to T3: the PHS by 20%, the PSS by 32%, and the TSDS by 23% and all differences were significant ($\alpha = 0.05$; $p < 0.0001$). These data, combined with the significant ($\alpha = 0.05$) reduction in the PID score, indicate that the intervention achieved its objective of relieving the dimension of pain that is related to patients' emotional and existential state, which responds poorly to drug

Table 5A
Mean NRS pain scores at T1 and T3 and PID scores in group A and B.

Patients	NRS pain score at T1 (± SD)	NRS pain score at T3 (± SD)	PID	Mean % change (± SD)	p-value (t-value)
Group A	4.11 (2.05)	2.28 (2.15)	**1.83**	44.52 (2.54)	< 0.0001 (4.87)
Group B	4.51 (2.39)	3.96 (3.04)	**0.55**	25.25 (2.14)	< 0.0001 (2.71)

*NRS, Numerical Rating Scale; PID, Pain Intensity Difference; SD, Standard Deviation.

Table 5B
Percent distribution of patients by group and PDI score.

Patients	Deterioration	No change	Improvement			
	−1/-4	**0**	**1**	**2**	**≥3**	**Total**
Group A	8.69	26.09	17.39	8.69	39.13	100.00
Group B	17.78	37.78	13.33	11.11	20.00	100.00
Total	**13.19**	**31.87**	**15.38**	**9.89**	**29.67**	**100.00**

*PID, Pain Intensity Difference.

treatment. The very limited change seen in the control group (9%, 1%, and 5%, respectively) is related to the fact that between T1 and T3 they received only pharmacological pain treatment. As shown in Tables 5A and 6, in group B the reduction was significant only for pain and the PHS, respectively.

When group A patients were asked whether they felt a greater control *over* their pain after the intervention, 65.2% answered *"yes"*, 24.9% answered *"no"*, and 10.9% were "not sure". The proportion of patients who denied a greater perceived control over pain was higher than that of patients who asked for rescue analgesics in the next 24 h. As regards pain in the 24 h period following the intervention, 80.4% of group A patients denied experiencing any episode of acute pain (Table 7). Of group B patients, who received only pain medications, 64.4% reported no episodes of acute pain. The data regarding the consumption of rescue analgesics reflect these figures. Application of the Chi-square test to the absolute frequency values indicated that acute pain and rescue analgesic administration depended on the group to which patients belonged ($\alpha = 0.05$).

6. Discussion

An RCT was designed to provide evidence of the effectiveness of GI and PMR in controlling pain in cancer patients receiving palliative care. Although a wide range of studies have assessed the effectiveness of a variety of complementary and alternative medicine approaches in such patients, data regarding the effectiveness of PMR and IGI in cancer patients receiving palliative care are not yet available. However, cancer patients are increasingly asking for and using complementary therapies to enhance their ability to fight cancer or to improve their physical and emotional wellbeing, as shown by a European survey [70] and by two surveys conducted in Italian hospices [54,55]. These studies highlight the role of PMR and IGI as adjuvant treatments that help relieve pain also in hospice patients at the end of life. Although the PID (NRS at T3 – NRS at T1) was significant in both patient groups, its average value was 1.83 in group A and 0.55 in group B, suggesting a greater effect of the PMR-IGI intervention compared with usual care. The notion that has been invoked to explain the effects of IGI on pain perception is the psychoneurological theory, whereby the creation of an image in a person's mind would activate the cerebral cortex, the limbic system and, subsequently the hypothalamus, which would then activate the autonomic nervous system [2].

Table 7
Episodes of acute pain and administration of rescue analgesics in the 24 h period following the intervention (T4).

Episodes of acute pain	No (%)	Yes (%)	Total (%)
Group A	80.43	19.57	100.00
Group B	64.44	35.56	100.00
Administration of rescue analgesics			
Group A	82.61	17.39	100.00
Group B	66.67	33.33	100.00

An RCT conducted by Kwekkeboom et al. [50,51] to investigate the contribution of PMR and IGI in relieving pain in 40 hospitalized cancer patients has found changes in pain intensity in 31% of the IGI group versus 8% of the control group. Another qualitative study involving 26 cancer patients compared their perception of PMR and IGI interventions to changes in their pain scores: eleven participants thought that PMR was effective in relieving pain and five described IGI as a successful pain-relieving intervention 24. In most cases, patients' perceptions of the effects of IGI and PMR matched the actual changes in their pain scores [24].

Another randomised clinical trial evaluated the efficacy of 3 brief cognitive-behavioural techniques – relaxation, distraction, and positive mood interventions – in 57 patients with cancer pain [71]. The relaxation and distraction techniques contributed to reduce pain intensity, but had only a short-term effect, whereas a small proportion (8.8%) of patients reported adverse effects such as no change or (mostly transient) pain exacerbation. These data are consistent with the findings of other studies [22]. The adverse effects can probably be ascribed, at least partly, to fatigue – a highly disabling concurrent symptom experienced by patients with advanced disease – which impairs their cognitive ability to direct or focus their attention or produce mental images. It is also reasonable to surmise that the imagery experience may have affected the self-evaluation of pain, as stressed in other studies where patients with greater imaging ability, more favourable expectations, and a lower TSDS achieved greater pain reduction [24]. Pain managed with drug treatment and a validated complementary therapy, which also reduces distress, can help clinicians optimise the quality of

Table 6
Changes in the ESAS-r score and subscores from T1 to T3 in each patient group.

