showed that the outcome was influenced by the following eight variables: %IBW and BMI, serum albumin concentration, coexistence of malignancy, dyspnea ranking (rank 4 and 5), FEV/FVC%, coexistence of bronchiectasis as determined by HRCT and hemoglobin level (hemoglobin <11.0 g/dl). Furthermore, multivariate analysis of predictors (Table 4) indicated the following three to be major factors worsening the outcome: %IBW(>85), ranking of dyspnea (rank 4 and 5), and coexistence of malignancy.

Previous reports have also suggested that nutrition is a major prognostic factor in cases of severe COPD [10-15]. The present data suggest that %IBW is a sensitive indicator of serum albumin concentration.

It has been known that poor daily activity of living was associated with a high mortality rate [19]. Although dyspnea at rest or exertion is not a criterion for LTOT, improvement of dyspnea with oxygen inhalation is known [18], and various mechanisms including improvement of ventilatory drive, minute ventilation, ventilatory muscle fatigue, or direct central perception have been speculated. However, perception of severe dyspnea is a major limiting factor for daily activity in elderly COPD patients [23]. Various benefits of LTOT for severe COPD patients are known [24] and the elderly patients who reach close to the average life expectancy may be benefitted as well. More recently the ANTADIR group has reported that severe COPD diagnosed on the basis of spirometry is associated with a survival similar to that among the hypoxemic patients[25]. However, the mean age of patients in their study was approximately 64 yr, which was 15 yr younger than in the present study. The present results indicate that the effects by LTOT must be studied in terms of improvement of quality of life in elderly COPD patients who already have the stated disability [26]. Particularly, it should lay particular emphasis on older patients whose age is close to the average life expectancy as in the present study. Further study is clearly needed.

In conclusion, we have analyzed factors that influence the outcome in elderly COPD patients receiving LTOT. The overall 5-year survival rate in COPD patients receiving LTOT was only 10.9% although LTOT might effect better outcome in younger patients. Three major variables were found to affect the outcome: %IBW, dyspnea ranking, and coexistence of malignancy. The dyspnea ranking is a major limiting factor in disabled elderly COPD patients. The benefits of LTOT should be assessed from this standpoint.

Figure Legends

Fig 1. Changes in cumulative survival rates in elderly COPD patients receiving long-term oxygen therapy.

Survival rates in the present study and in the general population were compared. The survival rates declined linearly until five years after the introduction of long-term oxygen therapy.

Fig 2. Changes in cumulative survival rates between groups aged over and under 80 yr of age.

The survival rates between the two groups did not differ.

Fig 3. Changes in cumulative survival rates among three groups according to FEV1.0/FVC (%).

The largest value of FEV1.0/FVC (%) was associated with the poorest survival rate, on the other hand the smallest value of FEV1.0/FVC (%) was associated with the longest survival rates among the three groups ($P<0.05$).

Fig 4. Changes in cumulative survival rates among three groups according to % ideal body weight.

The largest % ideal body weight (%IBW) associated with the best cumulative survival rates, whereas the smallest %IBW appeared to be associated with the poorest cumulative survival rate ($P<0.01$).

Fig 5. Changes in cumulative survival rate among three groups according to body mass index.

The largest body mass index (BMI) was associated with the best cumulative survival rates, whereas the smallest BMI appeared to be associated with the poorest cumulative survival rates ($P<0.01$).

Fig 6. Changes in cumulative survival rates among three groups according to serum albumin concentration.

The highest serum albumin concentration was associated with the best cumulative survival rates, whereas the smallest serum albumin concentration appeared to be associated with the poorest cumulative survival rates ($P<0.0X$).

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Table 1 The thirty-six variables analyzed in this study

Baseline disease	PaO_2	WBC
Cor pulmonale	$PaCO_2$	Lymphocyte number
Bronchiectasis	$AaDO_2$	Lymphocyte %
Gastric ulcer	$FEV_{1.0}$%predict	Body Height
Gastric ulcer (post therapy)	$FEV_{1.0}$/FVC%	Body Weight
Arrhythmia	MVV	IBW
Hypertension	%VC	%IBW
Ischemic heart disease	$FEV_{1.0}$	BMI
Malignancy	RV/TLC%	Arm span
Smoking history	$FEV_{1.0}$/VC	Total protein
Brinkman Index		Albumin
the duration of LTOT		Hb
Sex		
Age		

