



UNIVERSITA CAMPUS BIO-MEDICO DI ROMA

Criteria diagnostici: validità, limiti e potenziali alternative nell'anziano fragile

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Diagnosis of COPD 1(ATS/ERS)

- Diagnosis of COPD should be considered in any patient who has the following:
 - symptoms of cough
 - sputum production
 - dyspnoea
 - history of exposure to risk factors for the disease
- Spirometry should be obtained in all persons with the following history:
 - exposure to cigarettes and/or environmental or occupational pollutants
 - family history of chronic respiratory illness
 - presence of cough, sputum production or dyspnoea

Diagnosis of COPD 2 (ATS/ERS)

- **Spirometric classification of COPD:**
 - Post-bronchodilator FEV₁/forced vital capacity <0.7 confirms the presence of airflow limitation that is not fully reversible.

| Severity | Postbrochodilator FEV ₁ /FVC | FEV ₁ % pred |
|--|---|-------------------------|
| At risk Patients who: <ul style="list-style-type: none"> –smoke or have exposure to pollutants –have cough, sputum or dyspnoea •have family history of respiratory disease | >0.7 | ≥80 |
| Mild COPD | ≤0.7 | ≥80 |
| Moderate COPD | ≤0.7 | 50–80 |
| Severe COPD | ≤0.7 | 30–50 |
| Very severe COPD | ≤0.7 | <30 |



Ai fini diagnostici sono quindi indispensabili:

- Sintomatologia: codificata dall'esperienza nell'adulto
- Spirometria: interpretata in modo tradizionale

Ma i sintomi atipici, non rari nell'anziano,
possono ostacolare la diagnosi (Antonelli Incalzi et al, J Int
Med 2002; 252: 48)

| | Diagnosi corretta, n: 67 | Diagnosi errata, n: 13 | p |
|-------------|-----------------------------|---------------------------|-------|
| Dispnea | 60 | 3 | <.001 |
| Astenia | 21 | 10 | .002 |
| Edemi | 14 | 6 | .06 |
| Toracoalgia | 6 | 3 | .14 |
| Confusione | 3 | 1 | .63 |
| Vertigini | 4 | 2 | .24 |

Standard ATS/ERS di qualità della spirometria

(Miller MR et al. Eur Respir J 2005; 26: 319)

TABLE 5 Summary of within- and between-manoeuvre acceptability criteria

Within-manoeuvre criteria

Individual spirograms are "acceptable" if

They are free from artefacts [3]

Cough during the first second of exhalation

Glottis closure that influences the measurement

Early termination or cut-off

Effort that is not maximal throughout

Leak

Obstructed mouthpiece

They have good starts

Extrapolated volume <5% of FVC or 0.15 L, whichever is greater

They show satisfactory exhalation

Duration of ≥ 6 s (3 s for children) or a plateau in the volume–time curve or

If the subject cannot or should not continue to exhale

Between-manoeuvre criteria

After three acceptable spirograms have been obtained, apply the following tests

The two largest values of FVC must be within 0.150 L of each other

The two largest values of FEV₁ must be within 0.150 L of each other

If both of these criteria are met, the test session may be concluded

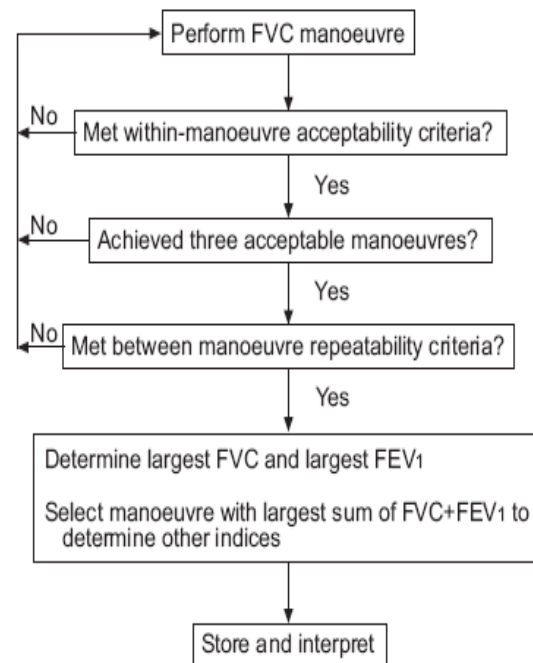
If both of these criteria are not met, continue testing until

Both of the criteria are met with analysis of additional acceptable spirograms or

A total of eight tests have been performed (optional) or

The patient/subject cannot or should not continue

Save, as a minimum, the three satisfactory manoeuvres



FVC: forced vital capacity; FEV₁: forced expiratory volume in one second.

..ma questi non sono standard per anziani (SaRA,
Am J Respir Crit Care Med 2000; 161: 1094-1100)

COMPLIANCE WITH ACCEPTABILITY
AND REPRODUCIBILITY CRITERIA*

| | Cases | Controls | p Value |
|---|------------|------------|---------|
| Acceptability, n (%) | 508 (83.6) | 747 (81.9) | NS |
| PEFT, n (%) | 405 (66.7) | 550 (60.3) | < 0.05 |
| BEV, n (%) | 526 (86.6) | 741 (81.2) | < 0.05 |
| FET, n (%) | 526 (86.6) | 748 (82) | < 0.05 |
| EEP, n (%) | 246 (40.5) | 538 (58.9) | < 0.001 |
| FEV ₁ reproducibility, n (%) | 573 (94.3) | 874 (95.8) | NS |
| FVC reproducibility, n (%) | 532 (87.6) | 830 (91) | NS |
| FEV ₁ , repr + accept, n (%) | 487 (80.2) | 725 (79.4) | NS |

Definition of abbreviations: BEV = back-extrapolated volume (acceptable if less than 150 ml or 5% of FVC); EEP = end-expiratory plateau (acceptable if no change in volume for at least 1 s); FET = forced exhalation time (acceptable if longer than 6 s); FEV₁ reproducibility = if the difference between the largest FEV₁ and the second largest FEV₁ was lower than 200 ml; FVC reproducibility = if the difference between the largest FVC and the second largest FVC was lower than 200 ml; PEFT = time-to-PEF (acceptable if less than 120 ms).

* No. (%) of tests that meet acceptability and reproducibility criteria.

Chi non riesce a fare una buona spirometria?

