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ORIGINAL ARTICLE

Impact of comprehensive pulmonary rehabilitation on anxiety and depression in hospitalized COPD patiens

G. Garuti, C. Cilione, D. Dell'Orso, P. Gorini*,
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ABSTRACT: ***Impact of comprehensive pulmonary rehabilitation on anxiety and depression in hospitalized COPD patiens. G. Garuti, C. Cilione, D. Dell'Orso, P. Gorini, M.C. Lorenzi, L. Totaro, G. Cirelli, E. Clini.***

To prospectively evaluate the effect of inpatient pulmonary rehabilitation (iPR) on anxiety and depression as outcome measures in patients with COPD, we studied 149 consecutive adults COPD referred to our iPR after an exacerbation. Patients were divided according to the GOLD staging into: Group 1 (stage 2a, n=48, FEV_1 63±9 %pred.), Group 2 (stage 2b, n=53, FEV_1 42±6 %pred.) and Group 3 (stage 3, n=48, FEV_1 25±7 %pred.). The iPR consisted of twelve 3-hours daily sessions.

Hospital Anxiety Depression (HAD) Scale as well as 6-minute walk (6MWD) with evaluation of dyspnea (D) and leg fatigue (F) at rest and end of effort, and health related quality of life by means of St. George Respiratory Questionnaire (SGRQ) were assessed before (T0) and after (T1) the iPR.

6MWD, D and F at end of effort and SGRQ total score similarly improved (p<0.001) in all groups after iPR. The mean level of HAD-anxiety (from 9.1±4.0 to 7.7±3.5, from 9.0±4.6 to 7.2±4.6 and from 8.1±4.1 to 6.7±4.3 in group 1,2 and 3 respectively) and HAD-depression (from 9.4±3.5 to 8.2±3.5, from 9.1±4.2 to 8.2±4.5 and from 9.0±4.0 to 7.4±4.5 respectively) similarly changed (p<0.0001) over time in all groups. The total percentage of patients with abnormal score (>10) of HAD-anxiety (from 31% to 21%) and HAD-depression (from 30% to 22%) significantly decreased (p<0.05) after the iPR.

Inpatient pulmonary rehabilitation may improve levels of anxiety and depression as well as symptoms, exercise capacity and health related quality of life in moderate to severe COPD patients after an acute exacerbation.
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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a disorder commonly associated with disability and impaired quality of life [1]. Patients with COPD have been shown to refer symptoms of raised anxiety and depression [2], the most severe patients being those presenting the highest levels of depression, which also appears to be under-recognized and under-treated [3].

Pulmonary rehabilitation (PR) is increasingly used to treat COPD patients of different degree of severity [4], bringing them benefits in terms of improved exercise capacity and quality of life [1, 5]. Some evidence also suggests that a shorter inpatient PR (iPR) is as useful and effective as a longer outpatient PR [6]. Furthermore, it has been shown that a short-stay iPR can improve psychological morbidity in patients with COPD [7]. Indeed, outpatient PR significantly improved the levels of anxiety and depression of COPD patients with a FEV1 lower than 40% of predicted value [8].

Still little is known about the effect of iPR on anxiety and depression in patients with less severe functional compromission and after acute exacerbation of their disease.

We therefore aimed to evaluate the impact of a short-stay iPR on anxiety and depression as outcome measures in patients with both moderate or severe COPD after an acute exacerbation.

Methods

Patients gave their informed consent to the study. All the procedure were conducted according to the declaration of Helsinki.

Patients

Patients with COPD consecutively admitted to our rehabilitation unit from July, 1st to December 31st, 2000 were studied. They were referred directly from acute care hospitals following an acute exacerbation of their disease. At the admission all patients were in stable condition as defined by stability in blood gas values. At this time none of the patients received systemic steroids; no change in the treatment with inhaled bronchodilators and steroid

(when appropriate) had been made in the six days preceding the admission to our hospital.

Eligibility criteria for iPR at this facility were: persisting symptomatic disease after exacerbation (e.g. dyspnea score ≥ 2 at the MRC scale), degree of disability and actual inability to perform most activity of daily living precluding participation to a outpatient program, FEV_1 lower than 80% of predicted and a FEV_1/FVC ratio below 70%, arterial PO_2 ≥ 60 mmHg breathing room air at rest, sufficient motivation and endurance to participate the rehabilitation therapy daily. Patients with any unstable medical condition, severe left ventricular dysfunction, resting hypoxemia, cancer, or inability to cooperate were excluded from the study.