Table 2 Characteristics of patients at the start of LTOT

Variables		All patients (n=157)
Age, y		79.2±6.01
Sex		
Male, %	n=121	77.1
Female, %	n=36	22.9
Period of LTOT, y		2.81
FEV_1, ℓ		0.80±0.39
FVC, ℓ		1.72±0.61
FEV_1/FVC, %		48±17
Body mass index, kg/m²	18.6±3.8	
%IBW, %		91.5±19.5
PaO_2, mmHg		67.0±12.95
$PaCO_2$, mmHg		42.8±8.56
Dyspnea ranking		3.79±0.89
Serum Albumin, g/dℓ		3.85±0.43
Hemoglobin, g/dℓ		12.47±1.66
Breakup of diagnosis of COPD		
COPD, %	n=83	52.9
COPD+BA, %	n=40	25.5
COPD+Post Tbc, %	n=34	21.6

IBW : Ideal Body Weight, BA : Bronchial asthma, Post Tbc : Post pulmonary tuberculosis sequelae

Table3 Univariate analysis of predictors of mortality in COPD patients receiving LTOT

Factors	poor outcome (no, no of %)	better outcome (no, no of %)	β-SE	Hazard Ratio	95% CI
%IBW	85≧ (70, 46.7%)	85< (80, 53.3%)	0.7660±0.2147	2.151***	1.41-3.28
BMI	18≧ (80, 53.3%)	18< (70, 46.7%)	0.7598±0.2215	2.138***	1.38-3.30
Alb	3.5≧ (39, 26.4%)	3.5< (109, 73.6%)	0.5940±0.2285	1.811**	1.16-2.83
Malignancy	yes (31, 19.7%)	no (126, 80.3%)	0.6134±0.2360	1.847**	1.16-2.93
Dyspnea ranking	4, 5 (102, 65.4%)	2, 3 (54, 34.6%)	0.5554±0.2445	1.743*	1.08-2.81
$FEV_{1.0}$/FVC%	50< (53, 34.9%)	50≧ (99, 65.1%)	0.4557±0.2167	1.577*	1.03-2.41
Bronchiectasis	yes (4, 2.5%)	no (153, 97.5%)	1.3757±0.5201	3.958**	1.43-10.97
Hb	11.0≧ (30, 19.5%)	11.0< (124, 80.5%)	0.6178±0.2398	1.855**	1.16-2.97

* p<0.05, ** p<0.01, *** p<0.001

Table 4 Multivariate analysis of predictors of mortality in COPD patients receiving LTOT

	Hazard Ratio	95% CI
%IBW (≦85 vs >85)	2.078 **	1.32-3.26
Albumin (≦3.5 vs >3.5)	1.424	0.88-2.30
Malignancy (yes vs no)	2.023 **	1.24-3.30
Dyspnea ranking (4, 5 vs 2, 3)	2.040 **	1.20-3.47
$FEV_{1.0}$/FVC% (≦50 vs >50)	0.521 **	0.33-0.82

** $p<0.01$

Figure 1 Survival rates in COPD patients receiving LTOT

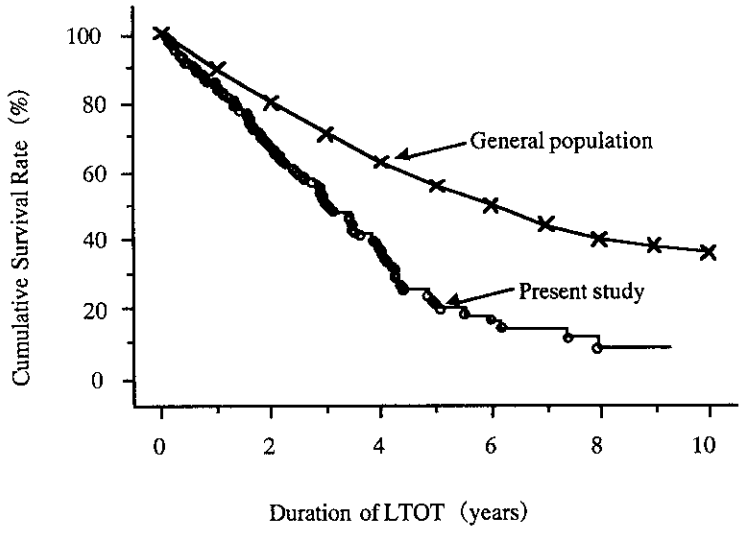


Figure 2 Changes in cumulative survival rates between groups aged over and under 80 yr of age.