(SaRA, Am J Respir Crit Care Med 2000; 161: 1094-1100)

STEPWISE LOGISTIC ANALYSIS

| Outcomes | Predictors | Odds Ratio | Confidence Interval | p Value |
|---------------------------------------|-------------------------------|------------|---------------------|---------|
| Poor acceptability | MMSE < 75th percentile | 1.59 | 1.07-2.37 | < 0.05 |
| | 6MWT < 75th percentile | 1.57 | 1.09-2.26 | < 0.05 |
| | Educational level \leq 5 yr | 1.54 | 1.08-2.20 | < 0.05 |
| Poor FEV ₁ reproducibility | Male sex | 3.04 | 1.44-6.42 | < 0.001 |
| | Age | 1.05 | 1.01-1.10 | < 0.05 |
| Poor FVC reproducibility | Respiratory drugs, n | 1.40 | 1.21-1.62 | < 0.001 |
| | Male sex | 1.99 | 1.26-3.12 | < 0.005 |
| Poor FEV ₁ repr + accept | Age | 1.04 | 1.01-1.07 | < 0.01 |
| | Age | 1.04 | 1.02-1.06 | < 0.001 |
| | Respiratory drugs, n | 1.17 | 1.05-1.32 | < 0.01 |
| | Male sex | 1.63 | 1.22-2.16 | < 0.01 |
| | MMSE < 75th percentile | 1.54 | 1.08-2.20 | < 0.05 |
| | Educational level \leq 5 yr | 1.39 | 1.04-1.87 | < 0.05 |

Non dimentichiamo i fattori operatore-dipendenti (SaRA, Am J Respir Crit Care Med 2000; 161: 1094-1100)

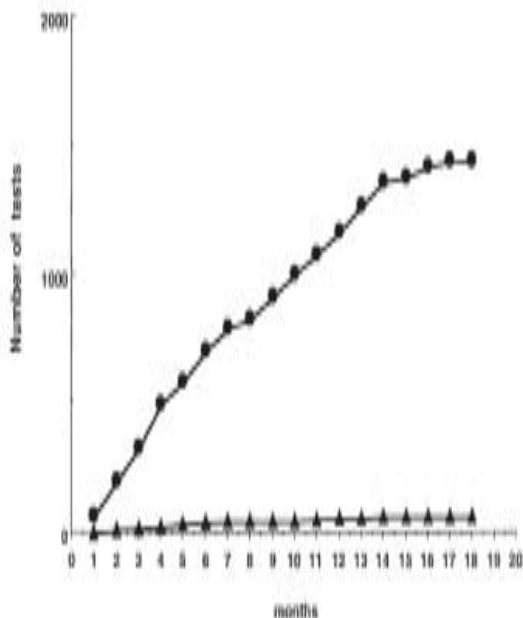
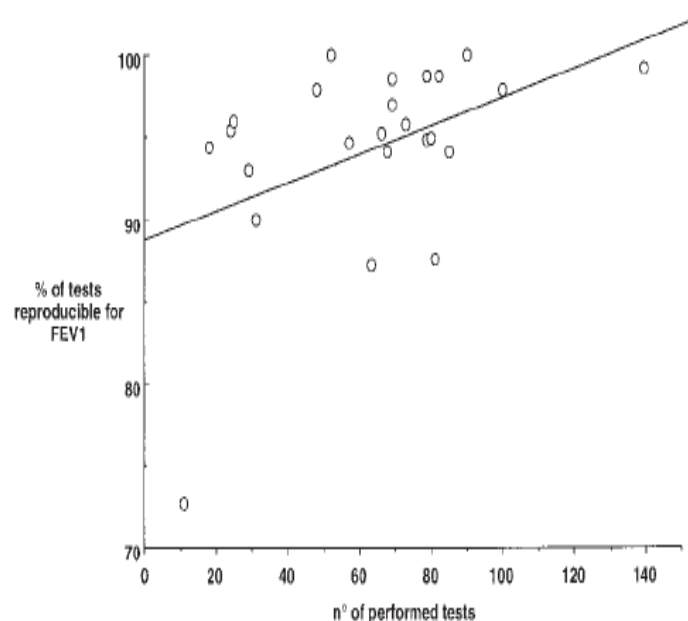


Figure 2. Representation of the cumulative number of reproducible (solid circles) and non-reproducible (open triangles) tests during the 20-mo study period. A significant trend to improvement was demonstrated (χ^2 for trends, $p < 0.05$).





Altre esperienze confermano le conclusioni del SaRA

Repeatability of Spirometry in 18,000 Adult Patients

Paul L. Enright, Kenneth C. Beck, and Duane L. Sherrill

“Patient characteristics, such as sex, age, height, smoking status, and FEV1 (% predicted), had very little effect on repeatability, explaining only 2 to 4% of the variation in repeatability (expressed in milliliters). We conclude that the ability of patients to meet or exceed spirometry repeatability goals does not depend on patient characteristics when testing is performed by experienced personnel.”



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Let's not forget: the GOLD criteria for COPD are based
on
post-bronchodilator FEV1

P.J. Sterk

Eur Respir J 2004; 23: 497–498

“The distinction of pre- and post-bronchodilator spirometry may not merely be a methodological detail. Is there not a good chance that the use of pre-bronchodilator FEV1/FVC values for the definition of COPD leads to potential overdiagnosis and over-estimation of the severity of this disease?”



