

**Table W1.** Demographic Characteristics of 43 Patients with GERD Symptoms but Did Not Provide the Duration Information.

| Characteristics                                    | ≤55 Years ( <i>n</i> = 13) | >55 Years ( <i>n</i> = 30) | <i>P</i> |
|--|----------------------------|----------------------------|----------|
| Sex, male, <i>n</i> (%)                            | 11 (84.6)                  | 24 (80.0)                  | .32*     |
| Smoking, yes, <i>n</i> (%)                         | 10 (76.9)                  | 25 (83.3)                  | .28*     |
| BMI at age 18 (mean ± SD), kg/m <sup>2</sup>       | 25.4 ± 5.8                 | 24.3 ± 3.5                 | .23      |
| BMI ≥ 25 kg/m <sup>2</sup> at age 18, <i>n</i> (%) | 7 (53.9)                   | 10 (33.3)                  | .21      |
| Stage, <i>n</i> (%)                                |                            |                            | .49      |
| I-II   | 5 (38.5)                   | 15 (50.0)                  |          |
| III-IV   | 8 (61.5)                   | 15 (50.0)                  |          |

\*Fisher exact test.

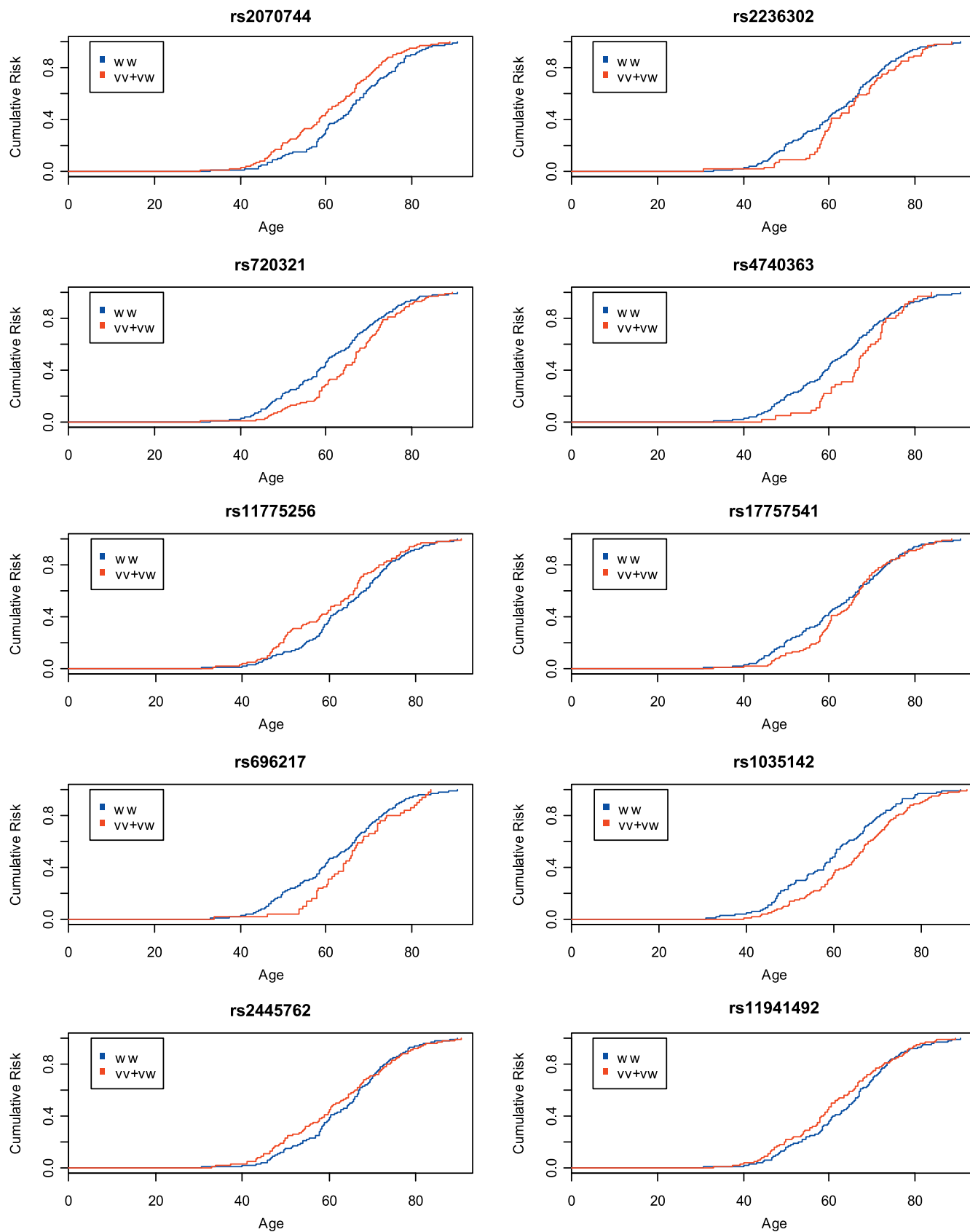
**Table W2.** Demographic Characteristics of 46 Patients with GERD Symptoms but Did Not Provide the Frequency Information.