The included patients were diagnosed and classified as COPD according to the GOLD staging and definition [9] and they were so divided into: Group 1 (stage 2a, n=48, FEV_1 63±9% pred.), Group 2 (stage 2b, n=53, FEV_1 42±6% pred.) and Group 3 (stage 3, n=48, FEV_1 25±7% pred.). All the included COPD patients had history of smoking (>20 pack-year) but they currently were non-smokers or ex-smokers.

Measurements

Functional measures

Baseline lung volumes and Forced Vital Capacity (FVC) were measured by means of a spirometer (Masterscope Jaeger GmbH, Hochberg-Germany). The predicted values according to QUANJER [10] were used. Arterial blood was sampled at the radial artery while the patients in the sitting position were breathing room air for at least one hour. PaO2, PaCO2 and pH were measured by means of an automated analyzer (Mod. 850, Chiron Diagnostics Co., Medfield-USA). Respiratory muscle strength was assessed by measuring MIP and MEP [11] using a respiratory module system (Masterscope PIMAX/PEMAX Module, Jaeger GmbH, Hochberg-Germany). The predicted values according to BRUSCHI *et al.* [12] were used.

Outcome measures

Measurement were taken baseline (T0) and at the end of iPR (T1). All measurements were performed and recorded under the supervision of personnel not involved in the study.

The timed walk distance was assessed by the 6 minute walking test (6MWD) [13] while patients breathed room air. Verbal encouragement was given at definite intervals during the test. Three practice tests were performed on 2 consecutive days and the highest value was recorded. Arterial oxygen saturation (SatO2) was indirectly monitored throughout the walk using a pulse oximeter. Perceived dyspnea (D) and leg fatigue (F) by pointing a number or phrase on a 10-point modified Borg scale [14] were obtained before (Resting) and immediately following (End of effort) the walk test.

Levels of anxiety and depression were measured using the Hospital Anxiety and Depression (HAD) Scale [15]. This is a equally divided 14 four-point questions scale: answers result into two separate scores (ranging from 0 to 21) for anxiety (HAD-anxiety) or depression (HAD-depression).

Health related quality of life was assessed by the validated Italian versions of the St. George's Respiratory Questionnaire (SGRQ) [16]: the four component scores (Total, Impact, Activity, Symptoms) of the questionnaire were considered for analysis.

Inpatient Pulmonary Rehabilitation

Our iPR is performed in patients admitted to a 85 bed ward. After initial evaluation by physician and respiratory therapist, a multidisciplinary team (consisting of chest physician, nurses, physical therapist, dietician and psychologist) assessed the patient thus formulating an individualized rehabilitation plan. Patients performed 12 sessions (6 days per week) which were held for 3 hours on a day basis.

All patients were instructed for compensatory breathing techniques, energy conservation, stress management and symptoms control. Moreover iPR included optimization of the pharmacological treatment.

Each session included: gait and balance training, supervised floor walking and stationary bicycle exercise, stair climbing, abdominal, upper and lower limb muscle activities lifting progressively light weights (300-500 gms), shoulder and full arm circling, instruction in activities of daily living and therapeutic recreation focused on community reentry, psychosocial counseling, nutritional programs (when appropriate).

Exercises were discontinued if vital signs, saturation or other parameters resulted inappropriate or dangerous to the patient; therapeutic oxygen was prescribed (if required) to protect against an increased oxygen demand. No assisted ventilation was used with any of the patients in study.

The scheduling of the rehabilitative therapies was organized with the goal to discharge the patient to independent function at the end of the programmed sessions.

Statistical analysis

Results are expressed as mean and standard deviation (SD). All analyses were performed using a specific software (StatSoft package 5.0 for Windows). Physiological data were analysed between and within groups with Anova for repeated measures; post-hoc test was then applied when appropriate. To detect between groups differences for non-parametric variables, the Kruskal-Wallis test was used, while the Friedman non-parametric test was used to detect differences within group (time course). A score of 10 or greater for HAD scores was taken as suggestive of clinically significant anxiety or depression [15]. Frequency distributions were analysed with χ^2 test. Spearman analysis was used to evaluate the linear correlation coefficient between the considered parameters. A p value <0.05 was considered to be significant.

