Section D: The SOF risk-scoring model is independent of CRS and their integration further improves the risk stratification of CRLM patients

Lin Qi

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1 Preparation

Loading data and functions.

```
library(ggplot2)
library(cowplot)
options(digits=6)
library(forestplot)
```

```
## Loading required package: grid
```

```
## Loading required package: magrittr
```

```
## Loading required package: checkmate
```

```
library(survival)
library(MASS)
library(parallel)
library(survminer)
```

```
## Loading required package: ggpubr
```

```
##
## Attaching package: 'ggpubr'
```

```
## The following object is masked from 'package:cowplot':
##
##     get_legend
```

```
source("./func/plot_KMCurve.R")
```

2 The SOF risk-scoring model is independent of CRS

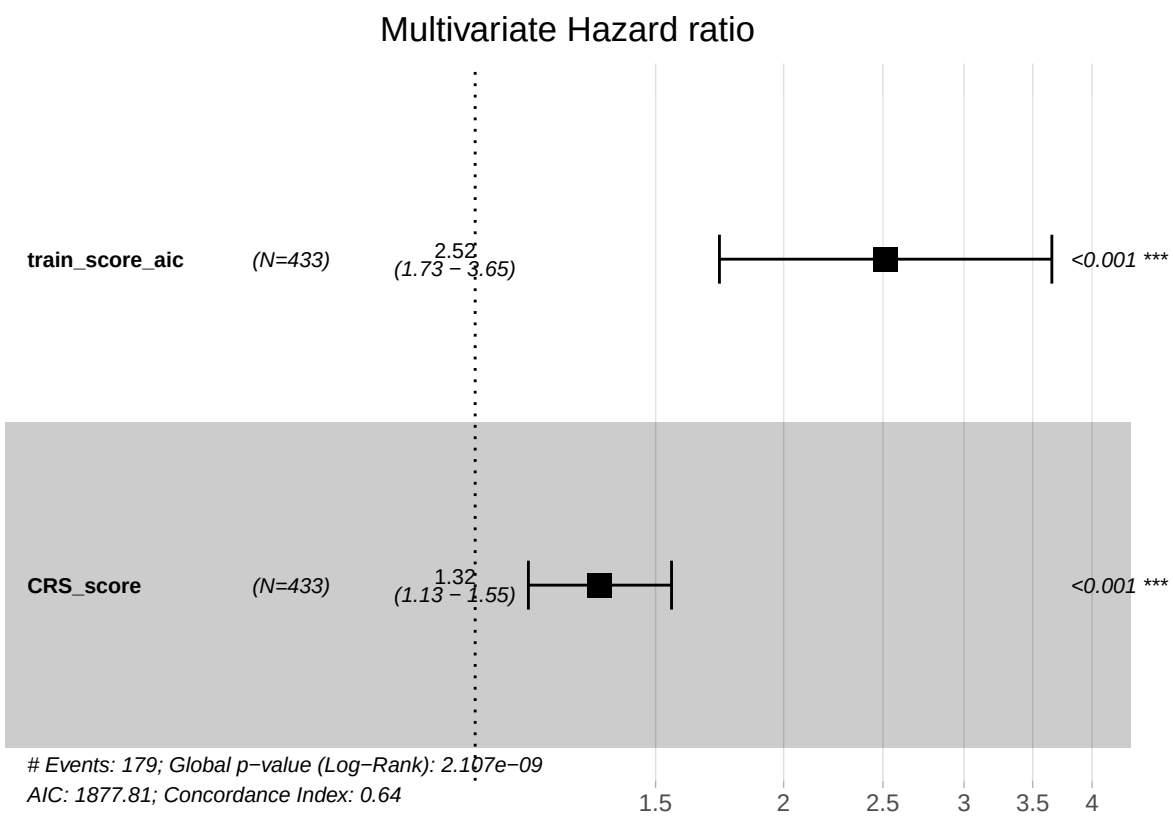
Multivariate Cox proportional hazards analysis demonstrated that SOF risk-scoring model was independent of CRS (Figure 5b).

```
load("./DataAndClinical.rdata")
BJCH_data <- BJCH_data[-which(BJCH_data$os.event==2 | BJCH_data$os.event==3 | BJCH_data$os.event==4),]
SYSUCC_data <- SYSUCC_data[-which(SYSUCC_data$os.time>120),]
BJCH_data <- BJCH_data[-which(BJCH_data$os.time>120),]

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)
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

zz_model2 <- coxph(Surv((os.time),(os.event))~train_score_aic+CRS_score,
                    data=SYSUCC_data)
summary(zz_model2)
```

```
## Call:
## coxph(formula = Surv((os.time), (os.event)) ~ train_score_aic +
```

```
##     CRS_score, data = SYSUCC_data)
##
##   n= 433, number of events= 179
##
##                    coef exp(coef) se(coef)    z Pr(>|z|)
## train_score_aic 0.9224    2.5153   0.1906 4.84  1.3e-06 ***
## CRS_score       0.2804    1.3237   0.0821 3.42  0.00063 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                 exp(coef) exp(-coef) lower .95 upper .95
## train_score_aic      2.52      0.398      1.73      3.65
## CRS_score            1.32      0.755      1.13      1.55
##
## Concordance= 0.644  (se = 0.023 )
## Likelihood ratio test= 40  on 2 df,   p=2e-09
## Wald test            = 39.7  on 2 df,   p=2e-09
## Score (logrank) test = 40.1  on 2 df,   p=2e-09
```

```r
ggforest(zz_model2,
        # data = SYSUCC_data,
        main = 'Multivariate Hazard ratio',
        # cpositions = c(0.05, 0.15, 0.35),
        # fontsize = 0.7,
        # refLabel = 'reference',
        noDigits = 3
      )
```



