Supplement for Multiple Imputation

Following the reporting guidelines of Sterne et al. (2009) about missing data, we show here some important details about the missing data and the method to handle them:

* Number of missing values for each variable of interest:

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Mobilized Iron | Major Iron Overload | LII-MRI | LII-MRI=3.4 | LII-MRI=2 | Alcohol overconsumption | Sex | BMI | Age | C282Y homozygous |
| Number of Complete cases | 58 | 58 | 72 | 72 | 72 | 64 | 72 | 70 | 72 | 72 |
| Number Missing values | 14 | 14 | 0 | 0 | 0 | 8 | 0 | 2 | 0 | 0 |

In the analysis, 72 patients were included of which 59 received a treatment for iron depletion and 13 received a trial treatment. The mobilized iron is unknown for the 13 patients that received the trial treatment, and for 1 patient that received the treatment but died before reaching depletion. So, in total we have 14 missing values for mobilized iron and major iron overload.

* Number of cases with complete data: 51/72
* Differences between complete and incomplete data:

In bold are the variables for which there is a sizeable difference in mean/proportion between complete and incomplete cases.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | N | Mean | Std. Deviation |
| **LII-MRI** | **Complete Cases** | **51** | **3,1411** | **2,33671** |
| **Incomplete Cases** | **21** | **1,9716** | **1,61348** |
| BMI | Complete Cases | 51 | 26,7168 | 3,83384 |
| Incomplete Cases | 19 | 26,6423 | 3,81670 |
| Age | Complete Cases | 51 | 59,75 | 12,568 |
| Incomplete Cases | 21 | 58,95 | 11,630 |
| **how many phlebotomies in depletion phase** | **Complete Cases** | **50** | **1,98** | **4,967** |
| **Incomplete Cases** | **7** | **2,57** | **2,936** |
| **how much apheresis in depletion** | **Complete Cases** | **50** | **6,72** | **7,923** |
| **Incomplete Cases** | **7** | **1,29** | **1,380** |
| Haemoglobin | Complete Cases | 48 | 9,267 | ,7093 |
| Incomplete Cases | 21 | 9,152 | ,8710 |
| Cholesterol | Complete Cases | 40 | 5,127 | 1,3700 |
| Incomplete Cases | 18 | 4,878 | 1,3662 |
| Triglycerides | Complete Cases | 38 | 2,0595 | 2,02758 |
| Incomplete Cases | 16 | 1,7556 | ,99740 |
| **ferritin** | **Complete Cases** | **51** | **1287,71** | **1199,996** |
| **Incomplete Cases** | **21** | **1472,57** | **2496,970** |
| Length | Complete Cases | 51 | 1,7632 | ,10284 |
| Incomplete Cases | 19 | 1,7753 | ,10658 |
| Weight | Complete Cases | 51 | 82,9275 | 12,88815 |
| Incomplete Cases | 19 | 83,6316 | 10,85521 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | Success | N | Proportion |
| **LII-MRI=3.4** | **Incomplete Cases** | **4** | **21** | **,190** |
| **Complete Cases** | **20** | **51** | **,392** |
| **LII-MRI=2** | **Incomplete Cases** | **6** | **21** | **,286** |
| **Complete Cases** | **28** | **51** | **,549** |
| **Alcohol overconsumption** | **Incomplete Cases** | **2** | **13** | **,154** |
| **Complete Cases** | **1** | **51** | **,020** |
| Sex (Males) | Incomplete Cases | 15 | 21 | ,714 |
| Complete Cases | 36 | 51 | ,706 |
| **C282Y homozygous** | **Incomplete Cases** | **3** | **21** | **,143** |
| **Complete Cases** | **22** | **51** | **,431** |
| **Is depletion reached** | **Incomplete Cases** | **7** | **21** | **,333** |
| **Complete Cases** | **50** | **51** | **,980** |
| **Treatment for depletion (full treatment versus trial)** | **Incomplete Cases** | **8** | **21** | **,381** |
| **Complete Cases** | **51** | **51** | **1,000** |
| **Erythrocyte apheresis performed** | **Incomplete Cases** | **16** | **21** | **,762** |
| **Complete Cases** | **48** | **51** | **,941** |
| Metabolic Syndrome | Incomplete Cases | 3 | 15 | ,200 |
| Complete Cases | 6 | 37 | ,162 |
| **Diabetes Mellitus** | **Incomplete Cases** | **4** | **21** | **,190** |
| **Complete Cases** | **5** | **51** | **,098** |
| Hypertension | Incomplete Cases | 10 | 21 | ,476 |
| Complete Cases | 21 | 51 | ,412 |
| **Hyperlipidaemia** | **Incomplete Cases** | **5** | **18** | **,278** |
| **Complete Cases** | **7** | **43** | **,163** |
| **Steatosis** | **Incomplete Cases** | **6** | **17** | **,353** |
| **Complete Cases** | **19** | **38** | **,500** |
| **fibrosis/cirrhosis** | **Incomplete Cases** | **0** | **19** | **,000** |
| **Complete Cases** | **6** | **41** | **,146** |
| Death (yes) | Incomplete Cases | 1 | 21 | ,048 |
| Complete Cases | 3 | 51 | ,059 |

* Missing data method: Missing data were handled with multiple imputation
  + Software and key setting: SPSS version 28, using the full conditional specification approach. Predictive-mean matching was used for continuous variables, and logistic regression for categorical variables.
  + Imputation model: the variables included in the imputation model can be classified in three groups: (i) all the variables used in the logistic regression including the outcome variable (i.e., LII-MRI=3.4, BMI, sex, C282Y homozygous, and major iron overload, see Table 4, main text), (ii) all variables related to the depletion process (i.e., how many phlebotomies in depletion phase, how much apheresis in depletion, start and end ferritin levels, is depletion reached, treatment for depletion (i.e., full treatment versus trial), erythrocyte apheresis performed, mobilized iron in the treatment or in the trial treatment, death) because predictive of the missing values, and (iii) other patient’s characteristics where a sizeable difference between complete and incomplete cases was found (i.e., LII-MRI, alcohol overconsumption, diabetes, hyperlipidaemia, steatosis, fibrosis/cirrhosis, see Tables above). The following variables were treated only as predictors in the imputation model: LII-MRI, LII-MRI=3.4 and 2, age, C282Y homozygous, is depletion reached, sex, treatment for depletion, erythrocyte apheresis performed, diabetes, death). The other variables were both predictor and outcome. No interactions were included in the imputation model.
  + Number of imputed datasets: 30, since approximately 30% of the patients has missing data in the variables of interest.