Results

The 149 COPD patients who entered the study represented 34% of the total patients consecutively admitted to our ward for rehabilitative purpose in the considered period.

Table 1 shows the general and demographic characteristics of patients in study divided into groups according to the GOLD staging (see Methods). Groups significantly differed for the level of airflow obstruction due to the pre-determined definition: nevertheless, the level of respiratory muscle strength was also significantly different across groups. Out of 149 patients, only 14 (9% of total, 4, 4 and 6 patients in group 1, 2 and 3 respectively) were taking antidepressant drug.

At baseline group 3 showed a significantly lower 6MWD ($p<0.05$ versus group 1 and 2) and higher D and F at end of effort ($p<0.01$ versus group 1) (see table 2).

Table 2 also shows the time course of symptoms and exercise capacity in the considered groups; the iPR determined a similar improvement in all groups when comparing the same outcome measures before (T0) and after (T1) the program.

Table 3 shows the time course of SGRQ and HAD mean scores in the three groups. All groups showed a similar improvement over time for HAD-anxiety and HAD-depression scores and for the SGRQ total score

Table 1. - Demographic, anthropometric and functional characteristics of patients at study entry. Data are as means (SD)

	Group 1	Group 2	Group 3	p (Anova)
Patients (n)	48	53	48	ns
Sex (M/F)	30/18	33/20	31/17	ns
Age (years)	70 (7)	68 (8)	68 (7)	ns
BMI (Kg x cm^{-2})	24 (3)	25 (4)	23 (6)	ns
FEV_1 (% pred)	63 (9)	42 (6)	25 (7)	< 0.001
FVC (% pred)	81 (13)	63 (12)	48 (12)	< 0.001
FEV_1/VC	68 (9)	57 (11)	46 (17)	< 0.001
MIP (cm H_2O)	55 (24)	46 (22)	49 (24)	< 0.05
MEP (cm H_2O)	83 (34)	78 (30)	71 (27)	< 0.05
$PaCO_2$ (mmHg)	39 (4)	40 (5)	42 (5)	ns
PaO_2 (mmHg)	68 (10)	69 (10)	63 (11)	ns

BMI: Body Mass Index; FEV_1 : pre-bronchodilator Forced Expiratory Volume in one second; FVC: pre-bronchodilator Forced Vital Capacity; MIP = Maximal Inspiratory Pressure; MEP = Maximal Expiratory Pressure; PaO_2: Arterial Oxygen Tension; $PaCO_2$: Arterial Carbon dioxide Tension.

Table 2. - Time course of symptoms and exercise capacity of patients in study. Data are as means (SD)

	Group 1		Group 2		Group 3	
	T0	T1	T0	T1	T0	T1
6MWD (meters)	361 (89)	429 (85) *	328 (113)	404 (101) *	272 (111) +	357 (106) *
End of effort-D	4.9 (1.3)	2.4 (1.3) §	5.3 (1.4)	3.0 (1.6) §	5.6 (1.5) °	3.5 (2.3) §
End of effort-F	5.5 (1.4)	3.6 (1.3) §	6.0 (2.1)	4.3 (1.5) §	6.4 (1.1) °	4.8 (2.0) §
Resting-D	3.6 (1.9)	3.5 (2.0)	4.0 (2.0)	4.0 (1.7)	4.1 (2.4)	3.9 (1.5)
Resting-F	3.7 (2.2)	3.8 (1.5)	3.9 (1.8)	4.1 (2.1)	4.0 (2.1)	3.8 (2.2)

6MWD: six minute walking capacity; End of effort-D: BORG score for dyspnea after exercise; End of effort-F: BORG score for leg fatigue after exercise; Resting-D: BORG score for dyspnea before exercise; Resting-F: BORG score for leg fatigue before exercise. * $p<0.0001$ versus T0; § $p<0.001$ versus T0; + $p<0.05$ versus group 1 and 2; ° $p<0.01$ versus group 1.

