Section B: Training and validation of a robust prognosticator for overall survival based on spatial organization features

Lin Qi

26/07/2022

Contents

1 Preparation: Loading data and functions

```
library(ggplot2)
library(cowplot)
library(survival)
library(MASS)
library(parallel)
options(digits=6)
load("./DataAndClinical.rdata")
source("./func/factor_analysis.R")
source("./func/optimal_cutoff.R")
source("./func/plot_KMCurve.R")
```

2 Univariate Cox regression analysis using clinical factors and SOFs

We performed univariate Cox regression analysis using clinical factors and SOFs (Table S2) in the SYSUCC discovery cohort. Eight SOFs showed significant association with overall survival (all $P < 0.05$, likelihood ratio tests, Table S2).

```
# Focus on 10 years OS
SYSUCC_data <- SYSUCC_data[-which(SYSUCC_data$os.time>=120),]

(factor_name <- colnames(SYSUCC_data)[c(4:16,18:38)])
```

```
##  [1] "Age"                           "Gender"
##  [3] "Primary_tumor_location"        "Pathological_Tstage"
##  [5] "Pathological_Nstage"           "Preoperative_chemotherapy"
##  [7] "Preoperative_CEA"              "Synchronous_liver_metastases"
##  [9] "Number_of_LM"                  "Largest_diameter_of_CRLM"
## [11] "Resection_margin"              "Concomitant_ablation"
## [13] "CRS_score"                     "Adjuvant_chemotherapy"
## [15] "Distal_Stroma_ratio"           "Distal_Debris_ratio"
## [17] "Distal_Lymphocyte_ratio"       "Distal_Hepatocyte_ratio"
## [19] "Distal_Mucus_ratio"            "Infiltrating_Stroma_ratio"
## [21] "Infiltrating_Debris_ratio"     "Infiltrating_Lymphocyte_ratio"
## [23] "Infiltrating_Hepatocyte_ratio" "Infiltrating_Mucus_ratio"
## [25] "TUM_STR_interaction"           "TUM_DEB_interaction"
## [27] "TUM_LYM_interaction"           "TUM_HEP_interaction"
## [29] "TUM_MUC_interaction"           "Overall_Stroma_ratio"
## [31] "Overall_Debris_ratio"          "Overall_Lymphocyte_ratio"
## [33] "Overall_Hepatocyte_ratio"      "Overall_Mucus_ratio"
```

```
# SYS
#clin_factors <- SYSUCC_data[,factor_name]
#SYS_cli_os <- SYSUCC_data[!is.na(as.numeric(SYSUCC_data$os.time)),]
#clin_factors_os <- clin_factors[!is.na(as.numeric(SYSUCC_data$os.time)),]
#os_time2 <- as.numeric(SYS_cli_os$os.time)
#os_event2 <- as.numeric(as.character(SYS_cli_os$os.event) )
#os2 <- cbind(os_time2,os_event2)
#os2 <- factor_analysis(clin_factors_os, os2, string = T, ignore.mul.auto = F, limit = NULL)
#os2 <- os2[,1:2]
```

```r
#SYS_os <- as.data.frame(os2)
os_time <- SYSUCC_data$os.time
os_event <- SYSUCC_data$os.event
res <- survival::Surv(os_time,os_event)
univ_formulas <- sapply(factor_name,function(x) as.formula(paste('res ~', x)))
univ_models <- lapply(univ_formulas, function(x){summary(survival::coxph(x, data=SYSUCC_data))})