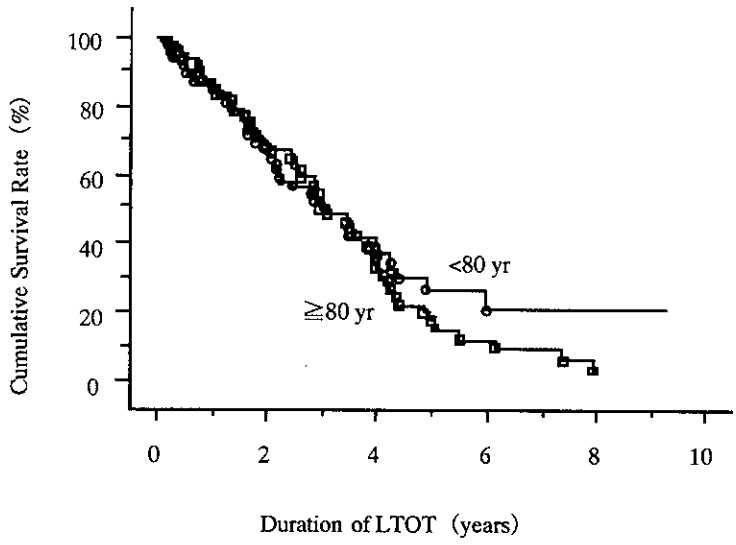


Figure 3 Changes in cumulative survival rates among three groups according to $FEV_{1.0}/FVC$ (%).

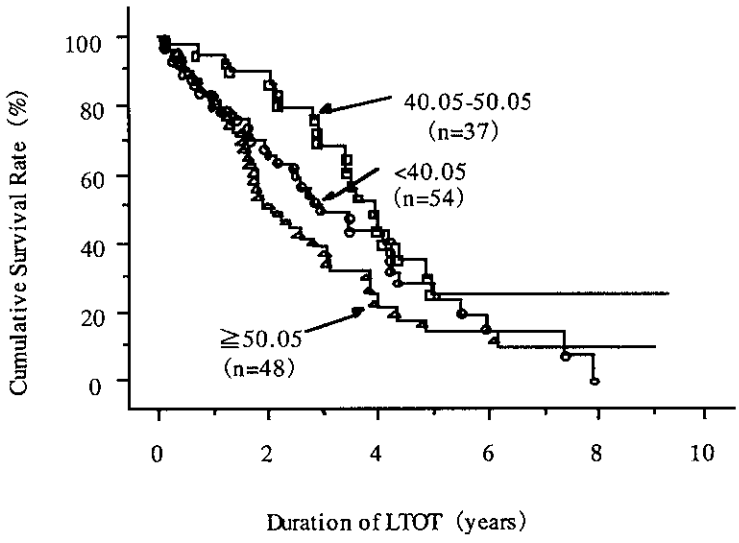


Figure 4 Changes in cumulative survival rates among three groups according to % ideal body weight.

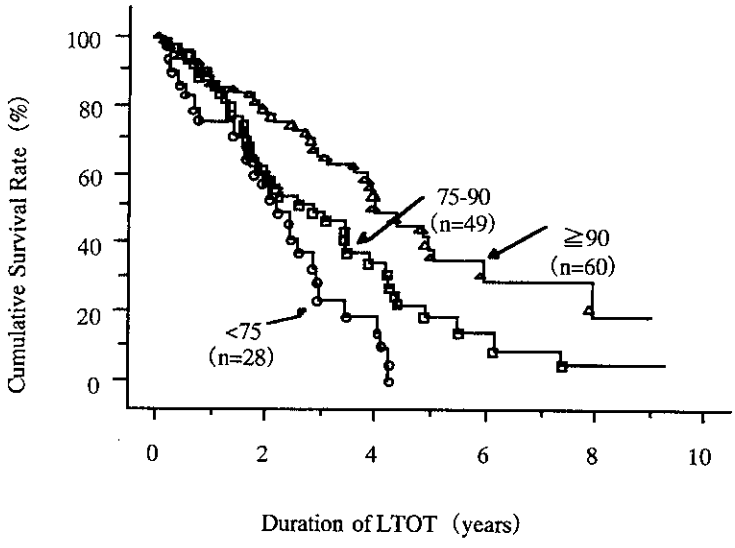


Figure 5 Changes in cumulative survival rate among three groups according to body mass index.