α

ECSC

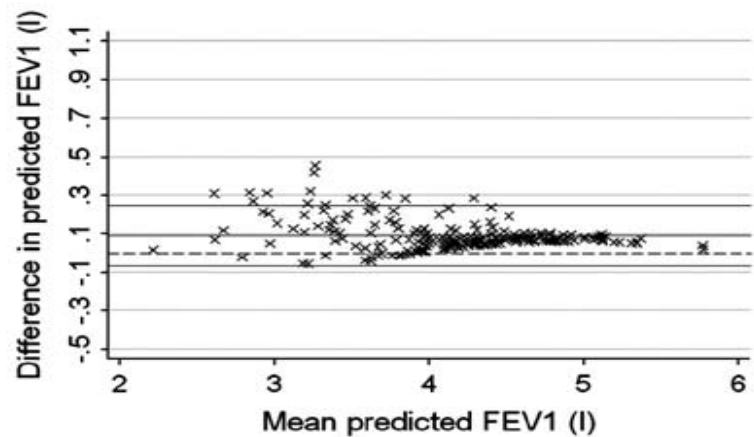
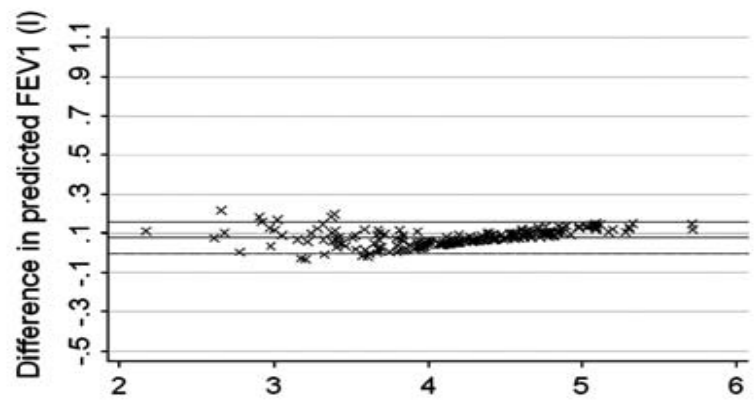
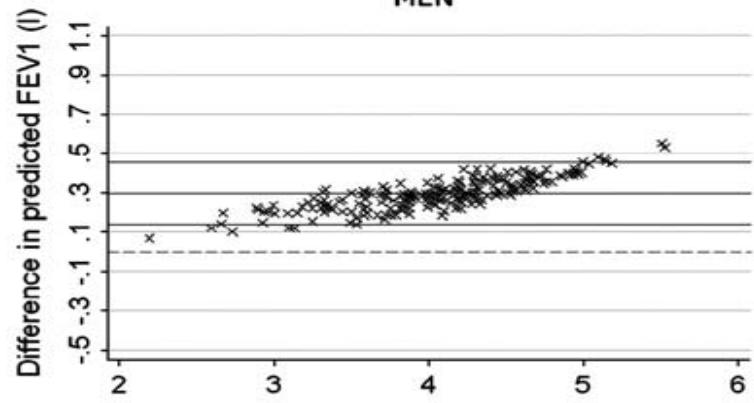
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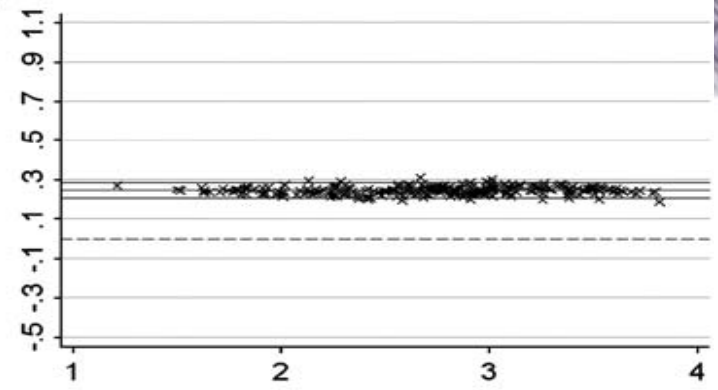
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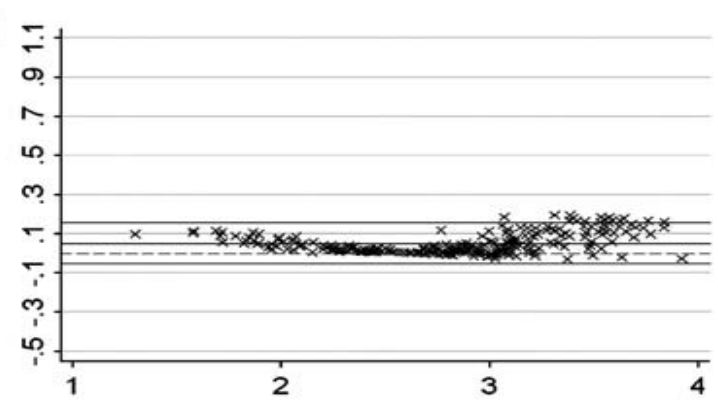


WOMEN

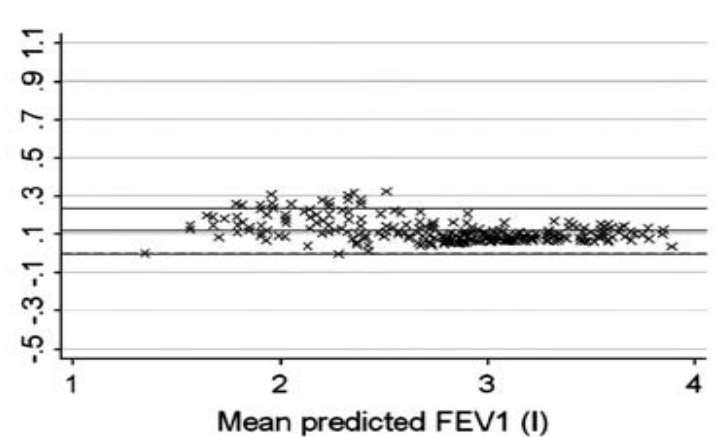
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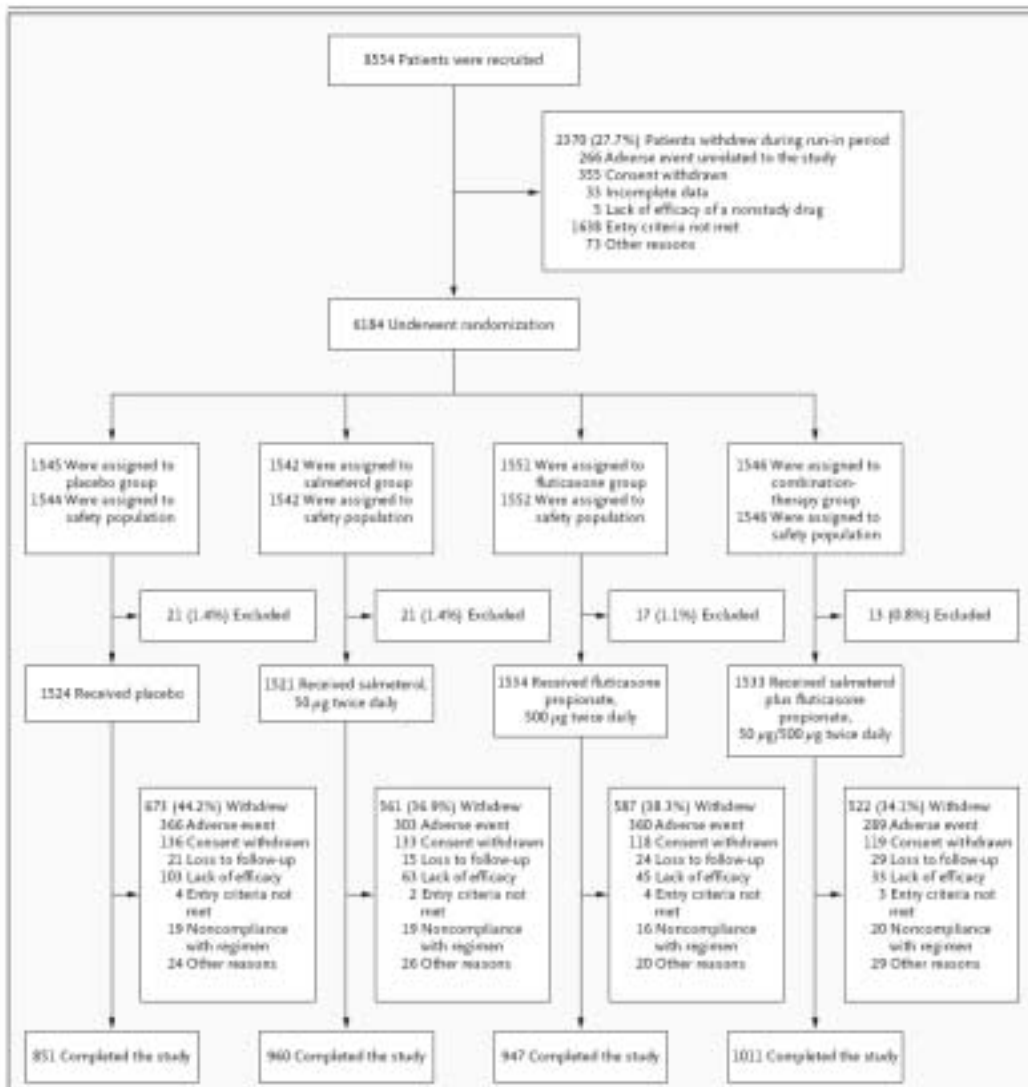