Table 3. - Time course of anxiety / depression and health related quality of life of patients in study. Data are as means (SD)

	Group 1		Group 2		Group 3	
	T0	T1	T0	T1	T0	T1
HAD-anxiety	9.1 (4.0)	7.7 (3.5) *	9.0 (4.6)	7.2 (4.6) *	8.1 (4.1)	6.7 (4.3) *
HAD-depression	9.4 (3.5)	8.2 (3.5) *	9.1 (4.2)	8.2 (4.5) *	9.0 (4.0)	7.4 (4.5) *
SGRQ-Total	53 (17)	48 (18) *	53 (18)	44 (20) *	60 (18)	53 (19) *
SGRQ-Impact	46 (22)	42 (22)	44 (20)	37 (22)	54 (21)	48 (23)
SGRQ-Activity	68 (18)	63 (19)	68 (19)	62 (22)	73 (20)	67 (23)
SGRQ-Symptoms	48 (23)	44 (25) §	50 (23)	37 (22) §	54 (22)	44 (23) §

HAD-anxiety: patients' anxiety level at the Hospital Anxiety Depression Scale; HAD-depression: patients' depression level at the Hospital Anxiety Depression Scale; SGRQ: St.George Respiratory Questionnaire. * $p<0.0001$ versus T0; § $p<0.05$ versus T0.

($p<0.0001$), the latter being mainly due to the significant change in the SGRQ symptoms component.

At T0 an abnormal level (>10) for both HAD-anxiety and HAD-depression scores was recorded in 31 and 30% respectively of the total sample. At this time, no significant differences were recorded among groups for an abnormal level (>10) of HAD-anxiety and HAD-depression scores. Figure 1 shows the frequency distribution of all patients according to the HAD scores at T0 and T1. The mean improvement in HAD-anxiety score was 1.4, 1.8 and 1.4 in group 1, 2 and 3 respectively, whereas HAD-depression score improved by 1.2, 0.9 and 1.6 respectively. The chi-square analysis showed a statistically significant difference ($p<0.05$) in the total number and percentage of patients with abnormal level of HAD-anxiety (which decreased from 51% to 35% and from 31% to 21%) and HAD-depression (which decreased from 50% to 38% and from 30% to 22%) before and after iPR. At T1, the number of patients with an abnormal score differently changed in group 1,2 and 3 ($p<0.05$) for HAD-anxiety (+5, -13 and -8%, respectively) and HAD-depression (-4, -8 and -10%).

The physiologic outcome measurements (symptoms and exercise capacity) did not show significant correlation with HAD-anxiety or HAD-depression scores at any time. HAD-anxiety and HAD-depression scores slightly but significantly ($p<0.05$) related with SGRQ total score both at T0 ($r=.42$ and $r=.41$ respectively) and T1 ($r=.53$ and $r=.49$ respectively). Moreover, % change in SGRQ total score also significantly, although weakly, related with % change in HAD-anxiety ($r=.20$, $p<0.05$), but not HAD-depression, score.

Discussion

This prospective study has demonstrated that a 12-sessions iPR can provide similar improvement in anxiety and depression as well as in exercise capacity and symptoms in both moderate or severe COPD patients after an acute exacerbation.

Overall, the value of pulmonary rehabilitation in COPD patients has been generally well established [9]. The relative efficacy of the specific components of this comprehensive program on physiological and psychological health has still to be definitively clarified in these patients. Our study shows that COPD patients of different severity may benefit from iPR in terms of physical performance and health-related quality of life, thus confirming previous results in COPD of different severity both as outpatients [4] or inpatients [7]. At the best of our knowledge, this is the first study documenting that a twelve daily sessions iPR may also improve levels of anxiety and depression in