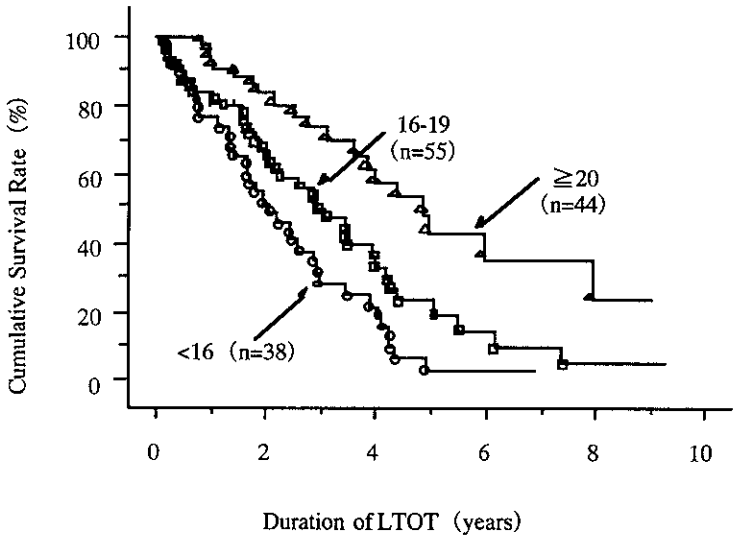
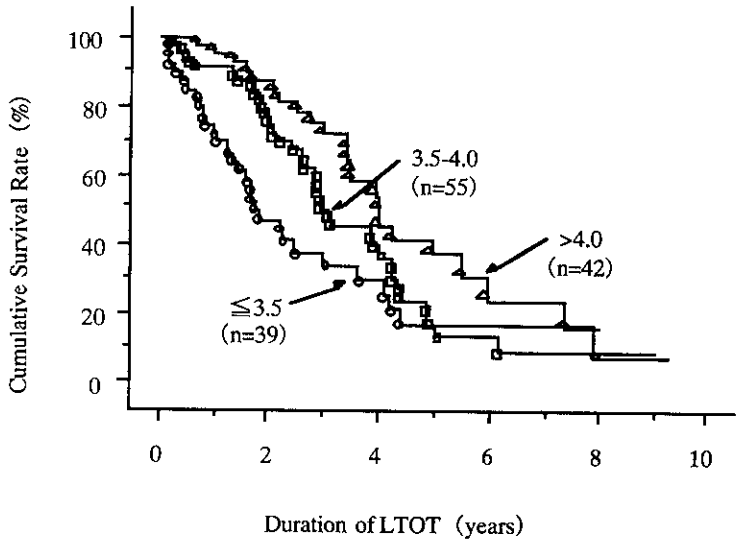


Figure 6 Changes in cumulative survival rates among three groups according to serum albumin concentration.



慢性閉塞性肺疾患患者における呼吸困難と quality of life に関する研究

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慢性閉塞性肺疾患患者における呼吸困難の程度と健康関連 quality of life（QOL）の障害についての検討を行った．呼吸困難の程度が進行すると，健康関連 QOL の障害がより強くなることが確認された．

キーワード：慢性閉塞性肺疾患、呼吸困難、QOL、SF-36

A．研究目的

近年，慢性疾患における健康関連 quality of life (QOL)の評価の重要性が指摘されている．慢性閉塞性肺疾患（COPD）においても，多くの研究が発表され，欧米では標準化された健康関連 QOL の調査票が多く存在する．しかし，全ての閉塞性肺疾患患者の健康関連 QOL を測定することは難しい．

慢性閉塞性肺疾患の重症度は，肺機能での 1 秒量（FEV1）の予測値に対する割合で決定される．例えば，米国胸部学会の定義によれば，Stage Ⅰは 50-79%予測値，Stage Ⅱは 35-49%予測値，Stage Ⅲは 35%予測値以下と分けられる．

