Techniques used in meta-analysis when estimate and SE were not directly available

Reconstructing survival data

In a number of studies (MTVOS: Araz et al. [1] and Chang et al. [2]; SUVOS and SUVPFS: Aktan et al. [3]) and Kwon et al. [4], the published Kaplan-Meier curves allowed reconstruction of the full set of survival data (i.e., both times of events, OS or PFS, and times of censoring). Thereby, data could be re-analyzed to obtain estimates of hazard ratio and its standard error.

Reconstructing survival curves

In a number of studies (MTVOS: Choi et al. (SCLC-ED) [5]; SUVOS: Go et al. [6] and Choi et al. (SCLC-LD) [5]; SUVPFS: Dinc et al. [7]), Kaplan-Meier curves were published that allowed reconstruction of the survival *distribution*, albeit not the complete set of observed times of events and censorings. Thereby, it was possible to simulate observations from the relevant distributions and estimate the hazard ratio. Furthermore, from the p-values for analyses where MTV or SUV were used as a quantitative covariate the standard error, SE, was estimated from the equation

$$p = P\left(\chi_1^2 > (\frac{\log(HR)}{SE})^2\right).$$

Reconstructing individual values of SUV and MTV

In the paper by Kwon et al. [4], a scatterplot of MTV versus SUV was presented from which the individual values, say x, could be read. The hazard ratio from a comparison of survival curves for patients with values of x (=MTV or SUV) below or above the median, M was then obtained as

$$HR = \frac{1}{3}\sum_t \frac{\log(S_+(t))}{\log(S_-(t))},$$

where t was chosen to get a baseline survival function S0(t) of 0.3, 0.5, or 0.7. Here

$$S_+(t) = \frac{1}{n/2}\sum_{i:x_i \geq M} S_0(t)^{\exp(\widehat{\beta}x_i)}, \quad S_-(t) = \frac{1}{n/2}\sum_{i:x_i < M} S_0(t)^{\exp(\widehat{\beta}x_i)}$$

and exp(β) is the hazard ratio when using x as quantitative covariate (given in the paper). Finally, the standard error of the HR was estimated using again the first equation for p. Robustness to the choices of t was investigated.

Reconstructing hazard ratios for high vs. low values from analyses with quantitative covariates

In a number of studies (MTVOS: Choi et al. (SCLC-LD) [5]; SUVOS: Yilmaz Demirci et al. [8], Choi et al. (SCLC-ED) [5]), only the hazard ratio and SE when using the covariate x(=MTV or SUV) were given, together with the sample size, n, and median, M and range, say x(1) to x(n) for x. Since the distributions of MTV and SUV tended to be right-skewed, they distribution of y=log(x) was approximated by a normal distribution with mean log(M) and some SD. For a sample of size n from a normal distribution with mean μ and SD σ, the expected value of the r'th smallest observation can be approximated by

$$E(y_{(r)}) = \mu + \Phi^{-1}\left(\frac{r - \frac{\pi}{8}}{n + 1 - \frac{2\pi}{8}}\sigma\right)$$

Using Blom G: 'Statistical estimates and transformed beta-variables' [9] for the minimum and maximum values (r=1 or r=n), the standard deviation, σ, can be estimated. Knowing the standard deviation, the expected value of y given above μ is

$$E(y \mid y > \mu) = \mu + \sigma\sqrt{\frac{2}{\pi}},$$

and, similarly the expected value given below the mean is the same formula with a '-' instead of a '+'. The difference between the expected values of x given above or below the median can, thus, be approximated by

$$D = M\exp(\sigma\sqrt{2/\pi}) - M/\exp(\sigma\sqrt{2/\pi})$$

and the log(HR) for comparing patients with values above and below the median is finally approximated by

Dβ with a standard error of D·SE, where exp(β) is the hazard ratio when using x as a quantitative covariate and SE its standard error (possibly calculated from a 95% confidence interval for exp(β)).

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