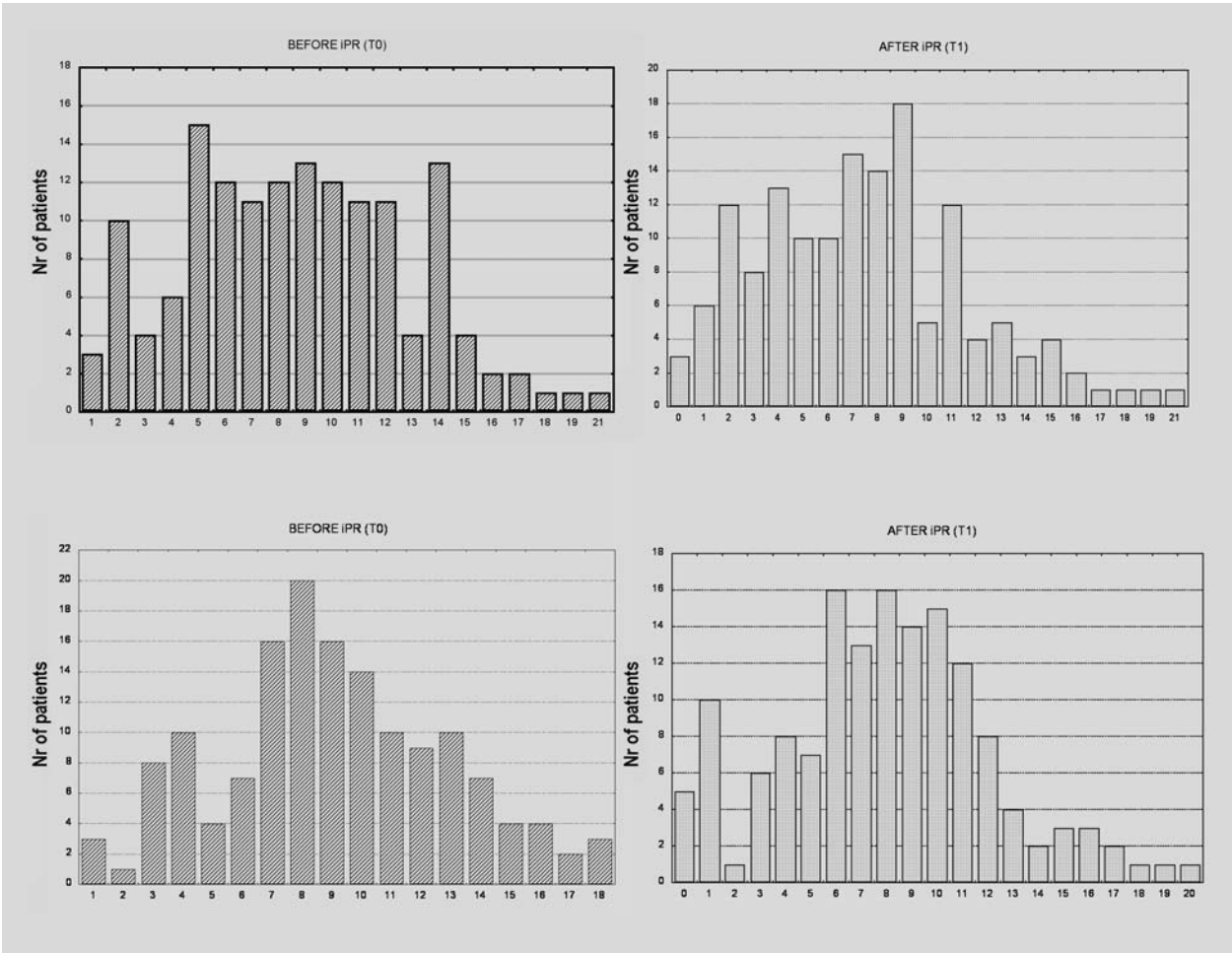

Fig. 1. - Frequency distribution of HAD-anxiety (upper panels) and HAD-depression (lower panels) scores at T0 (left) and T1 (right).

COPD patients with moderate and severe stage of their disease after an acute exacerbation.

Previous studies have documented high levels of anxiety and depression in these patients [5, 17, 18]. In particular, depressive symptoms are more prevalent in COPD patients than in age-matched subjects from a general population [19] and significantly contribute to the overall variance in functional status of the disease [20]. VOTTO *et al.* [7] have been able to show that a limited series of severely disabled (FEV_1 below 50% of predicted) COPD inpatients may decrease their anxiety and depression as assessed by means of partial components of the Pulmonary Functional Status Scale (PFSS) [21] after a short-term comprehensive rehabilitation program.

The HAD scale, that we use in our study, has been previously validated as the best tool for use in assessment of psychosocial morbidity [15] and provides more specific information as compared with other means to assess anxiety and depression [21, 22].

HAD scale has been used by WITHERS *et al.* [8] to test the individual's response to PR in stable severe COPD (FEV_1 below 40% of predicted) entering an outpatients program: they were able to demonstrate that both anxiety and depression significantly improved following PR, and that the levels reached by the HAD scores were maintained lower over 6 months. In our opinion, the present results extend those of that study [8], by showing that multidisciplinary PR may decrease the HAD levels in COPD inpatients following an acute exacerbation independent of the degree of severity.