Conseguenze della mancata esecuzione della spirometria

- I grandi trial farmacologici escludono o superselezionano gli anziani.
- Negli studi epidemiologici il ruolo prognostico del deficit ventilatorio è spesso ignorato.
- Le linee guida terapeutiche basate su classificazioni di gravità non trovano applicazione nell'anziano fragile.
- Scarsa conoscenza del declino età-correlato della funzione respiratoria

Un esempio di scarsa rappresentatività: Gli steroidi in via inalatoria (RCT)

| | CCHS | Euroscop | Isolde | LHS | TORCH |
|------------|-----------|-----------|-----------|-----------|-----------|
| Numero | 290 | 1277 | 990 | 1116 | 6112* |
| <u>Età</u> | <u>59</u> | <u>53</u> | <u>64</u> | <u>56</u> | <u>65</u> |
| FEV1 % | 86 | 77 | 50 | 64 | 44 |
| Revers. | 6.5 | 2.9 | 4.4 | 6.6 | 3.7 |



Esclusi
Torch 28%

Esclusi
Uplift 25%



Anche omettere la diagnosi di pneumopatia
restrittiva non è insignificante (SaRA Respir Med 2008;
102: 1349-1354)

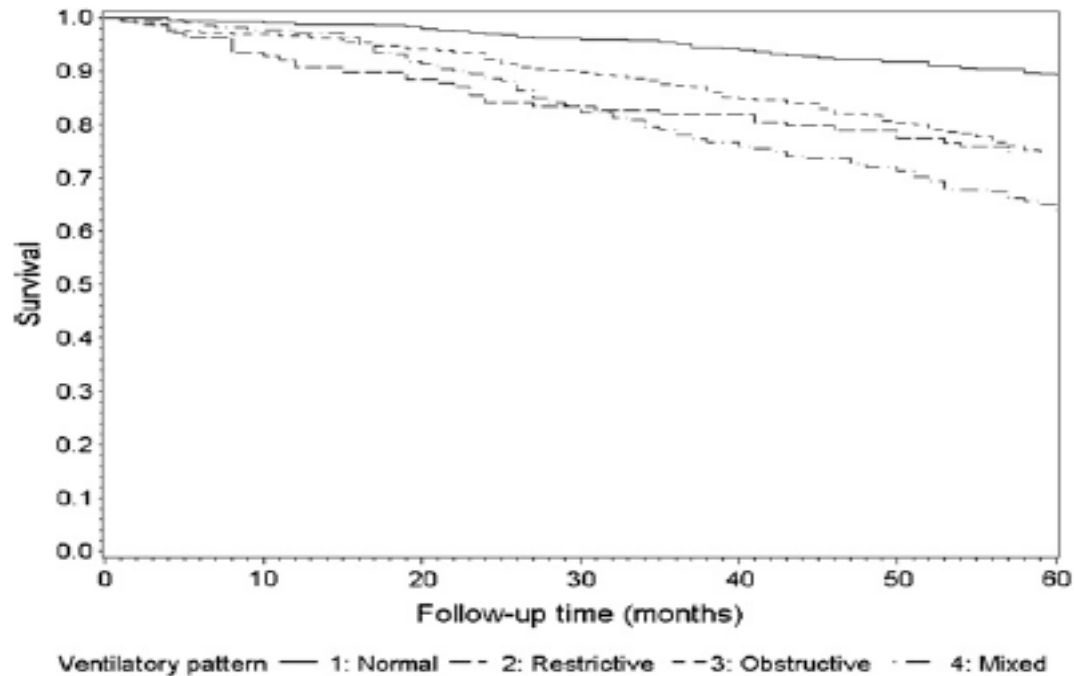


Figure 1 Survival of people with normal, restrictive, obstructive and mixed spirometric pattern.