Mean ESAS-r scores								
Total score	T1 and SD		T3 and SD		Change and SD		p-value (t-value)	% change
Group A (degrees of freedom, 45)								
Physical (0–70) PHS	25.37	(11.82)	20.26	11.16	5.11	8.21	< 0.0001 (4.22)	20
Psychological (0–20) PSS	9.17	5.63	6.24	5.09	2.93	4.53	< 0.0001 (4.39)	32
TSDS (0–100)	39.04	15.27	30.22	14.79	8.83	12.11	< 0.0001 (4.94)	23
Group B (degrees of freedom, 44)								
Physical (0–70) PHS	28.31	14.16	28.57	13.83	2.44	7.76	< 0.0001 (2.02)	9
Psychological (0–20) PSS	7.89	6.36	7.82	6.15	0.07	3.88	> 0.05 (0.11)	1
TSDS (0–100)	**40.00**	**17.54**	**38.16**	**18.76**	**1.84**	**9.93**	> **0.05 (1.25)**	**5**

*ESAS-r, Revised Edmonton Symptom Assessment Scale; TSDS, Total Symptom Distress Score; SD, Standard Deviation.

end-of-life care. Cognitive-behavioural strategies such as GI can thus provide a very useful tool.

In the present study the PMR-IGI intervention had a favourable impact on concurrent symptoms, including psychological distress, i.e. anxiety and depression, suggesting that it exerts effects on the emotional dimension of pain [38]. GI and PMR have proved effective in reducing depression and anxiety in cancer patients and induced changes in salivary cortisol and a-amylase [72]. A positive effect of PMR and IGI on anxiety has been reported in various studies of cancer patients, although in one study involving chemotherapy patients relaxation had no effect on stress, anxiety or quality of life [73].

Notably, and in line with recent studies [38], the images that provided actual benefits were those generated by participants, i.e. personal images, whose processing is therefore "individual" and whose suggestive power can be enhanced by the practitioner's ability to read the patient's responses and to adapt the GI to the unique characteristics of each subject. Patients often tended to visualise situations related to their own life and to describe past experiences that they subsequently relived in the form of a tale, in a regression similar to regressive hypnosis, rather than imagining new experiences. In such cases, the practitioner tried to steer the patient away from the evocation of past events and to encourage their replacement/integration with an imagery that was not closely tied to memories. Imagination is a conscious activity that consists in the ability to create a representation of any object or affective experience that is not present. Since imagination can replace the object or the absent affect, it has a useful function, alleviating the anxiety that can stem from the lack of the object or the absence of the affect. Imagery consists of a temporary emotional absorption in experiences, in which imagination has a key role. It has been reported that the imaginative ability of patients and their confidence in the intervention are better predisposing factors than their level of education or of pain/stress [49–51].

The favourable short-term response of group A patients, the limited number of acute pain episodes in the 24 h period after the intervention, and the modest need for rescue analgesics are highly encouraging, despite the typical fluctuating nature of pain in these patients. The present findings suggest that the PMR-IGI intervention may have had a positive impact on pain management. The greater control over pain, perceived by 65% of group A patients, resulted in a less passive attitude to their disease and to pain, as confirmed by the fact that only 17.4% of them asked for rescue analgesics in the next 24 h. As reported in previous studies [2,11,74], repeated delivery during the patients' stay at the hospice has the potential to further enhance their pain control ability and self-efficacy.

The main limitations of the study are related to the difficulties inherent in the palliative care setting, which is characterised by the extreme fragility of patients and their highly demanding care. Further limitations are related to extraneous variables that could not be controlled, like the possibility that patients' responses reflected demand characteristics (group A) or the absence of a therapist and interactions with an attentive other (group B). An attempt to control these effects was made by selecting for each centre a different, well-trained GI practitioner with strong experience in working with this type of patients, a feature that has been found useful in RCTs of complementary therapies [45]. Moreover, though invasive care procedures were avoided after the intervention and patients were recommended to lie quietly, other influences – including pleasant distractions – cannot be ruled out.

7. Conclusion

PMR and GI are highly flexible complementary therapies that can be administered at all cancer stages, for instance to help patients cope with the effects of chemotherapy and to alleviate symptoms at the end of life. They can be delivered at home, in hospital and in palliative care settings, where they can contribute to manage global pain and its affective components. The results of this study support the view that PMR and GI can be useful adjuvant techniques to alleviate pain distress in patients with terminal cancer. They also show that pain was significantly reduced both in the treated and the control group. Although this prevents drawing firm conclusions on the effectiveness of PMR and GI in controlling pain, their impact on total symptom distress and on emotional and existential components demonstrates that they exert a favourable, significant effect in relieving the personal dimension of pain, which responds poorly to medications. The intervention showed efficacy in reducing anxiety and distress, which are significant determinants in the personal experience of pain. PMR and GI may also be considered as aids in relieving the fear of experiencing pain again.

This study reports the findings of a one-off intervention. However, it can be assumed that repeated administration would improve the management of patients' pain distress. Training of palliative care operators and caregivers in delivering it would contribute to spread the adoption of PMR and GI in daily clinical practice, as proposed by Keefe [4, 75].

Complementary therapies should be offered to patients receiving palliative care, to integrate the multiprofessional palliative approach [54]. Despite the several problems affecting the planning and conduction of clinical trials involving terminally ill patients, further research should be performed to support and spread the use of effective CAM techniques even in this clinical context. Moreover, studies performed in palliative care settings do benefit from some very positive factors, such as patients' close relationship with the treatment team and the trust in the ethical nature of the study goals, which consistently aim to improve patients' quality of life.

Conflicts of interest

None.

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Appendix

ESAS-r cutoffs [69]

ESAS-r	Improvement	Deterioration	Total score
PHS	≥3	≤ −4	70
PSS	≥2	≤ −1	20
TSDS	≥3	≤ −4	100

*ESAS-r, Revised Edmonton Symptom Assessment Scale, PHS, physical subscore; PSS, psychological subscore; TSDS, Total Symptom Distress Score.

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