univ_results <- sapply(1:length(univ_models), function(i){
    x <- univ_models[[i]]
    p <- x$logtest[3]
    HR <- x$conf.int[1,c(1,3,4)]
    p <- as.numeric(p)
    aa <- c(HR,p)
    return(aa)
})
colnames(univ_results) <- factor_name
rownames(univ_results) <- c("HR","L95","H95","logtest_P")
univ_results <- t(univ_results)
data.frame(HR=sprintf("%3.2f (%3.2f - %3.2f)",
                                    univ_results[, 1], univ_results[, 2], univ_results[, 3]),
                          P=signif(univ_results[, 4], 3))
```

```
##                                              HR        P
## Age                             1.01 (0.99 - 1.02) 3.57e-01
## Gender                          1.06 (0.77 - 1.46) 7.17e-01
## Primary_tumor_location          0.94 (0.66 - 1.33) 7.19e-01
## Pathological_Tstage             0.77 (0.47 - 1.28) 3.34e-01
## Pathological_Nstage             1.46 (1.08 - 1.99) 1.34e-02
## Preoperative_chemotherapy       1.52 (1.10 - 2.09) 8.91e-03
## Preoperative_CEA                1.00 (1.00 - 1.00) 3.70e-02
## Synchronous_liver_metastases    1.01 (0.99 - 1.02) 4.01e-01
## Number_of_LM                    1.04 (1.01 - 1.07) 2.16e-02
## Largest_diameter_of_CRLM        1.08 (1.01 - 1.15) 4.20e-02
## Resection_margin                2.11 (1.46 - 3.07) 2.44e-04
## Concomitant_ablation            1.64 (1.11 - 2.42) 1.92e-02
## CRS_score                       1.39 (1.18 - 1.63) 5.71e-05
## Adjuvant_chemotherapy           0.69 (0.49 - 0.96) 3.58e-02
## Distal_Stroma_ratio             1.02 (0.76 - 1.37) 8.94e-01
## Distal_Debris_ratio             1.71 (1.27 - 2.32) 3.92e-04
## Distal_Lymphocyte_ratio         0.71 (0.52 - 0.96) 2.29e-02
## Distal_Hepatocyte_ratio         0.66 (0.49 - 0.89) 6.03e-03
## Distal_Mucus_ratio              1.10 (0.82 - 1.48) 5.24e-01
## Infiltrating_Stroma_ratio       0.89 (0.66 - 1.20) 4.46e-01
## Infiltrating_Debris_ratio       1.57 (1.16 - 2.11) 3.15e-03
## Infiltrating_Lymphocyte_ratio   0.75 (0.56 - 1.02) 6.30e-02
## Infiltrating_Hepatocyte_ratio   1.22 (0.91 - 1.65) 1.83e-01
## Infiltrating_Mucus_ratio        1.24 (0.92 - 1.68) 1.57e-01
## TUM_STR_interaction             1.10 (0.82 - 1.49) 5.16e-01
## TUM_DEB_interaction             1.13 (0.84 - 1.52) 4.13e-01
## TUM_LYM_interaction             0.69 (0.51 - 0.93) 1.29e-02
## TUM_HEP_interaction             1.38 (1.03 - 1.85) 3.29e-02
## TUM_MUC_interaction             1.30 (0.97 - 1.74) 8.43e-02
## Overall_Stroma_ratio            0.87 (0.65 - 1.17) 3.64e-01
## Overall_Debris_ratio            1.69 (1.26 - 2.28) 5.06e-04
## Overall_Lymphocyte_ratio        0.64 (0.47 - 0.86) 3.12e-03
```

```
## Overall_Hepatocyte_ratio      0.77 (0.57 - 1.03) 7.93e-02
## Overall_Mucus_ratio           1.23 (0.91 - 1.65) 1.73e-01
```