Terapia della BPCO in base allo stadio: spirometria-dipendente

I: Lieve

II: Moderato

III: Grave

IV: Molto Grave

- $VEMS/CVF < 0.7$
- $VEMS \geq 80\%$ del predetto

- $VEMS/CVF < 0.7$
- $50\% \leq VEMS < 80\%$ del predetto

- $VEMS/CVF < 0.7$
- $30\% \leq VEMS < 50\%$ del predetto

- $VEMS/CVF < 0.7$
- $VEMS < 30\%$ del predetto
o $VEMS < 50\%$ del predetto più insufficienza respiratoria cronica

Riduzione attiva dei fattori di rischio; vaccinazione antinfluenzale, vacc. anti-pneumococcica

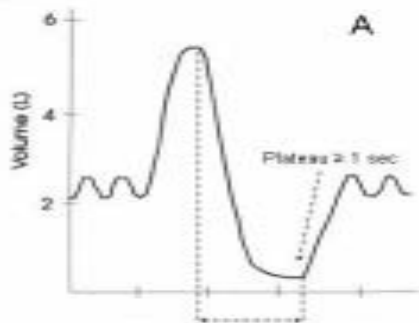
Aggiungere broncodilatatori a breve durata d'azione (quando necessario)

Aggiungere un trattamento regolare con broncodilatatori a lunga durata d'azione (quando necessario); **Aggiungere** riabilitazione

Aggiungere glucocorticosteroidi inalatori in caso di ripetute riacutizzazioni

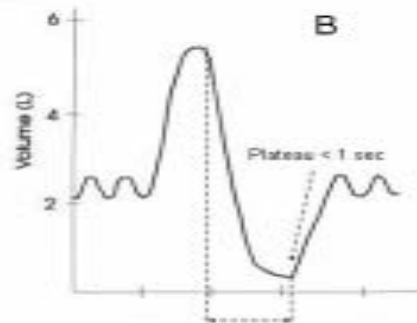
Aggiungere ossigenoterapia a lungo termine in caso di insufficienza respiratoria **Prendere in considerazione** la terapia chirurgica

Servono quindi misure spirometriche “per anziani fragili”



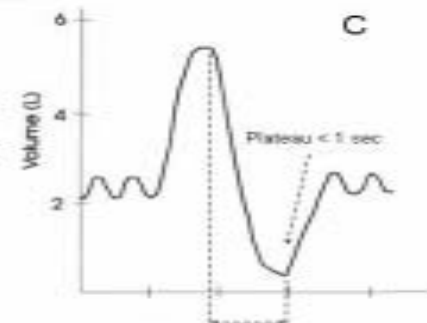
Forced expiratory time ≥ 6 sec

FVC: measurable
FEV6: measurable
SFVC: measurable



Forced expiratory time ≥ 6 sec

FVC: not measurable
FEV6: measurable
SFVC: measurable



Forced expiratory time < 6 sec

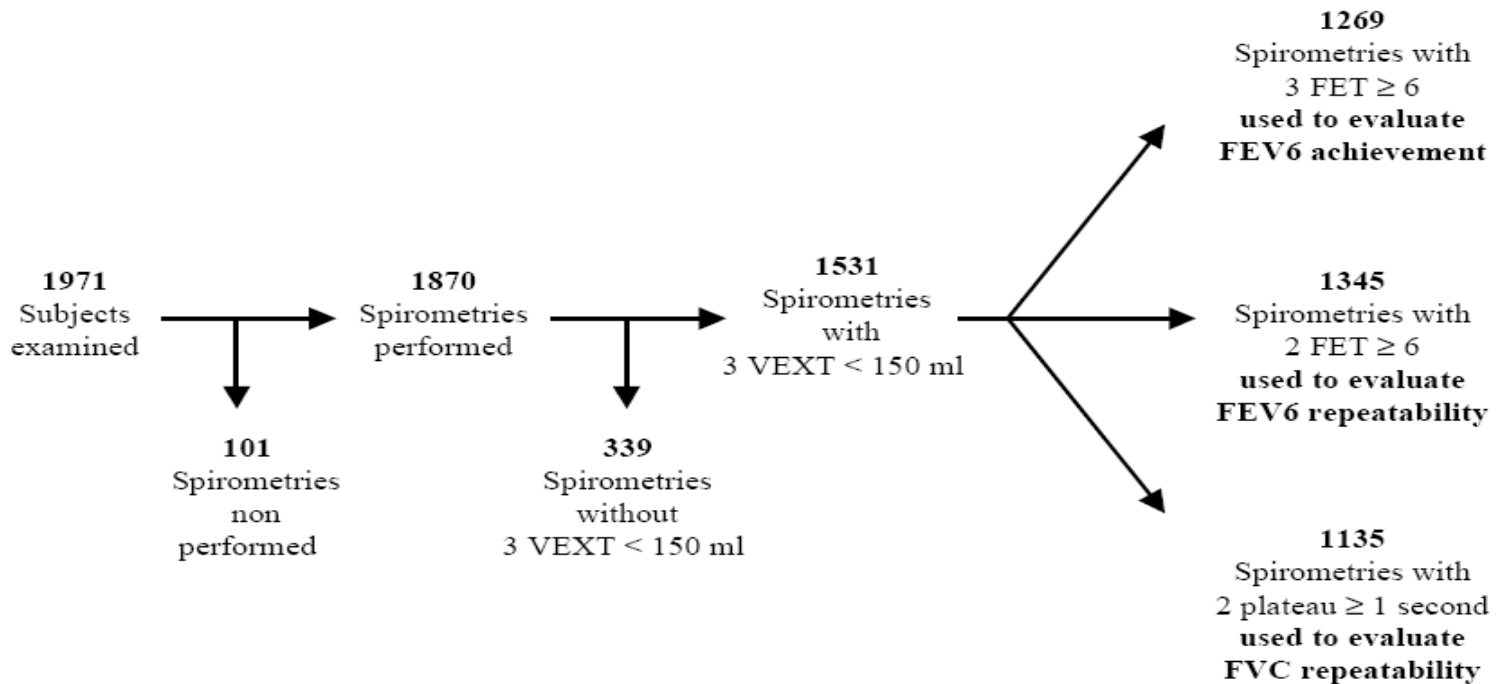
FVC: not measurable
FEV6: not measurable
SFVC: measurable



Il FEV6: molto più che una promessa

- Predice il declino della funzione respiratoria nei fumatori (Enright R. L. *Respir Med* 2002;96:444)
- E' un valido surrogato di FVC per la diagnosi di ostruzione e restrizione (Swanney M. P. *Am J Respir Crit Care Med* 2000;162:917)
- Ne esistono valori di riferimento su alcune popolazioni (Hankinson J. L. *Chest* 2003;124:1805; Garcia-Rio F. *Eur Respir J* 2004;24:397)

..ma anche il FEV6 non è per tutti (SaRA, Thorax 2008;
63: 60-66)



