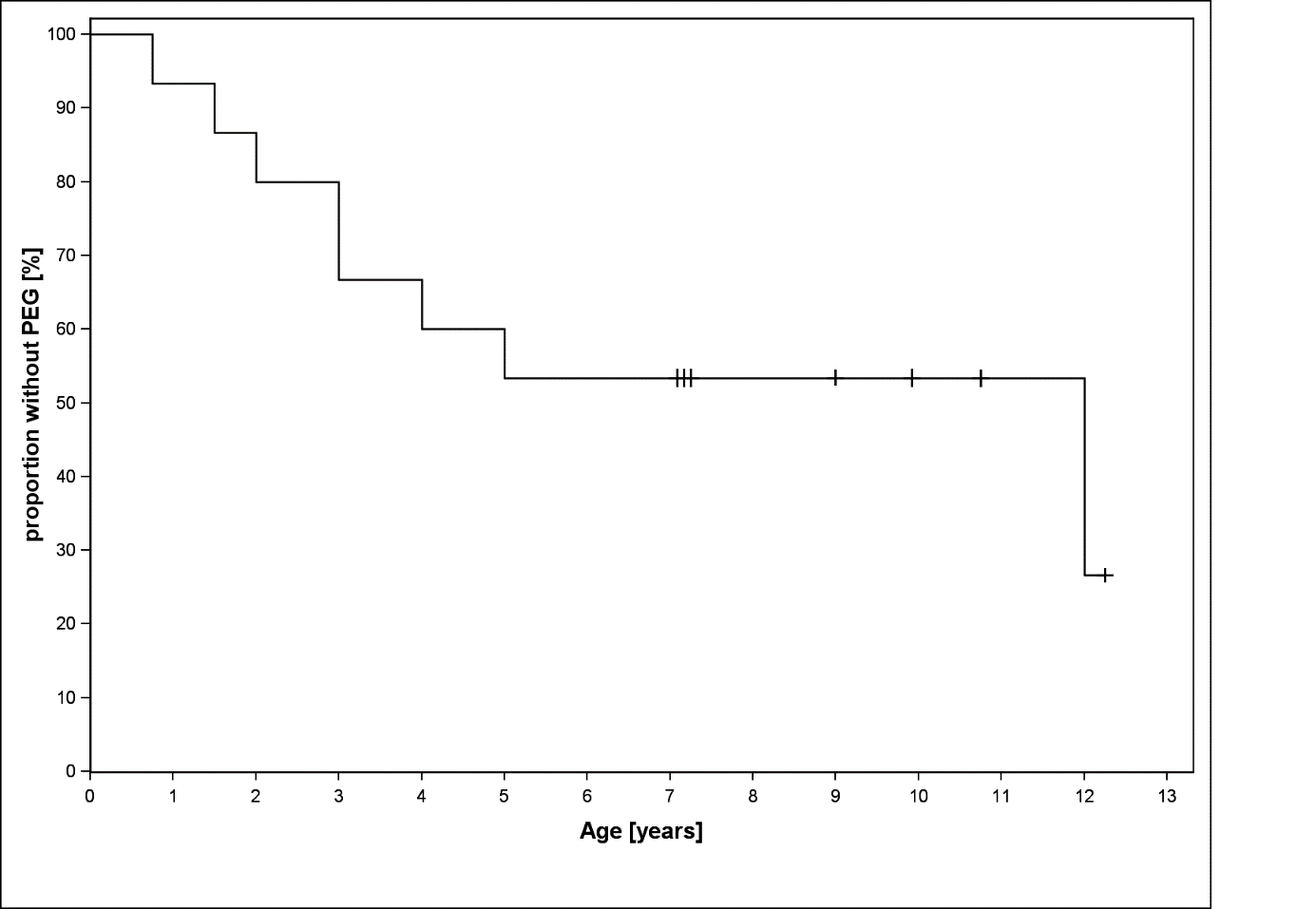


**Supplemental Figure 1 A*:*** Ventilator-free survival of 15 IOPD patients



**Supplemental Figure 1 B:** Gastrostomy-free survival in 15 IOPD patients

**Supplemental Table 2:** Results of the standardized scoring of magnetic resonance imaging abnormalities in patients with IOPD

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Patient | Age | PWM centrum semiovale | PWM frontal/ occipital | Corpus callosum | PLIC | ALIC | External capsule | Sub-cortical | U-fibres | Decus-satio | Cortico-spinal | Widened lateral ventricle | Widened 4th ventricle | Basal ganglia |
| 11 | 1.1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6 | 1.7 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 1.9 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 11 | 2.1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 3.0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6 | 3.2 | 2 | 2 | 1 | 1 | 1 | 2 | 2 | 0 | 1 | 2 | 0 | 0 | 0 |
| 3 | 3.6 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| 4 | 3.11 | 2 | 2 | 1 | 2 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 0 |
| 15 | 4.0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 11 | 7.3 | 2 | 2 | 1 | 2 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| 11 | 8.2 | 2 | 2 | 2 | 2 | 0 | 2 | 1 | 0 | 0 | 0 | 1 | 1 | 1 |
| 10 | 9.2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

The shades of grey reflect the severity of involvement: from light (restricted, stage 1) to dark (widespread, stage 3). 0 = normal, 1 = slightly abnormal, 2 = abnormal. PWM, periventricular white matter; PLIC, posterior limb of internal capsule; ALIC, anterior limb of internal capsule.

MRI white matter changes in: **stage 0**: none, **stage 1**: supratentorial region: frontal and occipital periventricular white matter, centrum semiovale, corpus callosum, external capsule, posterior and anterior limb of the internal capsule; **stage 2**: subcortical white matter and U-fibres; **stage 3**: infratentorial region: decussation and cortical spinal tract at the brain-stem level

**Supplemental Table 3:** Motor milestones and ventilator status in relation to dosage regimen for 15 patients with IOPD

|  |  |  |
| --- | --- | --- |
| **Treatment regimen** | **Loss of previously acquired motor milestones** | **Respiratory deterioration with need for ventilation** |
| Standard dosage (n = 4) | 3 (75%) | 3 (75%) |
| Intermediate dosage (n = 4) | 2 (50%) | 2 (50%) |
| High dosage (n = 7) | 0 (0%) | 0 (0%) |