3 Model optimization with a stepwise feature selection algorithm

Finally, the model with overall debris ratio, overall lymphocyte ratio, tumor-distal hepatocyte ratio and tumor-hepatocyte interaction achieved the minimum AIC value and was selected for the following analysis (Figure 3b).

```
BJCH_data <- BJCH_data[-which(BJCH_data$os.event==2 | BJCH_data$os.event==3 | BJCH_data$os.event==4),]
BJCH_data <- BJCH_data[-which(BJCH_data$os.time>120),] # Focus on 10 years OS

# SOFs which performed significant prognostic power in univariate cox analysis and
# passed the correlation-based selection.

fit1 <- coxph(Surv((os.time),(os.event))~Overall_Debris_ratio+Overall_Lymphocyte_ratio+
                Distal_Hepatocyte_ratio+Infiltrating_Debris_ratio+
                TUM_LYM_interaction+TUM_HEP_interaction,
              data=SYSUCC_data)
fit2 <- coxph(Surv((os.time),(os.event))~1,
              data=SYSUCC_data)
```

3.1 Methods 1

```
a1 <- stepAIC(fit1,direction="backward")
```

```
## Start:  AIC=1896.27
## Surv((os.time), (os.event)) ~ Overall_Debris_ratio + Overall_Lymphocyte_ratio +
##     Distal_Hepatocyte_ratio + Infiltrating_Debris_ratio + TUM_LYM_interaction +
##     TUM_HEP_interaction
##
##                              Df  AIC
## - Infiltrating_Debris_ratio  1 1895
## - TUM_LYM_interaction        1 1895
## <none>                         1896
## - Overall_Lymphocyte_ratio   1 1897
## - Distal_Hepatocyte_ratio    1 1897
## - Overall_Debris_ratio       1 1898
## - TUM_HEP_interaction        1 1900
##
## Step:  AIC=1894.67
## Surv((os.time), (os.event)) ~ Overall_Debris_ratio + Overall_Lymphocyte_ratio +
##     Distal_Hepatocyte_ratio + TUM_LYM_interaction + TUM_HEP_interaction
##
##                             Df  AIC
## - TUM_LYM_interaction       1 1893
## <none>                        1895
## - Overall_Lymphocyte_ratio  1 1895
## - Distal_Hepatocyte_ratio   1 1896
## - TUM_HEP_interaction       1 1898
## - Overall_Debris_ratio      1 1900
##
```

```
## Step:  AIC=1893.38
## Surv((os.time), (os.event)) ~ Overall_Debris_ratio + Overall_Lymphocyte_ratio +
##     Distal_Hepatocyte_ratio + TUM_HEP_interaction
##
##                            Df  AIC
## <none>                        1893
## - Distal_Hepatocyte_ratio   1 1896
## - TUM_HEP_interaction       1 1896
## - Overall_Lymphocyte_ratio  1 1898
## - Overall_Debris_ratio      1 1899
```

```
print("Final model:----------------------------------------------------")
```

```
## [1] "Final model:----------------------------------------------------"
```

```
a1
```

```
## Call:
## coxph(formula = Surv((os.time), (os.event)) ~ Overall_Debris_ratio +
##     Overall_Lymphocyte_ratio + Distal_Hepatocyte_ratio + TUM_HEP_interaction,
##     data = SYSUCC_data)
##
##                             coef exp(coef) se(coef)     z      p
## Overall_Debris_ratio       0.432     1.541    0.159  2.71 0.0067
## Overall_Lymphocyte_ratio -0.386     0.680    0.155 -2.50 0.0126
## Distal_Hepatocyte_ratio  -0.347     0.707    0.166 -2.09 0.0363
## TUM_HEP_interaction        0.336     1.400    0.156  2.16 0.0309
##
## Likelihood ratio test=28.4  on 4 df, p=1.05e-05
## n= 433, number of events= 179
```

3.2 Methods 2

```
a2 <- stepAIC(fit2,direction="forward",scope=list(upper=fit1,lower=fit2))
```

```
## Start:  AIC=1913.76
## Surv((os.time), (os.event)) ~ 1
##
##                              Df  AIC
## + Overall_Debris_ratio        1 1904
## + Overall_Lymphocyte_ratio    1 1907
## + Infiltrating_Debris_ratio   1 1907
## + Distal_Hepatocyte_ratio     1 1908
## + TUM_LYM_interaction         1 1910
## + TUM_HEP_interaction         1 1911
## <none>                          1914
##
## Step:  AIC=1903.67
## Surv((os.time), (os.event)) ~ Overall_Debris_ratio
##
##                              Df  AIC
## + Overall_Lymphocyte_ratio    1 1897
## + TUM_LYM_interaction         1 1900
## + TUM_HEP_interaction         1 1901
## + Distal_Hepatocyte_ratio     1 1903
```

```
## <none>                           1904
## + Infiltrating_Debris_ratio  1 1904
##
## Step:  AIC=1896.99
## Surv((os.time), (os.event)) ~ Overall_Debris_ratio + Overall_Lymphocyte_ratio
##
##                             Df  AIC
## + TUM_HEP_interaction        1 1896
## + Distal_Hepatocyte_ratio    1 1896
## <none>                           1897
## + Infiltrating_Debris_ratio  1 1898
## + TUM_LYM_interaction        1 1898
##
## Step:  AIC=1895.83
## Surv((os.time), (os.event)) ~ Overall_Debris_ratio + Overall_Lymphocyte_ratio +
##     TUM_HEP_interaction
##
##                             Df  AIC
## + Distal_Hepatocyte_ratio    1 1893
## <none>                           1896
## + TUM_LYM_interaction        1 1896
## + Infiltrating_Debris_ratio  1 1896
##
## Step:  AIC=1893.38
## Surv((os.time), (os.event)) ~ Overall_Debris_ratio + Overall_Lymphocyte_ratio +
##     TUM_HEP_interaction + Distal_Hepatocyte_ratio
##
##                             Df  AIC
## <none>                           1893
## + TUM_LYM_interaction        1 1895
## + Infiltrating_Debris_ratio  1 1895
```

```
print("Final model:----------------------------------------------------")
```

```
## [1] "Final model:----------------------------------------------------"
```

```
a2
```

```
## Call:
## coxph(formula = Surv((os.time), (os.event)) ~ Overall_Debris_ratio +
##     Overall_Lymphocyte_ratio + TUM_HEP_interaction + Distal_Hepatocyte_ratio,
##     data = SYSUCC_data)
##
##                              coef exp(coef) se(coef)     z      p
## Overall_Debris_ratio      0.432     1.541    0.159  2.71 0.0067
## Overall_Lymphocyte_ratio -0.386     0.680    0.155 -2.50 0.0126
## TUM_HEP_interaction       0.336     1.400    0.156  2.16 0.0309
## Distal_Hepatocyte_ratio  -0.347     0.707    0.166 -2.09 0.0363
##
## Likelihood ratio test=28.4  on 4 df, p=1.05e-05
## n= 433, number of events= 179
```