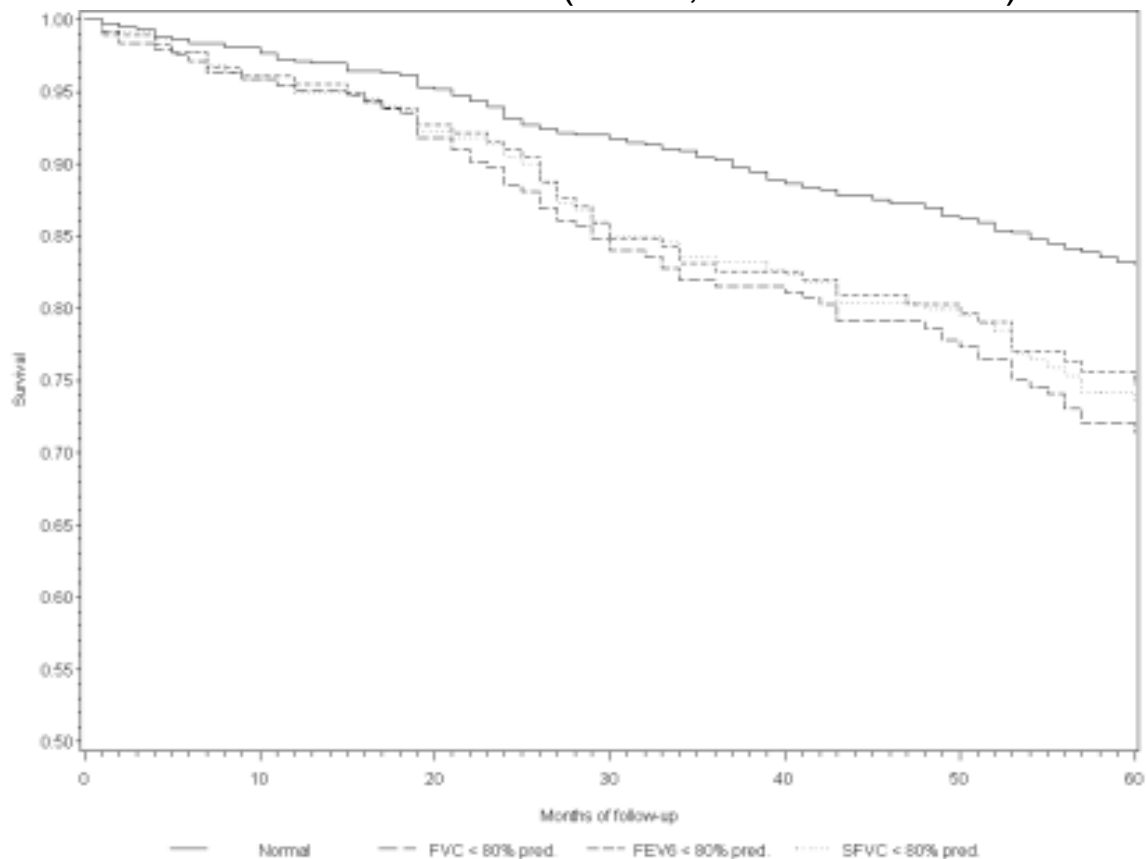
Chi non riesce a conseguire il FEV6 (SaRA, Thorax 2008; 63: 60-66)

Table 3 - *Factors negatively influencing FEV6 achievement. Multivariable logistic analysis on 1531 subjects with a satisfactory start of test.*

| | Odds ratio | P value | 95% confidence interval |
|----------------------------------|------------|---------|-------------------------|
| Older age (for 5 year) | 1.42 | < 0.001 | 1.25 – 1.59 |
| Female sex | 1.58 | 0.022 | 1.08 – 2.31 |
| Lower education * | 1.77 | 0.001 | 1.25 – 2.51 |
| Depression † | 1.54 | 0.045 | 1.12 – 2.13 |
| Cognitive impairment ‡ | 1.61 | 0.009 | 1.09 - 2.37 |
| Spirometric restriction § | 1.98 | < 0.001 | 1.37 – 2.86 |

Also corrected by smoking habit, Barthel index and 6-Minute Walking Test,

La “sFVC” (s=surrogate) può essere la soluzione? (SaRA, in elaborazione)



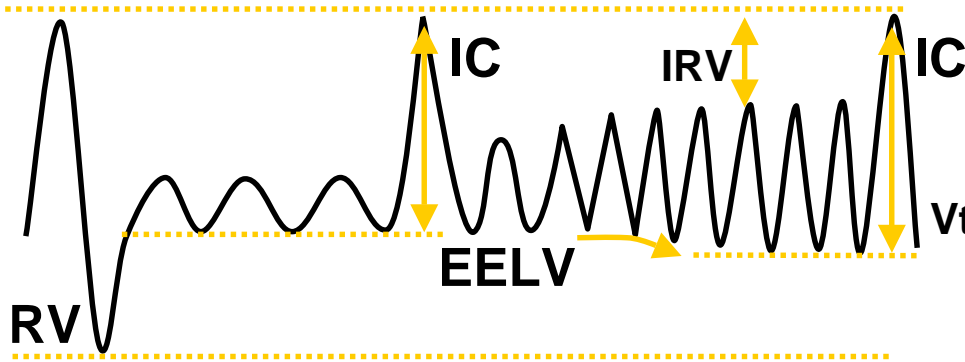


Indici di limitazione al flusso espiratorio

- Correlano con la gravità della dispnea da sforzo
- Aggiungono a FEV1 e FVC un elemento interpretativo della sintomatologia
- Non sostituiscono FEV1 e FVC a scopo diagnostico