| Characteristics                                    | ≤55 Years ( <i>n</i> = 14) | >55 Years ( <i>n</i> = 32) | <i>P</i> |
|--|----------------------------|----------------------------|----------|
| Sex, male, <i>n</i> (%)                            | 12 (85.7)                  | 27 (84.4)                  | 1.00     |
| Smoking, yes, <i>n</i> (%)                         | 10 (71.4)                  | 27 (84.4)                  | .42      |
| BMI at age 18 (mean ± SD), kg/m <sup>2</sup>       | 26.1 ± 5.7                 | 24.7 ± 4.1                 | .36      |
| BMI ≥ 25 kg/m <sup>2</sup> at age 18, <i>n</i> (%) | 7 (50.0)                   | 12 (37.5)                  | .52      |
| Stage, <i>n</i> (%)                                |                            |                            | .35      |
| I-II   | 5 (35.7)                   | 17 (53.1)                  |          |
| III-IV   | 9 (64.3)                   | 15 (46.9)                  |          |

**Table W3.** Allele Frequencies of the SNPs Significantly Associated with Age of EA Onset.

| SNP                          | ≤55 Years ( <i>n</i> = 89), % |      |      | >55 Years ( <i>n</i> = 246), % |      |      |
|------------------------------|-------------------------------|------|------|--------------------------------|------|------|
|                              | AA                            | AB   | BB   | AA                             | AB   | BB   |
| <i>NOS2</i> rs2070744        | 19.1                          | 51.7 | 29.2 | 40.7                           | 39.8 | 19.5 |
| <i>MMP14</i> rs2236302       | 92.1                          | 7.9  | 0    | 75.2                           | 24.4 | 0.4  |
| <i>BCL2</i> rs720321*        | 82.0                          | 16.9 | 1.1  | 64.2                           | 32.9 | 2.9  |
| <i>ABL1</i> rs4740363        | 96.9                          | 3.4  | 0    | 82.9                           | 15.9 | 1.2  |
| <i>TNFRSF10A</i> rs11775256  | 47.2                          | 43.8 | 9.0  | 64.6                           | 30.9 | 4.5  |
| <i>BCL2</i> rs17757541*      | 80.9                          | 18.0 | 1.1  | 64.6                           | 31.7 | 3.7  |
| <i>GHRL</i> rs696217         | 94.4                          | 5.6  | 0    | 81.3                           | 18.3 | 0.4  |
| <i>CASP8</i> rs1035142       | 50.6                          | 37.1 | 12.4 | 33.7                           | 50.0 | 16.3 |
| <i>CYP19A1</i> rs2445762     | 46.1                          | 41.6 | 12.3 | 58.5                           | 36.6 | 4.9  |
| <i>VEGFR2/KDR</i> rs11941492 | 52.8                          | 32.6 | 14.6 | 58.9                           | 36.2 | 4.9  |

\*Correlation coefficient of the two SNPs  $r^2 = -0.04$ ,  $P = .47$ .