3.3 Methods 3

```
a3 <- stepAIC(fit2,direction="both",scope=list(upper=fit1,lower=fit2))
```

```
## Start:  AIC=1913.76
## Surv((os.time), (os.event)) ~ 1
##
##                              Df  AIC
## + Overall_Debris_ratio        1 1904
## + Overall_Lymphocyte_ratio    1 1907
## + Infiltrating_Debris_ratio   1 1907
## + Distal_Hepatocyte_ratio     1 1908
## + TUM_LYM_interaction         1 1910
## + TUM_HEP_interaction         1 1911
## <none>                          1914
##
## Step:  AIC=1903.67
## Surv((os.time), (os.event)) ~ Overall_Debris_ratio
##
##                              Df  AIC
## + Overall_Lymphocyte_ratio    1 1897
## + TUM_LYM_interaction         1 1900
## + TUM_HEP_interaction         1 1901
## + Distal_Hepatocyte_ratio     1 1903
## <none>                          1904
## + Infiltrating_Debris_ratio   1 1904
## - Overall_Debris_ratio        1 1914
##
## Step:  AIC=1896.99
## Surv((os.time), (os.event)) ~ Overall_Debris_ratio + Overall_Lymphocyte_ratio
##
##                              Df  AIC
## + TUM_HEP_interaction         1 1896
## + Distal_Hepatocyte_ratio     1 1896
## <none>                          1897
## + Infiltrating_Debris_ratio   1 1898
## + TUM_LYM_interaction         1 1898
## - Overall_Lymphocyte_ratio    1 1904
## - Overall_Debris_ratio        1 1907
##
## Step:  AIC=1895.83
## Surv((os.time), (os.event)) ~ Overall_Debris_ratio + Overall_Lymphocyte_ratio +
##     TUM_HEP_interaction
##
##                              Df  AIC
## + Distal_Hepatocyte_ratio     1 1893
## <none>                          1896
## + TUM_LYM_interaction         1 1896
## + Infiltrating_Debris_ratio   1 1896
## - TUM_HEP_interaction         1 1897
## - Overall_Lymphocyte_ratio    1 1901
## - Overall_Debris_ratio        1 1906
##
## Step:  AIC=1893.38
```

```
## Surv((os.time), (os.event)) ~ Overall_Debris_ratio + Overall_Lymphocyte_ratio +
##     TUM_HEP_interaction + Distal_Hepatocyte_ratio
##
##                              Df  AIC
## <none>                          1893
## + TUM_LYM_interaction         1 1895
## + Infiltrating_Debris_ratio   1 1895
## - Distal_Hepatocyte_ratio     1 1896
## - TUM_HEP_interaction         1 1896
## - Overall_Lymphocyte_ratio    1 1898
## - Overall_Debris_ratio        1 1899
```

```
print("Final model:----------------------------------------------------")
```

```
## [1] "Final model:----------------------------------------------------"
```

```
a3
```

```
## Call:
## coxph(formula = Surv((os.time), (os.event)) ~ Overall_Debris_ratio +
##     Overall_Lymphocyte_ratio + TUM_HEP_interaction + Distal_Hepatocyte_ratio,
##     data = SYSUCC_data)
##
##                             coef exp(coef) se(coef)     z      p
## Overall_Debris_ratio       0.432     1.541    0.159  2.71 0.0067
## Overall_Lymphocyte_ratio -0.386     0.680    0.155 -2.50 0.0126
## TUM_HEP_interaction        0.336     1.400    0.156  2.16 0.0309
## Distal_Hepatocyte_ratio  -0.347     0.707    0.166 -2.09 0.0363
##
## Likelihood ratio test=28.4  on 4 df, p=1.05e-05
## n= 433, number of events= 179
```