一方，慢性閉塞性肺疾患患者の症状で最も多いのは，呼吸困難である．その呼吸困難は，主観的な感覚ではあるが，種々の調査票を用いて，重症度別に分類することができる．例えば，Medical Research Council (MRC) dyspnea scale は，どの程度の日常活動をしたときに呼吸困難を感じるかに基づいて 5 段階のスコアで評価する．

今回，FEV1 によるステージと呼吸困難を用いた分類が，どのように慢性閉塞性肺疾患患者の健康関連 QOL の障害を反映しているかを検討した．

B．研究方法

1. 対象

京都大学医学部附属病院通院中の慢性閉塞肺疾患患者男性 194 名．閉塞肺疾患の定義は，米国胸部学会の定義による．

2. 評価方法

肺機能は，FEV1，FVC を指標とした．FEV1 の予測値に対する割合によって米国胸部学会の定義に従い，患者を Stage Ⅰ，ⅡおよびⅢの 3 群に分類した．呼吸困難は，MRC dyspnea scale を用いて評価し，その scale により MRC scale=1，MRC scale=2，MRC scale≧3 の 3 群に患者を分類した．又，健康関連 QOL は，一般的な質問票である SF-36 を用いて評価した．SF-36 のスコアは 0 から 100 点に換算さ

れ，スコアが高いほど QOL が良いことを示す．

C．研究結果

対象患者の背景を Table 1 に示す

	mean SD	Range
Age (years)	70 ± 8	48 - 91
FEV_1 (L)	1.10 ± 0.43	0.39 - 2.56
FEV_1 (%pred)	41.5 ± 15.6	15.1 - 77.8
MRC scale	2 ± 1	1 - 5
SF-36†		
Physical Functioning	74.6 ± 17.8	5 - 100
Social Functioning	80.9 ± 21.1	13 - 100
Role-Physical	58.0 ± 41.4	0 - 100
Role-Emotional	63.7 ± 44.1	0 - 100
Mental Health Index	75.0 ± 18.6	24 - 100
Vitality	78.9 ± 22.7	21 - 100
Bodily Pain	65.5 ± 21.3	0 - 100
General Health	50.2 ± 19.7	0 - 97

MRC: Medical Research Council;

SF-36: Short form 36 health survey questionnaire.

Table 1. 検討対象症例の背景と SF-36 スコア

57 名の患者が Stage Ⅰであり，62 名が Stage Ⅱ，75 名が Stage Ⅲであった．一方，MRC scale=1 であったのは 59 名で，MRC scale=2 は 82 名，MRC scale≧3 の呼吸困難を示したのは 53 名であった．

Stage 毎の SF-36 の各領域のスコア分布を Figure 1 に示す．Physical function, Social function, Role-physical, Role-emotional, Mental health, Vitality, General health の各領域で，Stage2 と Stage3 のスコアは Stage1 に対して有意に低い傾向にあった(Fisher's LSD method, $p<0.05$)．しかし，どの領域においても Stage2 と Stage3 の 2 群間に有意な差は認めなかった．

MRC scale に基づいて 3 群に分けた場合の SF-36 の各領域のスコア分布を Figure 2 に示す．Bodily pain と General health の領域をのぞいて，MRC scale≧3 の群は有意に，MRC scale=1 および MRC scale=2 の両群に対してスコアが低い傾向にあった（Fisher's LSD method, $p<0.05$)．

D．考察

今回の検討では，患者の呼吸困難を元に分類することが，健康関連 QOL をより反映し，その障害の大まかな予測に役立つことが示唆された．

呼吸困難は，元来，慢性閉塞性肺疾患患者の健康関連 QOL の障害に最も関連しているといわれる．これまでの研究でも，健康関連 QOL 調査票スコアと呼吸困難との相関関係は中等度以上であることが知られている．

我々が用いた MRC scale は非常に簡便であり，外来診察の問診の際に簡単に聴取できる．このような scale を用い，患者を大まかに 3 群に分けることで，SF-36 のほとんどの領域のスコア分布が分かれたことは興味深い．

一方，米国胸部学会の定義に基づいた重症度の分類では，Stage Ⅱ以上の 2 群での健康関連 QOL の差が明らかではなかった．これは，2 群の患者における QOL の障害の程度のばらつきが大きいためであり，肺機能上の閉塞性障害が強いことが必ずしも QOL の障害とは関連していないことを示している．