Similar prognostic performance was observed in the Kaplan–Meier analyses (Figure 3c-d, Figure S6). Together, these observations demonstrated comparative but independent prognostic power between the SOF risk-scoring model and CRS.

3 Integrating the SOF and CRS scoring systems

We next sought to integrate the SOF and CRS scoring systems for better prognostic stratification. For simplicity, we attributed the low-risk group to 0 point and the high-risk group to 1 point on both scoring systems. The SOF-CRS integrated grading resulted in three groups (Combined low-risk: 0 points, medium-risk: 1 point, high-risk: 2 points) with substantially different overall survival, showing superior overall performance (Figure 5f).

```
# Figure 5f
# SYSUCC stratify ------------------------------------------------------------
cutoff <- -0.346837
labels <- factor(SYSUCC_data$train_score_aic >= (cutoff),levels = c("FALSE","TRUE"),
                 labels = c("SOF-Low","SOF-High"))
labels <- as.character(labels)
labels[which(SYSUCC_data$CRS_group=="0")] <- paste0(
  "CRS-Low+",labels[which(SYSUCC_data$CRS_group=="0")])
labels[which(SYSUCC_data$CRS_group=="1")] <- paste0(
  "CRS-High+", labels[which(SYSUCC_data$CRS_group=="1")])
labels[which(labels=="CRS-High+SOF-High")] <- "High Risk"
labels[which(labels=="CRS-High+SOF-Low")] <- "Mid Risk"
labels[which(labels=="CRS-Low+SOF-High")] <- "Mid Risk"
labels[which(labels=="CRS-Low+SOF-Low")] <- "Low Risk"
labels <- factor(labels,levels = c("High Risk","Mid Risk","Low Risk"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(SYSUCC_data$os.time,SYSUCC_data$os.event))
input$V1 <- as.numeric(input$V1)
SYSUCC_3 <- plot_KMCurve(input,labels,font = "sans",risk.table = T,risk.table.ratio = 0.4,
                         title = "SYSUCC SOFs+CRS risk",legend.pos = c(0.75,0.88),
                         xlab="Follow up",ylab = "Overall survival")

# BJCH stratify --------------------------------------------------------------
labels_bj <- factor(BJCH_data$bj_predict_aic >= (cutoff),levels = c("FALSE","TRUE"),
                    labels = c("SOF-Low","SOF-High"))
labels_bj <- as.character(labels_bj)
labels_bj[which(BJCH_data$CRS_group=="0")] <- paste0(
  "CRS-Low+",labels_bj[which(BJCH_data$CRS_group=="0")])
labels_bj[which(BJCH_data$CRS_group=="1")] <- paste0(
  "CRS-High+",labels_bj[which(BJCH_data$CRS_group=="1")])
labels_bj[which(labels_bj=="CRS-High+SOF-High")] <- "High Risk"
labels_bj[which(labels_bj=="CRS-High+SOF-Low")] <- "Mid Risk"
labels_bj[which(labels_bj=="CRS-Low+SOF-High")] <- "Mid Risk"
labels_bj[which(labels_bj=="CRS-Low+SOF-Low")] <- "Low Risk"
labels_bj <- factor(labels_bj,levels = c("High Risk","Mid Risk","Low Risk"))
legend.labs <- as.vector(na.omit(unique(labels_bj)))
input <- as.data.frame( cbind(BJCH_data$os.time,BJCH_data$os.event))
input$V1 <- as.numeric(input$V1)
BJCH_3 <- plot_KMCurve(input,labels_bj,font = "sans",risk.table = T,risk.table.ratio = 0.4,
                       title = "BJCH SOFs+CRS risk",legend.pos = c(0.75,0.88),
                       xlab="Follow up",ylab = "Overall survival")
```

```
plot_grid(SYSUCC_3,BJCH_3,ncol = 2,byrow = T,align = "hv")
```