4 Optimal cutoff for dichotomizing patients into high- and low-risk groups

The cutoff for dichotomizing the SOF risk score was selected by stepwise optimization from 20 to 80 percentiles with steps of 1000. The cutoffs that displayed the highest prognostic significance with the log-rank test were selected [1].

```
zz_model_aic <- coxph(Surv((os.time),(os.event))~Overall_Debris_ratio+Overall_Lymphocyte_ratio+
                        Distal_Hepatocyte_ratio+TUM_HEP_interaction,
                      data=SYSUCC_data)
summary(zz_model_aic)
```

```
## Call:
## coxph(formula = Surv((os.time), (os.event)) ~ Overall_Debris_ratio +
##     Overall_Lymphocyte_ratio + Distal_Hepatocyte_ratio + TUM_HEP_interaction,
##     data = SYSUCC_data)
##
##   n= 433, number of events= 179
##
##                             coef exp(coef) se(coef)     z Pr(>|z|)
## Overall_Debris_ratio       0.432     1.541    0.159  2.71   0.0067 **
## Overall_Lymphocyte_ratio -0.386     0.680    0.155 -2.50   0.0126 *
```

```
## Distal_Hepatocyte_ratio  -0.347     0.707    0.166 -2.09   0.0363 *
## TUM_HEP_interaction       0.336     1.400    0.156  2.16   0.0309 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                           exp(coef) exp(-coef) lower .95 upper .95
## Overall_Debris_ratio          1.541      0.649     1.127     2.106
## Overall_Lymphocyte_ratio      0.680      1.471     0.502     0.921
## Distal_Hepatocyte_ratio       0.707      1.415     0.511     0.978
## TUM_HEP_interaction           1.400      0.714     1.031     1.900
##
## Concordance= 0.619  (se = 0.023 )
## Likelihood ratio test= 28.4  on 4 df,   p=1e-05
## Wald test            = 28  on 4 df,   p=1e-05
## Score (logrank) test = 28.5  on 4 df,   p=1e-05
```

```
train_score_aic <- predict(zz_model_aic)
SYSUCC_data$train_score_aic <- train_score_aic
bj_predict_aic <- predict(zz_model_aic,BJCH_data)
BJCH_data$bj_predict_aic <- bj_predict_aic

print("Cutoff is:")
```

```
## [1] "Cutoff is:"
```

```
(cutoff = as.numeric(opti_cut(SYSUCC_data=SYSUCC_data,lowThresh=0.1,highThresh=0.9,steps=10000)))
```

```
## [1] -0.346837
```

5 Independent validation for the prognostic performance of SOFs risk-scoring

Applying the same risk-scoring model and cutoff to the BJCH cohort, we were able to independently validate the prognostic performance (Figure 3c-d and Figure S6). Even after adjusting for other clinicopathological factors significantly associated with OS, the SOF risk-scoring score still demonstrated a significant prognostic power in the two cohorts (both $P < 0.001$, Table S5-S6).

```
# Table S5
# Univariate and multivariate Cox proportional hazards analysis of SOF risk scores
# and clinicopathological factors in the SYSUCC cohort
summary(coxph(Surv((os.time),(os.event))~Pathological_Nstage+Number_of_LM+
                Largest_diameter_of_CRLM+Preoperative_CEA+
                Preoperative_chemotherapy+Resection_margin+Concomitant_ablation+
                Adjuvant_chemotherapy+train_score_aic,
              data=SYSUCC_data))
```

