Early diagnosis of Late Onset Pompe Disease in patients with respiratory failure (PneumoLoped Study preliminary data)

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Background

Late Onset Pompe Disease (LOPD) is a metabolic, autosomal recessive disease due to a reduced functionality of protein α-glucosidase (GAA), which leads to an accumulation of glycogen in skeletal muscle tissue and in other organs. 70% of LOPD patients develops progressive respiratory failure (RF) with vital capacity reduction and risk of mechanical ventilation.
Recent data suggest the importance of an early LOPD diagnosis.

Objectives

- Prevalence of LOPD suspect in patients with respiratory failure
- Optimize the diagnostic process in pulmonology units, encouraging early diagnosis

Methods

- Real-life study, conducted in 18 Pulmonology Italian Centers (Fig. 1), aimed to enroll 500 adult patients with unexplained RF and follow the diagnostic algorithm for suspected LOPD (Fig. 2a-2b)
- For each patient, clinicians collected a drop of blood on Dried Blood Spot (DBS) for the measurement of GAA, executed in a centralized laboratory
- Muscular disability was assessed with Walton Gardner Medwin Scale (WGMS).

Fig. 1 – Centers distribution

Fig. 2a - LOPD diagnostic algorithm (1)

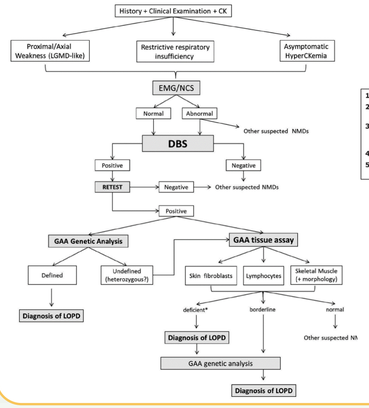
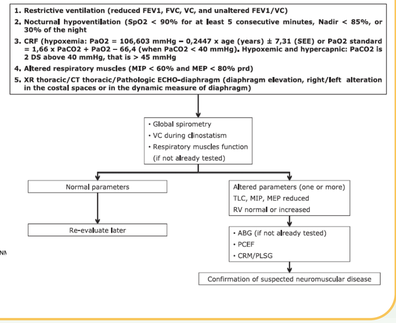


Fig. 2b - Diagnostic flow chart to confirm the diagnosis of LOPD on the basis of different respiratory dysfunctional patterns (2)



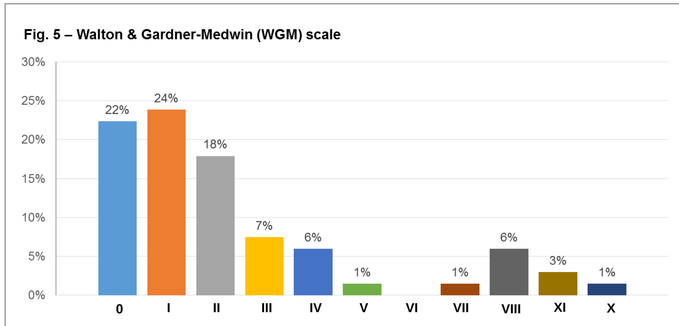
Preliminary Results

PneumoLoped started in February 2015 (enrollment is ongoing). **67 patients have been enrolled at the date of this analysis** (characteristics in Table 1 and Fig. 3-7):

- 43% acceded for respiratory reasons
- 45% was hospitalized and 33% needed mechanical ventilation
- Hyperckemia was reported in 39% of patients
- The majority of cases (78%) presented a WGMS between 0 and 5

