Section C: The SOF risk-scoring model is a robust biomarker for adjuvant chemotherapy in patients without pretreatment

Lin Qi

26/07/2022

Contents

1 Preparation

Loading data and functions.

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

2 Robust biomarker for adjuvant chemotherapy in patients without pretreatment

No statistically significant OS benefit was observed in patients treated with adjuvant CTx compared to patients not treated with adjuvant CTx in both cohorts. However, further stratification analyses in patients without pretreatment indicated that adjuvant CTx brought consistently significant OS benefit for the SOF high-risk subgroups in both cohorts, while no difference of OS was observed between patients with or without adjuvant CTx in the SOF low-risk subgroups.

```
# Figure 4: Patients without pretreatment
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)
```

```
## 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 )
```

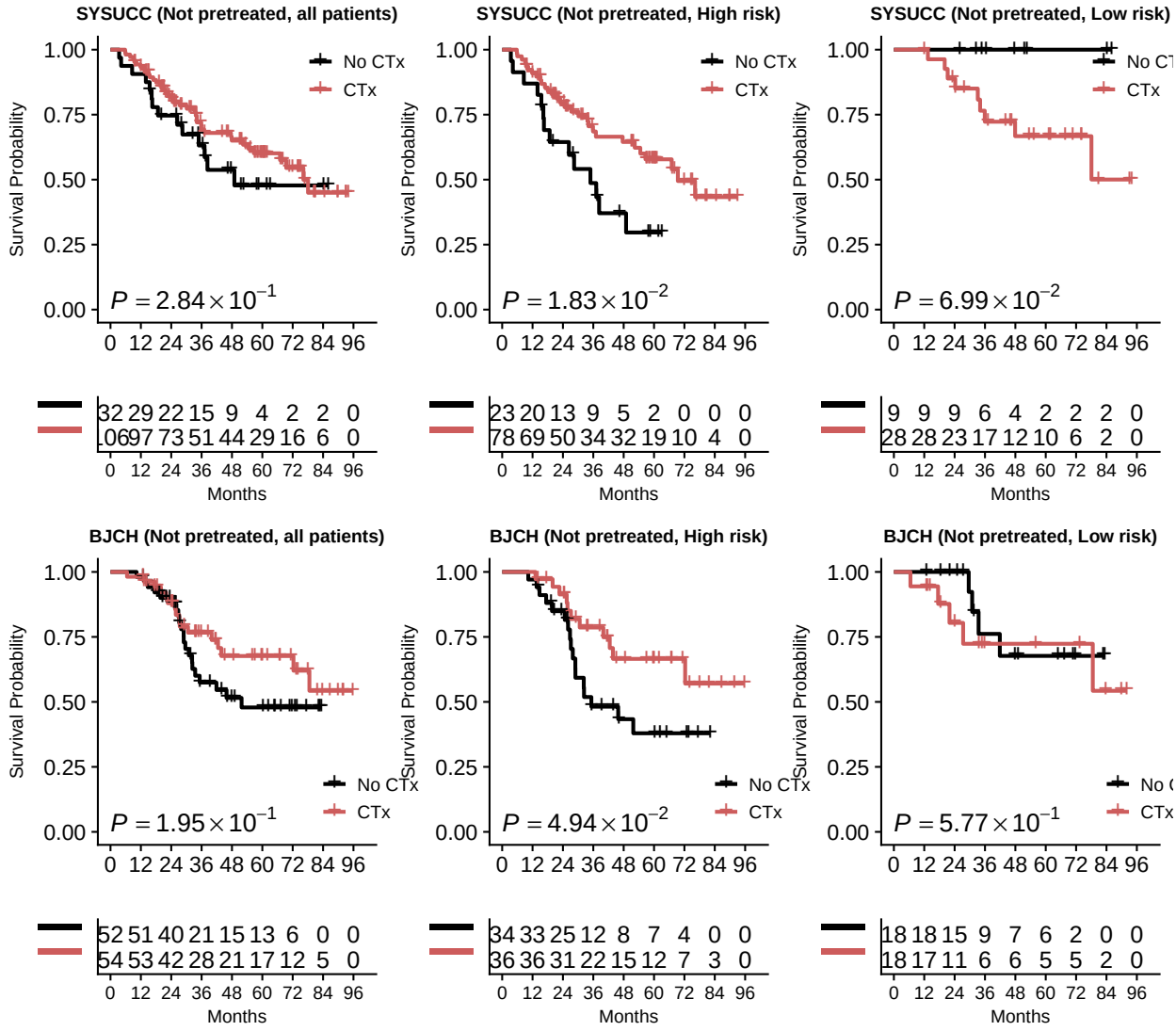
```
## Likelihood ratio test= 28.4  on 4 df,   p=1e-05
## Wald test            = 28  on 4 df,   p=1e-05
## Score (logrank) test = 28.5  on 4 df,   p=1e-05
```

```
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

cutoff = -0.346837
```