The mean improvements in HAD-anxiety score (1.4, 1.8 and 1.4 in group 1, 2 and 3 respectively) and in HAD-depression score (1.2, 0.9 and 1.6, respectively) were higher than those observed in the whole population of the Withers study [8]. This effect may be mainly due to the different populations studied; our COPD patients followed an acute episode requiring hospitalization and baseline HAD scores were higher than those of WITHERS *et al.* [8]. Indeed, hypoxaemia *per se* may reduce ability to face the activity of daily living, impair cognitive function [23] and increase depression [3] of COPD patients. Nonetheless, percentage distribution of patients with HAD levels (>10) suggestive for anxiety and depression at admission (not higher than 30% of the total sample) in our study was quite similar to that of WITHERS *et al.* [8], thus suggesting that exacerbation might have influenced the score but not the prevalence of symptoms within our study population.

At difference with previous study [8], it is noteworthy that a similar improvement on anxiety and depression following PR has been obtained in a heterogeneous population of COPD (FEV_1 ranging from 79 to 11% of predicted) although the number of patients with an abnormal score (>10) after iPR differently changed across groups (see Results section). This change was higher in the most compromised COPD (group 2 and 3). Therefore, this result demonstrated that the most obstructed among COPD patients may benefit the best from a comprehensive iPR on the associated levels of anxiety and depression. Nonetheless, the most severely impaired individuals are those who may better improve their physiological outcomes after pulmonary rehabilitation [24].

Recent research [25] has shown that higher levels of catastrophic withdrawals coping strategies and lower levels of self-efficacy of symptoms management is associated with higher levels of depression and a reduced quality of life in COPD patients.

Our study confirmed that poor correlation exists between HAD and the physiological measurements in COPD patients [26, 27], whereas HAD scores significantly related with SGRQ total component (as assessed by absolute value or percentage change). HAJIRO *et al.* [18] have also found that HAD score significantly correlated (r=0.51) with SGRQ in mild and severe stable COPD patients.

The differences in correlation coefficients recorded in that study [18] and in our study between HAD and SGRQ could be due to the different condition of the patients included. However, the finding of only partial correlation between HAD and SGRQ scores probably means that psychological features cannot be completely explained by dimensions linked with health-related quality of life [28]. Therefore, future studies should be better addressed to find the links (if any) among these dimensions in order to maximize the effects of PR by including more specific evaluations and interventions.

The major limitation of the study are the folloing. The overall improvement that we observed in our sample should be interpreted with caution. Firstly, iPR patients were not compared with a untreated control group. However, these COPD patients were specifically referred to our unit for rehabilitative purpose, so it would have been unethical not to treat them. Secondly, the positive effect of iPR could have been mainly related to the continued medical improvement during convalescence. Nonetheless, the gains in all the pre-determined outcome measures, covering both physiological, psychological and quality of life areas, were independent of the degree of illness severity and suggested that iPR was probably the major causal factor. In addition, the mean change in health-related quality of life scores paralleled and were (although weakly) significantly related to those obtained in terms of anxiety and depression which have been previously shown as two of the most important components of psychosocial improvement after PR [7]. Undoubtedly, the substantial improvement observed in physiological variables may have reflected the marked baseline limitations (which was also a pre-determined criteria of study entry) of this population. Finally, we did not followed our patients after discharge to look at any variation in the anxiety and depression status, possibly related to the long-term effects of our iPR.

In conclusion, our study shows that iPR may improve levels of anxiety and depression as well as symptoms, exercise capacity and health related quality of life in moderate to severe COPD patients

after an acute exacerbation. Psychological measures may be included as outcomes entering the comprehensive assessment that may quantify the burden of COPD referred to inpatient rehabilitation.

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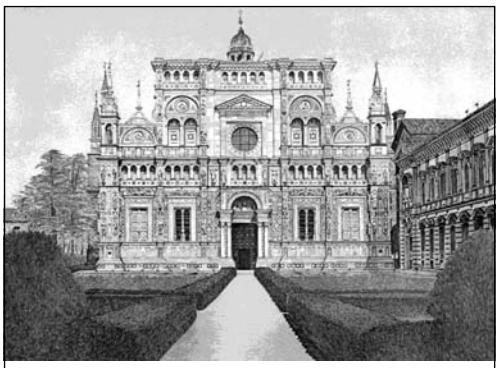

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