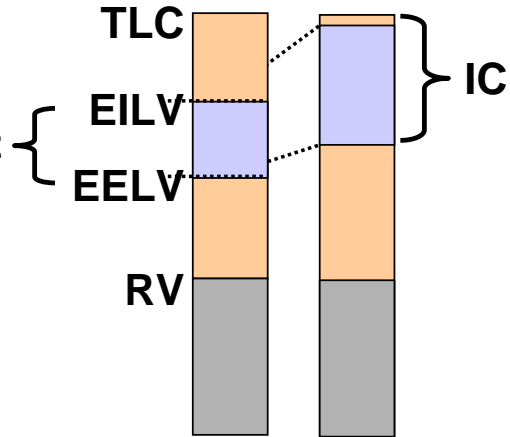
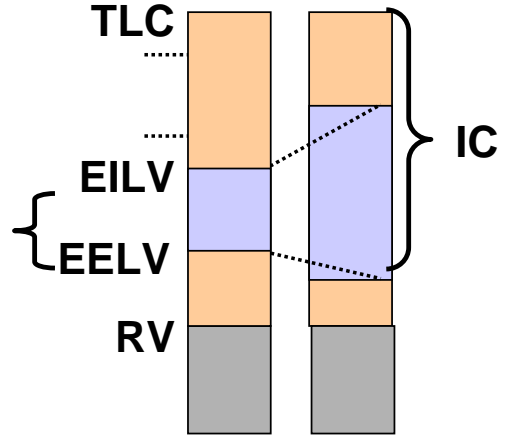
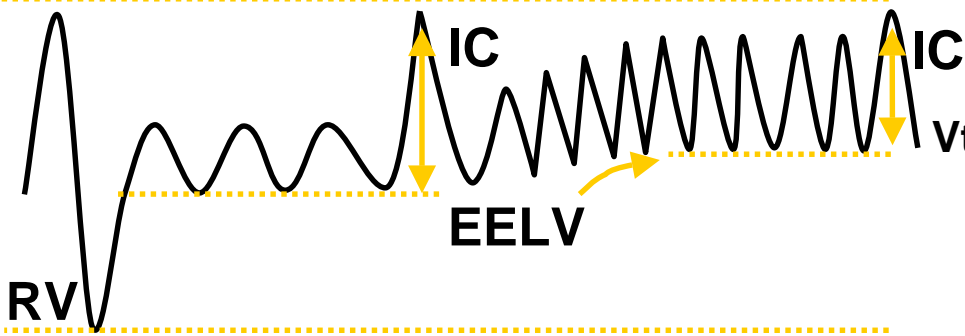
TLC Lung Volume Response to Exercise

Health



TLC

COPD

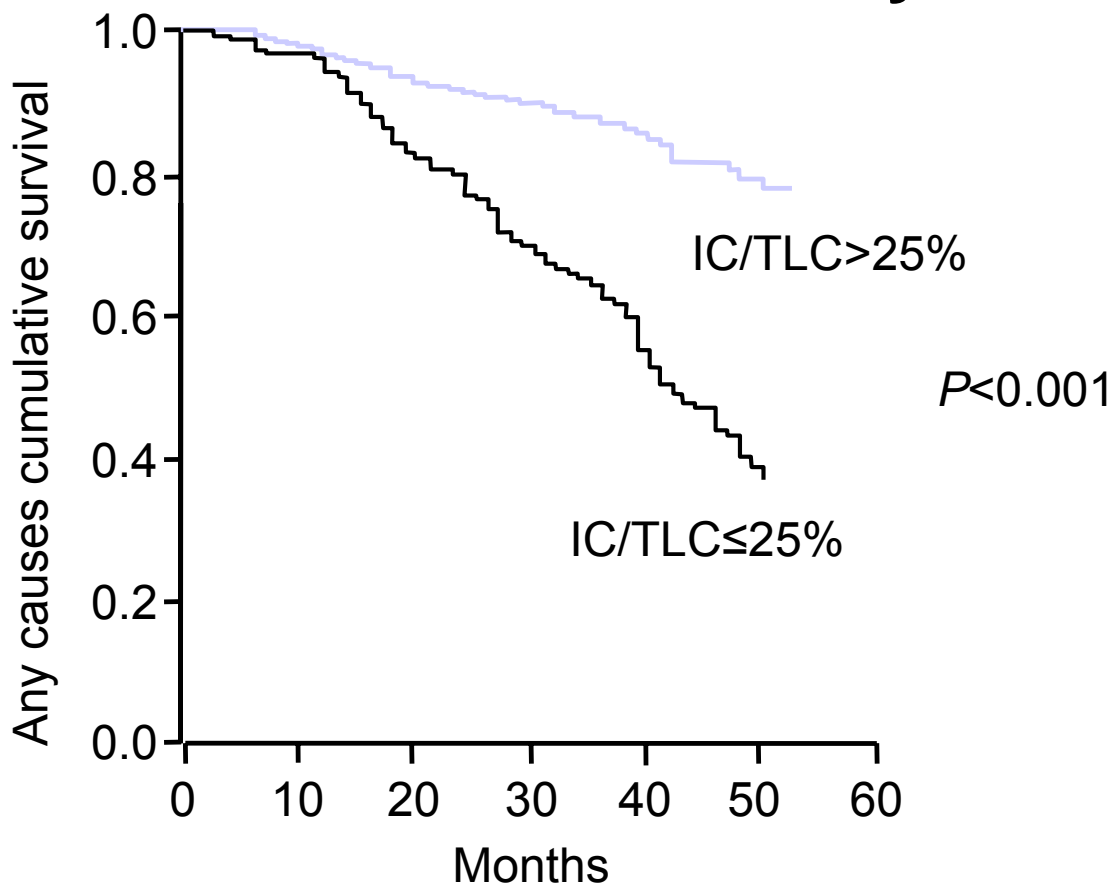


Rest Exercise

IRV=inspiratory reserve volume.

Cooper et al. *Am J Med.* 2006;119:S21-S32 (A).