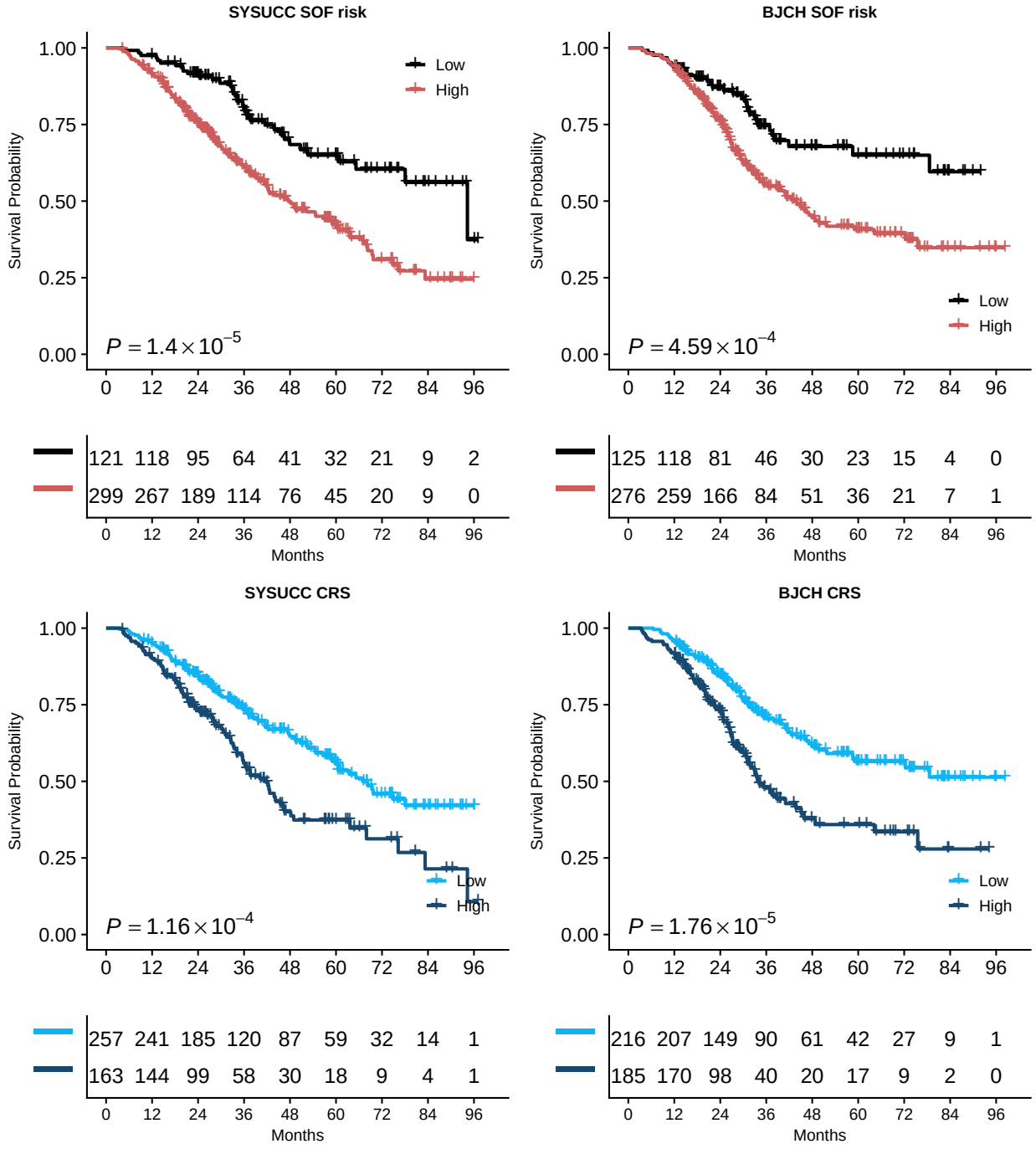
```
## Call:
## coxph(formula = Surv((os.time), (os.event)) ~ Pathological_Nstage +
##     Number_of_LM + Largest_diameter_of_CRLM + Preoperative_CEA +
##     Preoperative_chemotherapy + Resection_margin + Concomitant_ablation +
##     Adjuvant_chemotherapy + train_score_aic, data = SYSUCC_data)
##
##   n= 404, number of events= 169
##    (29 observations deleted due to missingness)
```

```
##
##                                 coef exp(coef)  se(coef)     z Pr(>|z|)
## Pathological_Nstage1        0.251134  1.285482  0.163803  1.53    0.125
## Number_of_LM                0.002384  1.002386  0.019342  0.12    0.902
## Largest_diameter_of_CRLM   -0.000535  0.999465  0.042244 -0.01    0.990
## Preoperative_CEA            0.000728  1.000728  0.000637  1.14    0.253
## Preoperative_chemotherapy1  0.403261  1.496697  0.179804  2.24    0.025 *
## Resection_margin1           0.354976  1.426147  0.218653  1.62    0.104
## Concomitant_ablation        0.283997  1.328429  0.245079  1.16    0.247
## Adjuvant_chemotherapy      -0.304545  0.737459  0.178520 -1.71    0.088 .
## train_score_aic             0.944156  2.570644  0.208898  4.52  6.2e-06 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                            exp(coef) exp(-coef) lower .95 upper .95
## Pathological_Nstage1           1.285      0.778     0.932      1.77
## Number_of_LM                   1.002      0.998     0.965      1.04
## Largest_diameter_of_CRLM       0.999      1.001     0.920      1.09
## Preoperative_CEA               1.001      0.999     0.999      1.00
## Preoperative_chemotherapy1     1.497      0.668     1.052      2.13
## Resection_margin1              1.426      0.701     0.929      2.19
## Concomitant_ablation           1.328      0.753     0.822      2.15
## Adjuvant_chemotherapy          0.737      1.356     0.520      1.05
## train_score_aic                2.571      0.389     1.707      3.87
##
## Concordance= 0.663  (se = 0.023 )
## Likelihood ratio test= 49.2  on 9 df,   p=2e-07
## Wald test            = 51.2  on 9 df,   p=6e-08
## Score (logrank) test = 53.4  on 9 df,   p=2e-08
```

```r
