**S3 Table 8.** Characteristics of severe lactic acidosis cases (lactate ≥5.0 mmol/l and pH <7.35) and matched controls

|  |  |  |
| --- | --- | --- |
| **Lactate ≥5.0****mmol/l** | **Cases** | **Controls** |
| **All** | (n=34) | (n=810) |
| **Age**, median (IQR) | 74 (70 - 83) | 74 (70 - 83) |
| **Gender** |  |  |
|  Male | 21 (61.8%) | 498 (61.5%) |
|  Female | 13 (38.2%) | 312 (38.5%) |
| **Use of metformin** |  |  |
|  Non-usea | 17 (50.0%) | 373 (46.0%) |
|  Recent useb | 4 (11.8%) | 43 (5.3%) |
|  Current usec | 13 (38.2%) | 394 (48.6%) |
| **Diabetes duration** |  |
|  0-1 years | 3 (8.8%) | 71 (8.8%) |
|  2-5 years | 11 (32.4%) | 156 (19.3%) |
|  6-9 years | 4 (11.8%) | 111 (13.7%) |
|  10+ year | 16 (47.1%) | 472 (58.3%) |
| **Charlson comorbidity index** |  |  |
|  0 | 12 (35.3%) | 490 (60.5%) |
|  1 | 3 (8.8%) | 120 (14.8%) |
|  ≥2 | 19 (55.9%) | 200 (24.7%) |
| **Laboratory values** |  |  |
| **eGFR**d,e, mean (SD) | 65.2 (26.8) | 69·0 (22.7) |
| **HbA1c**f.g, mean (SD) | 6.8 (0.8) | 6·9 (1.1) |

a. Non-use of metformin is “never use of metformin or occurrence of a metformin prescription dated more than 365 days before admission with lactic acidosis”.

b. Recent use of metformin is “occurrence of a metformin prescription in the past dated 91 to 365 days before admission with lactic acidosis”.

c. Current use is “occurrence of a metformin prescription within the past dated 90 days before admission with lactic acidosis”.

d. Three cases (8.8%) and 161 controls (19.9%) had a missing value for eGFR.

e. eGFR calculated by the MDRD fourmula.

f. Five cases (14.7%) and 157 controls (19.4%) had a missing value for HbA1c.

g. HbA1c (glycated hemoglobin), % of total hemoglobin.