健康関連 QOL を評価対象とする研究が多くでてきているが，FEV1 に基づく患者群の分別のほかに，呼吸困難を元に患者を分けることがより慢性閉塞性肺疾患患者の多様性の検討に役立つ可能性がある．

E．結論

閉塞性肺疾患患者を呼吸困難の程度によって分類することが，健康関連 QOL の視点から重要であることが示唆された．慢性閉塞性肺疾患患者のケアにおいて，客観的な肺機能の指標とともに，主観的である呼吸困難に対する考慮が必要であろう．

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Figure 1

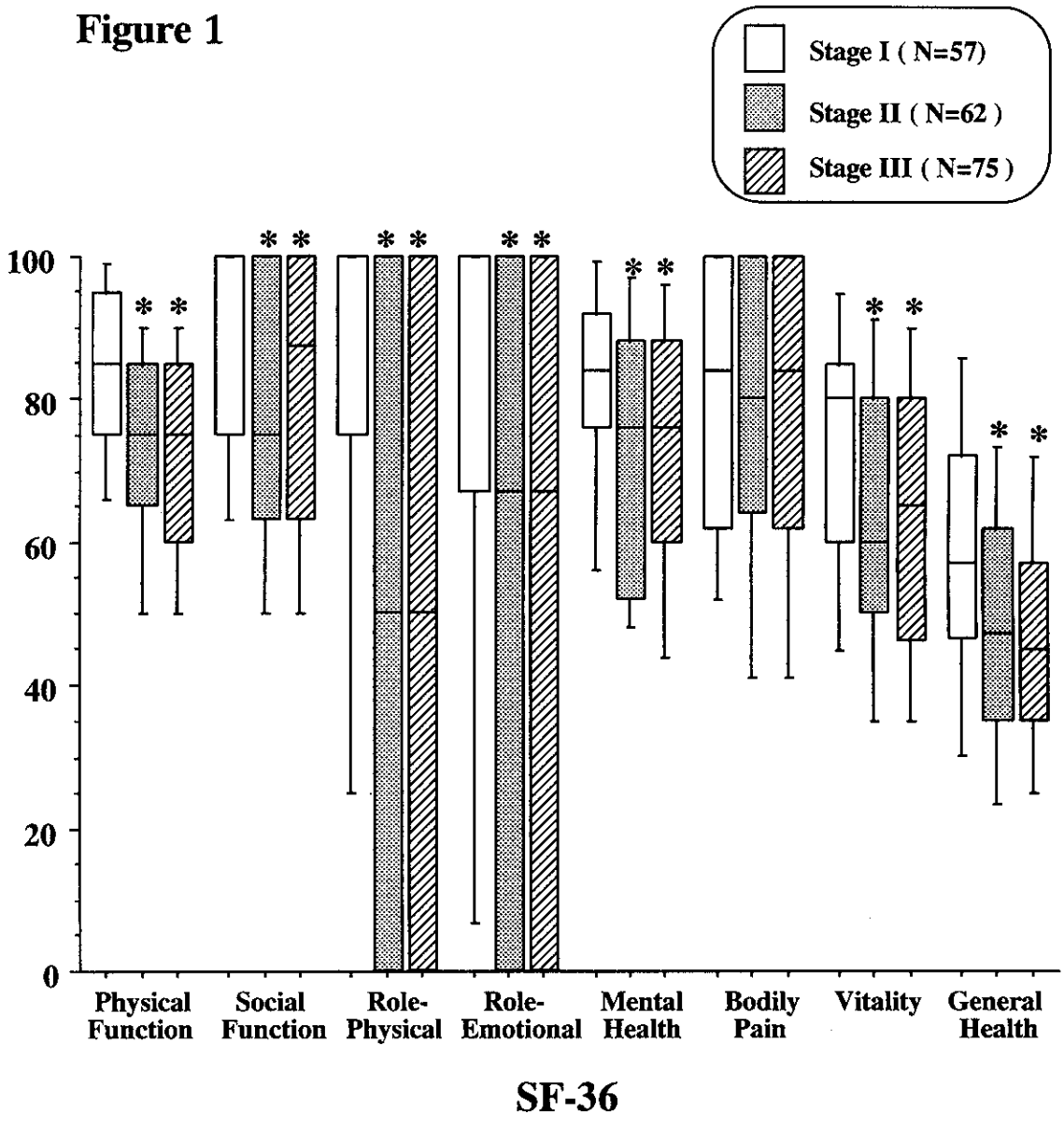
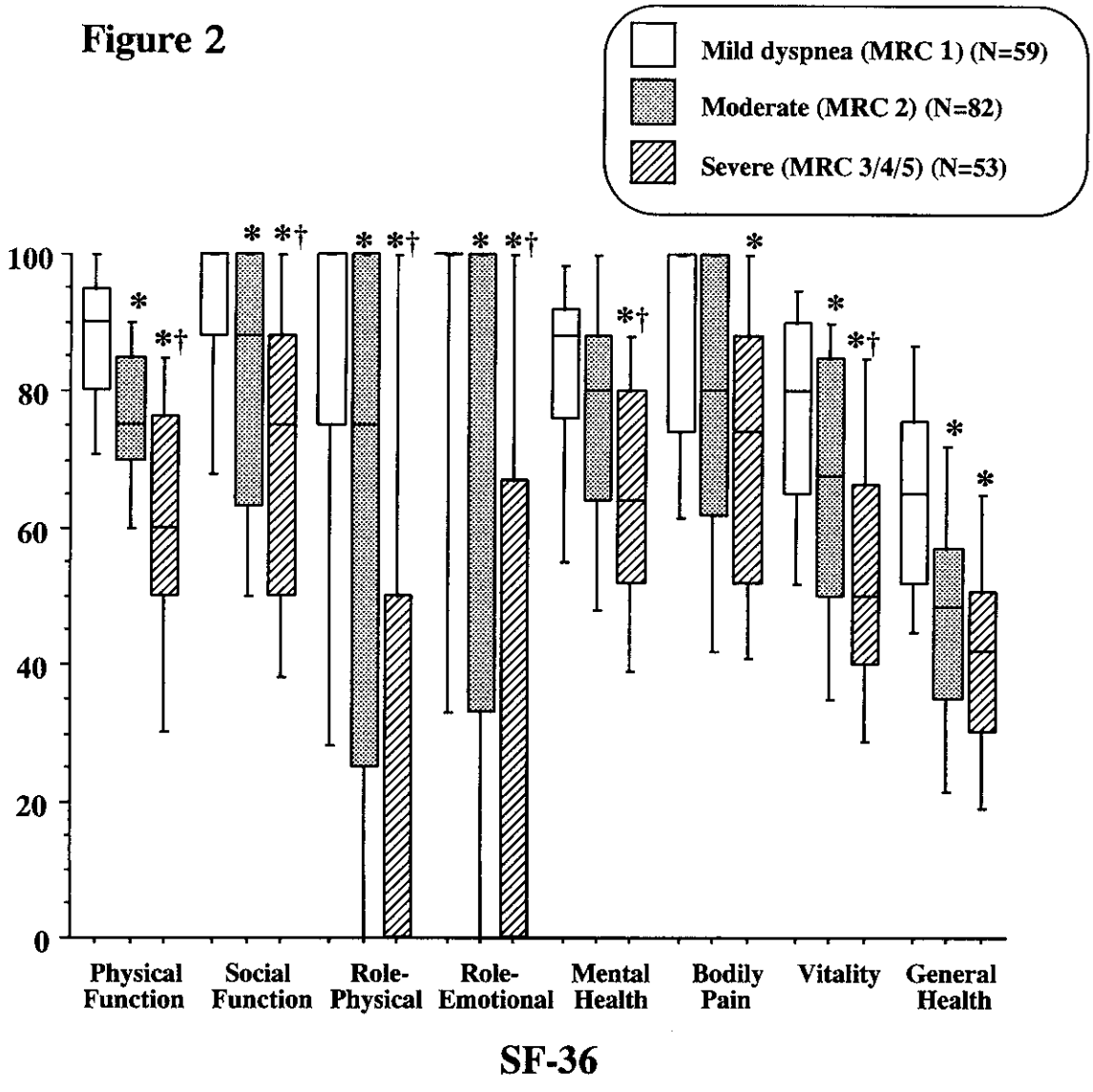


Figure 1. 対象患者のステージ別の SF-36 の各領域のスコア分布.

Figure 2



*; vs. MRC scale 1, †; vs. MRC scale 2.

Figure 2. 対象患者の MRC scale 別の SF-36 の各領域のスコア分布.