**Figure W1.** Kaplan-Meier curves: cumulative risk and age of cancer diagnosis associated with the wide-type (ww) or variant types (v + w) of the 10 SNPs.

**Table W4.** COX Regression Model of the 10 SNPs.

| SNP                          | OR (95% CI)      | <i>P</i> | FDR   |
|------------------------------|------------------|----------|-------|
| <i>NOS2</i> rs2070744        | 1.40 (1.13-1.76) | .004     | 0.02  |
| <i>MMP14</i> rs2236302       | 0.84 (0.64-1.10) | .196     | 0.28  |
| <i>BCL2</i> rs720321         | 0.77 (0.61-0.97) | .029     | 0.10  |
| <i>ABL1</i> rs4740363        | 0.82 (0.60-1.13) | .226     | 0.28  |
| <i>TNFRSF10A</i> rs11775256  | 1.21 (0.97-1.50) | .093     | 0.23  |
| <i>BCL2</i> rs17757541       | 0.94 (0.75-1.19) | .619     | 0.69  |
| <i>GHRL</i> rs696217         | 0.80 (0.59-1.07) | .137     | 0.27  |
| <i>CASP8</i> rs1035142       | 0.68 (0.54-0.85) | .0007    | 0.007 |
| <i>CYP19A1</i> rs2445762     | 1.02 (0.82-1.26) | .868     | 0.87  |
| <i>VEGFR2/KDR</i> rs11941492 | 1.16 (0.93-1.44) | .185     | 0.28  |

**Table W5.** Independent and Interactive ORs of the Top 10 SNPs and Age on EA Risk among 335 Cases and 319 Controls.

| SNP*                         | Age ≤ 55 Years   |          | Age > 55 Years   |          | Interaction OR* (95% CI) | <i>P</i> |
|------------------------------|------------------|----------|------------------|----------|--------------------------|----------|
|                              | OR               | <i>P</i> | OR               | <i>P</i> |                          |          |
| <i>NOS2</i> rs2070744        | 3.69 (1.45-9.38) | .006     | 0.75 (0.46-1.20) | .228     | 4.02 (1.57-10.29)        | .004     |
| <i>MMP14</i> rs2236302       | 0.29 (0.09-0.91) | .033     | 1.65 (0.94-2.89) | .081     | 0.20 (0.06-0.65)         | .008     |
| <i>BCL2</i> rs720321         | 0.78 (0.34-1.81) | .565     | 1.54 (0.94-2.53) | .084     | 0.54 (0.21-1.36)         | .191     |
| <i>ABL1</i> rs4740363        | 0.08 (0.02-0.44) | .003     | 1.06 (0.57-1.98) | .861     | 0.12 (0.02-0.62)         | .011     |
| <i>TNFRSF10A</i> rs11775256  | 1.72 (0.84-3.53) | .136     | 1.07 (0.67-1.70) | .787     | 1.48 (0.66-3.32)         | .336     |
| <i>BCL2</i> rs17757541       | 0.41 (0.17-0.98) | .044     | 0.76 (0.47-1.21) | .247     | 0.61 (0.24-1.53)         | .297     |
| <i>GHRL</i> rs696217         | 0.63 (0.17-2.38) | .495     | 1.46 (0.79-2.69) | .230     | 0.40 (0.10-1.61)         | .195     |
| <i>CASP8</i> rs1035142       | 0.81 (0.40-1.63) | .554     | 1.06 (0.65-1.71) | .821     | 0.73 (0.32-1.65)         | .450     |
| <i>CYP19A1</i> rs2445762     | 2.06 (1.01-4.17) | .046     | 0.79 (0.50-1.25) | .317     | 2.40 (1.08-5.34)         | .032     |
| <i>VEGFR2/KDR</i> rs11941492 | 1.25 (0.62-2.53) | .535     | 0.86 (0.54-1.37) | .527     | 1.44 (0.65-3.18)         | .371     |

\*SNPs in dominant model and age dichotomized by 55 years.