IC/TLC and mortality



NEP: diagnostica limitazione al flusso e null'altro

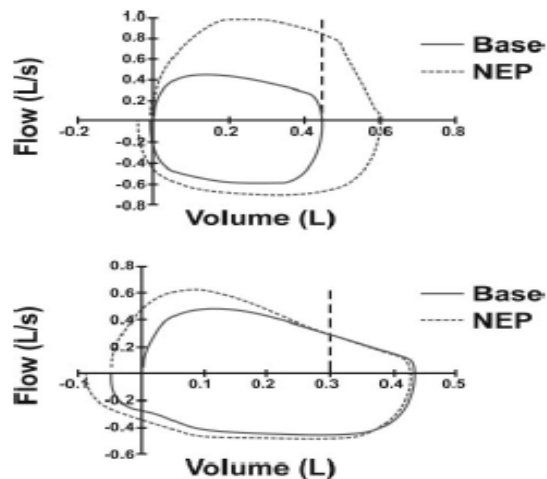
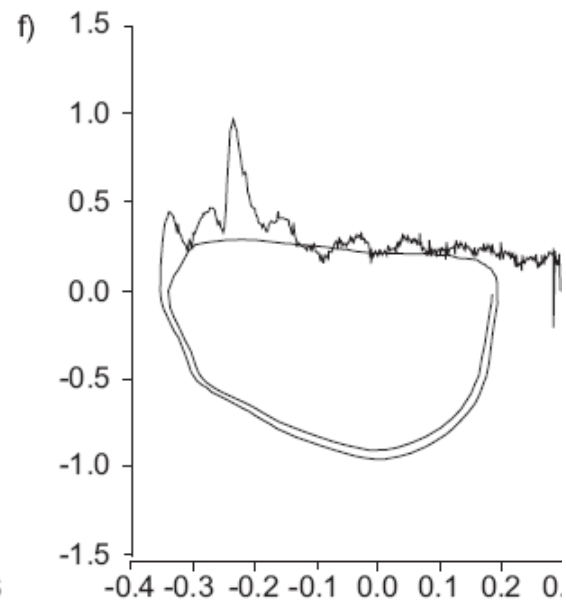
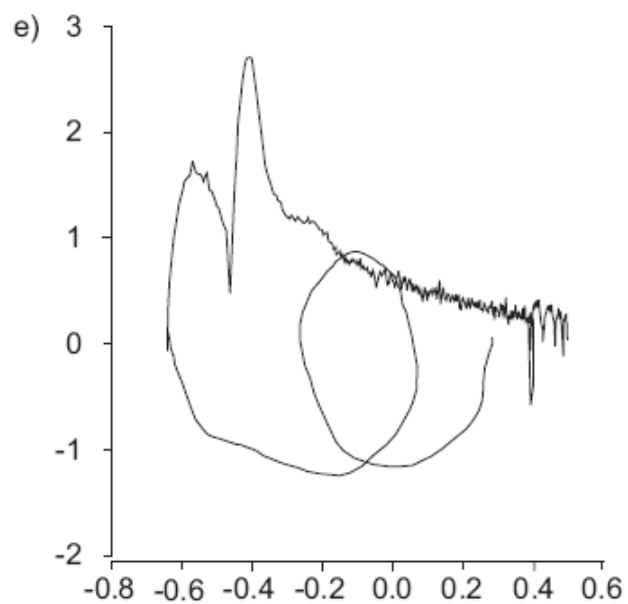
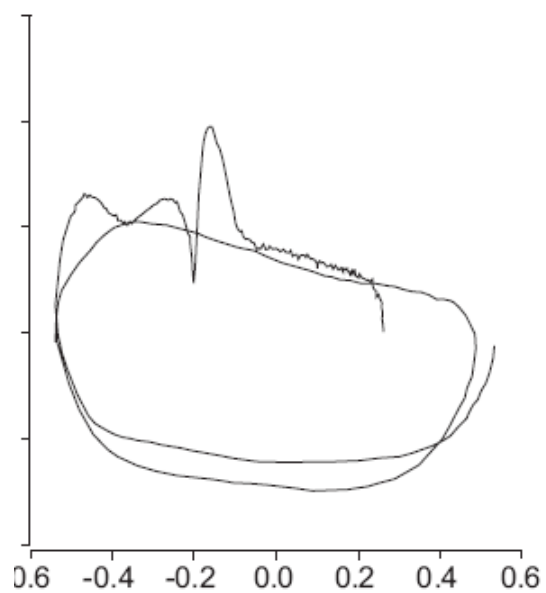
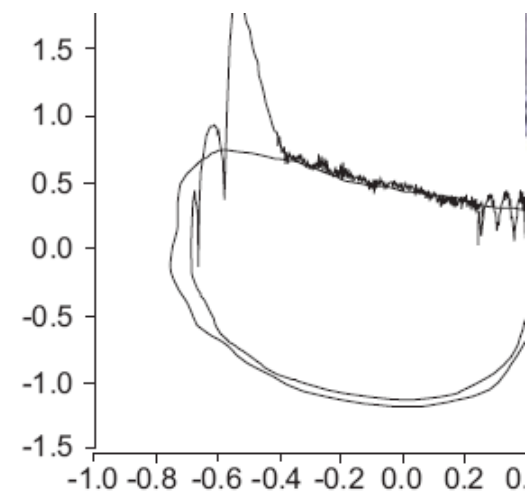
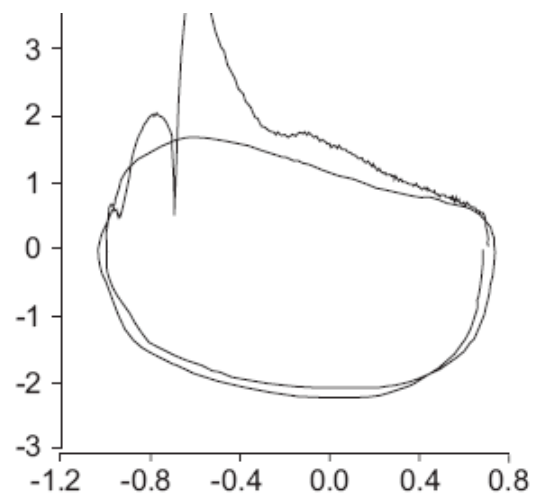
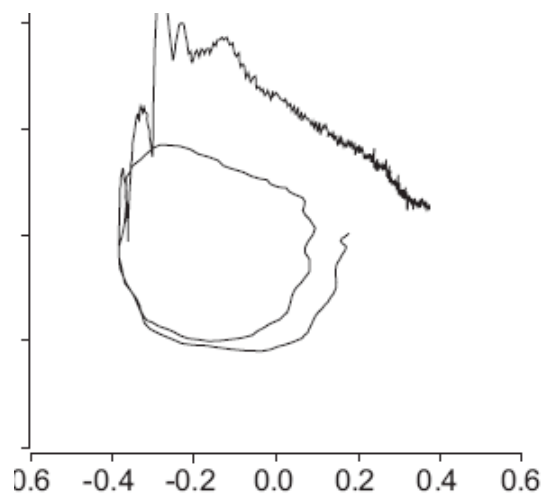


FIGURE 1. NEP technique in representative subjects without EFL (*top*) and with EFL (*bottom*).



Volume L

Volume L

Volume L

FIG 2. a, b and c): Representative examples of flow-volume loops during negative expiratory pressure (NEP) manoeuvre for a) non-flow-limited, b) partially flow-limited, and c) flow-limited conditions.



Diagnosi di BPCO nell'anziano: prospettive

Integrazione tra clinica e funzione respiratoria

Profilo di rischio

Clinica: selezione di sintomi e segni tipici

Spirometria: ricerca di parametri convenienti (FEV6, forse "sFVC")

Analisi del modello ventilatorio: rapporto T_e/T_{tot} basale e sotto sforzo