# Figure 3c-d: Kaplan-Meier plots showing the difference in OS according to SOF risk score
#              classification in (c) the SYSUCC cohort and (d) the BJCH cohort.
# Figure S6: Kaplan-Meier analyses of patients stratified by the CRS risk scores in
#            (a) the SYSUCC and (b) the BJCH cohorts.
# SYSUCC SOF risk
labels <- factor(SYSUCC_data$train_score_aic >= (cutoff),levels = c("FALSE","TRUE"),
                 labels = c("Low","High"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(SYSUCC_data$os.time,SYSUCC_data$os.event))
input$V1 <- as.numeric(input$V1)
SYSUCC_im <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                          risk.table = T,risk.table.ratio = 0.4,title = "SYSUCC SOF risk",
                          legend.pos = c(0.75,0.88),xlab="Months")
# SRSUCC CRS group
labels <- factor(SYSUCC_data$CRS_group,levels = c("0","1"),labels = c("Low","High"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(SYSUCC_data$os.time,SYSUCC_data$os.event))
input$V1 <- as.numeric(input$V1)
SYSUCC_CRS <- plot_KMCurve(input,labels,font = "sans",color = c("#10B4F3","#164870"),
                           risk.table = T,risk.table.ratio = 0.4,title = "SYSUCC CRS",
                           legend.pos = c(0.8,0.18),xlab="Months")
# SYSUCC SOF risk
labels <- factor(BJCH_data$bj_predict_aic >= (cutoff),levels = c("FALSE","TRUE"),
                 labels = c("Low","High"))
```

```r
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(BJCH_data$os.time,BJCH_data$os.event))
input$V1 <- as.numeric(input$V1)
BJCH_im <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                        risk.table = T,risk.table.ratio = 0.4,title = "BJCH SOF risk",
                        legend.pos = c(0.8,0.18),xlab="Months")
#
labels <- labels <- factor(BJCH_data$CRS_group,levels = c("0","1"),labels = c("Low","High"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(BJCH_data$os.time,BJCH_data$os.event))
input$V1 <- as.numeric(input$V1)
BJCH_CRS <- plot_KMCurve(input,labels,font = "sans",color = c("#10B4F3","#164870"),
                         risk.table = T,risk.table.ratio = 0.4,title = "BJCH CRS",
                         legend.pos = c(0.8,0.18),xlab="Months")

plot_grid(SYSUCC_im,BJCH_im,SYSUCC_CRS,BJCH_CRS,ncol = 2,byrow = T,align = "hv")
```



6 References

[1] Maley, C. C., Koelble, K., Natrajan, R., Aktipis, A. & Yuan, Y. An ecological measure of immune-cancer colocalization as a prognostic factor for breast cancer. Breast Cancer Res. 17, 131 (2015).