Table 1 – Patients characteristics (n. 67) [*m.s. = missing data*]	
Gender (n, %)	M: 41 (61%), F: 26 (39%)
Age, Y (mean±sd)	59±18
NM Family history (n, %)	3 (4%)
FEV1 % pred (n,%)	normal: 25 (37%); low: 33 (49%); *14% m.s.*
FEV1/VC% (n,%)	normal: 40 (60%); low: 16 (24%); *16% m.s.*
MIP (n,%)	normal: 5 (7%); low: 41 (61%); *32% m.s.*
MEP (n,%)	normal: 12 (18%); low: 34 (51%); *31% m.s.*
SpO2 (n,%)	>30% of night time < 90%: 11 (16%); at least 5 min <90%: 16 (24%); at nadir <85%: 2 (3%); *57% m.s.*
PaO2 (n,%)	normal: 22 (33%); hypoxemia: 31 (46%); respiratory failure: 4 (6%); *15% m.s.*
PaCO2 (n,%)	normal: 29 (43%); hypocapnia: 7 (10%); hypercapnia: 21 (31%); *16% m.s.*
PH (n,%)	compensated: 48 (72%); alkalosis: 6 (9%); acidosis: 3 (4%); *15% m.s.*
Bicarbonates (n,%)	normal: 29 (43%); low: 3 (4%); high: 23 (34%); *19% m.s.*
CK (n,%)	≤ 195: 21 (31%); >195: 26 (39%); *30% m.s.*

Fig. 5 – Walton & Gardner-Medwin (WGM) scale



Grade 0 = all activities normal
Grade I = normal gait, unable to run freely, myalgia, atrophy
Grade II = unable to walk on tiptoes, waddling gait
Grade III = evident muscle weakness, stepping gait, climbing stairs with banister
Grade IV = difficulty in rising from the floor, presence of Gowers' sign
Grade V = unable to rise from the floor
Grade VI = unable to climb stairs
Grade VII = unable to rise from a chair
Grade VIII = unable to walk without assistance
Grade IX = unable to eat, drink or sit unassisted
Grade X = respiratory muscles compromised, tetraplegic

Fig. 7 - Other diaseases

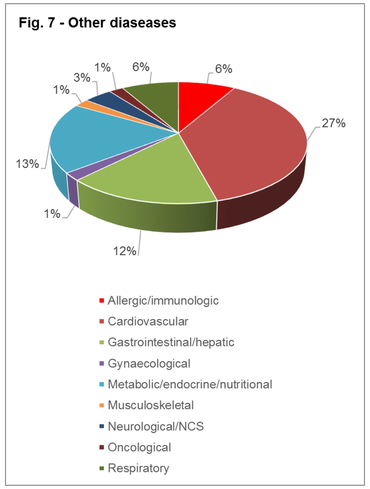


Fig. 3 – Cause of visit

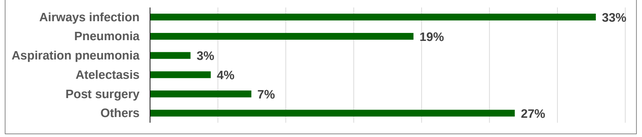


Fig. 4 – Patient access

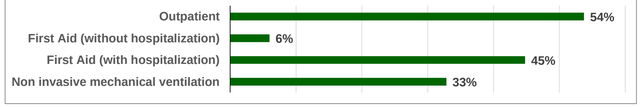
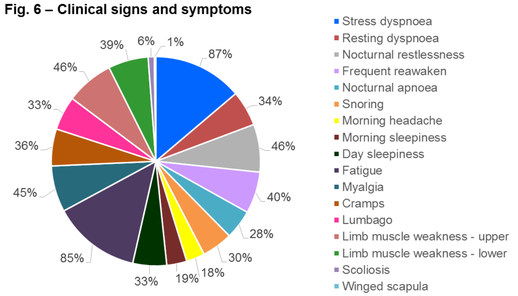


Fig. 6 – Clinical signs and symptoms



GGA Activity measurements

- **66 blood samples** has been collected on DBS (1 is going to be collected)
- **64 has been already analyzed** in a centralized laboratory through *tandem mass spectrometry*

Results:

- 63 cases resulted negative [>1,86 micromol/L/h]
- **1 subject resulted positive** [0,48 micromol/L/h at first test; 0,36 micromol/L/h at second test]

Conclusions

PneumoLoped could provide original data to better highlight the role of pulmonologists in the management of acute respiratory failure associated to neuromuscular diseases, and in the assistance of subjects with genetic rare disorders such as Late onset Pompe Disease.

References

(1) Toscano A, Montagnese F, Musumeci O. ***Early is better? A new algorithm for early diagnosis in Late Onset Pompe Disease (LOPD)*** Acta Myologica 2013; XXXII: 78-81

(2) Ambrosino N, Confalonieri M, Crescimanno G et Al. ***The role of respiratory management of Pompe disease.*** Respiratory Medicine 2013; 107: 1124-1132