**Pre-existing Neurocognitive Disorder (NCD)**

Before surgery, all patients performed a neuropsychological test battery consisting of paper-based (among others: Trail-Making-Test (TMT) Part B, Grooved Pegboard Task (GPT)) and computerized subtests (CANTAB, Cambridge Cognition Ltd., UK: among others: Paired Associates Learning (PAL), Verbal Recognition Memory (VRM)). Furthermore, we preoperatively assessed the Instrumental Activities of Daily Living (IADL) (1), the Geriatric Depression Scale (GDS) (2, 3) and the health status instrument EQ5D (4).

For these four test parameters, a composite score was calculated and compared to the corresponding mean baseline value of an age-matched non-surgical control group. Neurocognitive disorder (NCD) was defined following the 5th edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-5) definition (5) of the American Psychiatric Association for neurocognitive disorders.

**Mild NCD** was classified as:

1. Cognitive Test performance lies 1-2 standard deviations (SD) below controls in composite score of PAL first trial memory score, VRM delayed recognition, GP time dominant hand and TMT-B time
2. AND cognitive concern
3. AND lack of functional impairment

OR

1. Cognitive Test performance is ≥ 2 SD below controls in composite score of PAL first trial memory score, VRM delayed recognition, GP time dominant hand and TMT-B time
2. AND lack of cognitive concern
3. AND lack of functional impairment

**Major NCD** was classified as:

1. Cognitive Test performance impaired ≥ 2 SD below controls in summary score of PAL first trial memory score, VRM delayed recognition, GP time dominant hand and TMT-B time
2. AND functional impairment (irrespective of cognitive concern).

Cognitive concern was defined as present if item 10 of the GDS was positive (2, 3). Functional impairment was defined as present if there was an interference with independence in everyday activities (impairment in IADL: < 8 points (1) AND/*OR* impairment in usual activities of the EQ5D (4)).

**Frailty Status**

The Frailty Phenotype is based on the Fried Criteria (6). Five criteria were considered: weight loss, exhaustion, low physical activity, muscle weakness and slow gait speed. A patient was classified as frail if at least three criteria were met and as pre-frail if one or two criteria were met.

**Weight loss** was defined as either > 3 kilograms (kg) within the last 3 months (according to Mini Nutritional Assessment (MNA) Question B (7)) OR ≥ 5% of body weight within the last year (according to Study of Osteoporotic Fractures (SOF) index (8)).

**Exhaustion** was either indicated through the SOF index OR question 13 of the GDS (both surrogates).

**Low Physical Activity** was defined as < 15 points on item 6 of the Barthel Index (9-11).

**Muscle Weakness** was defined through handgrip strength (HGS). The cutoffs are based on sex and body mass index (6), scoring the average of three trials from the dominant hand (if information was available, otherwise the best mean value left or right was used).

Male: Female:

BMI ≤24: ≤29 kg BMI ≤23: ≤17 kg

BMI 24.1-26: ≤30kg BMI 23.1-26: ≤17.3kg

BMI 26.1-28: ≤30 kg BMI 26.1-29: ≤18 kg

BMI >28: ≤32kg BMI >29: ≤21kg

BMI: Body-Mass-Index

**Impairment of Gait Speed** was defined as slowness in Timed-Up and Go (TUG) test (cut-off ≥ 10 seconds (12)).

Table S1: Overview over surgical sites of the surgical procedures (n=838)

|  |  |
| --- | --- |
| **Surgical Site** | **Frequency (Percentage)** |
| Nervous System | 41 (4.9%) |
| Endocrine Glands | 10 (1.2%) |
| Eyes | 31 (3.7%) |
| Ears | 8 (1%) |
| Nose and the Paranasal Sinuses | 15 (1.8%) |
| Face and in the Oral Cavity | 22 (2.6%) |
| Pharynx, Larynx and Trachea | 5 (0.6%) |
| Lung and Bronchus | 19 (2.3%) |
| Heart | 42 (5%) |
| Blood Vessels | 15 (1.8%) |
| Lymphatic Vessels | 19 (2.3%) |
| Digestive Tract | 155 (18.5%) |
| Urinary Organs | 47 (5.6%) |
| Male Genital Organs | 52 (6.2%) |
| Female Genital Organs | 51 (6.1%) |
| Jaw and Craniofacial Bone | 14 (1.7%) |
| Locomotor System Organs | 233 (27.8%) |
| Mamma | 11 (1.3%) |
| Skin and Underlying Tissue | 17 (2%) |
| Diagnostic Procedures (in general anesthesia) | 26 (3.1%) |

Table S2: Frequency of Groups of Substances of preoperative long-term medication (n=751).

|  |  |  |  |
| --- | --- | --- | --- |
| **Number** | **Group** | **n** | **%** |
| 0 | others | 32 | 0.8 |
| 1 | stomatological preparations | 4 | 0.1 |
| 2 | drugs for acid related disorders | 263 | 6.8 |
| 3 | drugs for functional gastrointestinal disorders | 11 | 0.3 |
| 4 | bile and liver therapy | 9 | 0.2 |
| 5 | drugs for constipation | 29 | 0.8 |
| 6 | antidiarrheals | 18 | 0.5 |
| 7 | digestives | 18 | 0.5 |
| 8 | drugs used in diabetes | 236 | 6.1 |
| 9 | vitamins | 72 | 1.9 |
| 10 | mineral supplements | 4 | 0.1 |
| 11 | antithrombotic agents | 371 | 9.6 |
| 12 | antihemorrhagics | 2 | 0.1 |
| 13 | antianemic preparations | 30 | 0.8 |
| 14 | cardiac therapy | 74 | 1.9 |
| 15 | antihypertensives | 29 | 0.8 |
| 16 | diuretics | 262 | 6.8 |
| 17 | beta blocking agents | 318 | 8.3 |
| 18 | calcium channel blockers | 163 | 4.2 |
| 19 | agents acting on the renin-angiotensin system | 437 | 11.3 |
| 20 | lipid modifying agents | 288 | 7.5 |
| 21 | dermatologicals | 19 | 0.5 |
| 22 | sex hormones and modulators of the genital system | 12 | 0.3 |
| 23 | urologicals | 91 | 2.4 |
| 24 | pituitary and hypothalamic hormones and analogues | 5 | 0.1 |
| 25 | corticosteroids for systemic use | 46 | 1.2 |
| 26 | thyroid therapy | 137 | 3.6 |
| 27 | antibacterials for systemic use | 25 | 0.6 |
| 28 | antivirals for systemic use | 4 | 0.1 |
| 29 | antineoplastic and immunomodulating agents | 46 | 1.2 |
| 30 | antiinflammatory and antirheumatic products | 89 | 2.3 |
| 31 | antigout preparations | 73 | 1.9 |
| 32 | drugs for treatment of bone diseases | 16 | 0.4 |
| 33 | opioids | 110 | 2.9 |
| 34 | other analgesics and antipyretics | 58 | 1.5 |
| 35 | antiepileptics | 69 | 1.8 |
| 36 | anti-parkinson drugs | 43 | 1.1 |
| 37 | psycholeptics | 60 | 1.6 |
| 38 | psychoanaleptics | 67 | 1.7 |
| 39 | other nervous system drugs | 11 | 0.3 |
| 40 | drugs for obstructive airway diseases | 163 | 4.2 |
| 41 | antihistamines for systemic use | 4 | 0.1 |
| 42 | ophthalmologicals | 33 | 0.9 |

751 patients took a total of 3851 substances. These were divided into 43 groups of substances (according to Anatomical Therapeutic Chemical classification system). Data are expressed as frequencies (percentages) in relation to 3851 substances.

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