3 In patients without pretreatment

```
SYSUCC_data$riskgroup <- factor(SYSUCC_data$train_score_aic>=cutoff,labels = c("0","1"))
BJCH_data$riskgroup <- factor(BJCH_data$bj_predict_aic>=cutoff,labels = c("0","1"))
SYSUCC_data <- SYSUCC_data[!is.na(SYSUCC_data$Adjuvant_chemotherapy),]
BJCH_data <- BJCH_data[!is.na(BJCH_data$Adjuvant_chemotherapy),]


# 1. all not having pre patients
SYSUCC_data0 <- SYSUCC_data[which(SYSUCC_data$Preoperative_chemotherapy==0),]
labels <- factor(SYSUCC_data0$Adjuvant_chemotherapy,levels = c("0","1"),labels = c("No CTx","CTx"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(SYSUCC_data0$os.time,SYSUCC_data0$os.event))
input$V1 <- as.numeric(input$V1)
pre0_sysu <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                                risk.table = T,risk.table.ratio = 0.4,
                           title = "SYSUCC (Not pretreated, all patients)",
                                legend.pos = c(0.75,0.88),xlab="Months")
BJCH_data0 <- BJCH_data[which(BJCH_data$Preoperative_chemotherapy==0),]
labels <- factor(BJCH_data0$Adjuvant_chemotherapy,levels = c("0","1"),labels = c("No CTx","CTx"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(BJCH_data0$os.time,BJCH_data0$os.event))
input$V1 <- as.numeric(input$V1)
pre0_bj <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                               risk.table = T,risk.table.ratio = 0.4,
                          title = "BJCH (Not pretreated, all patients)",
                               legend.pos = c(0.8,0.18),xlab="Months")

# 2. not having pre + SOF high patients
SYSUCC_data0 <- SYSUCC_data[which(SYSUCC_data$Preoperative_chemotherapy==0
                                  & SYSUCC_data$riskgroup==1),]
labels <- factor(SYSUCC_data0$Adjuvant_chemotherapy,levels = c("0","1"),labels = c("No CTx","CTx"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(SYSUCC_data0$os.time,SYSUCC_data0$os.event))
input$V1 <- as.numeric(input$V1)
pre0SOFH_sysu <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                                  risk.table = T,risk.table.ratio = 0.4,
                               title = "SYSUCC (Not pretreated, High risk)",
                                  legend.pos = c(0.75,0.88),xlab="Months")
BJCH_data0 <- BJCH_data[which(BJCH_data$Preoperative_chemotherapy==0
                               & BJCH_data$riskgroup==1),]
```

```r
labels <- factor(BJCH_data0$Adjuvant_chemotherapy,levels = c("0","1"),labels = c("No CTx","CTx"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(BJCH_data0$os.time,BJCH_data0$os.event))
input$V1 <- as.numeric(input$V1)
pre0SOFH_bj <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                            risk.table = T,risk.table.ratio = 0.4,
                          title = "BJCH (Not pretreated, High risk)",
                            legend.pos = c(0.8,0.18),xlab="Months")

# 3. not having pre + SOF low patients
SYSUCC_data0 <- SYSUCC_data[which(SYSUCC_data$Preoperative_chemotherapy==0
                                  & SYSUCC_data$riskgroup==0),]
labels <- factor(SYSUCC_data0$Adjuvant_chemotherapy,levels = c("0","1"),labels = c("No CTx","CTx"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(SYSUCC_data0$os.time,SYSUCC_data0$os.event))
input$V1 <- as.numeric(input$V1)
pre0SOFL_sysu <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                              risk.table = T,risk.table.ratio = 0.4,
                            title = "SYSUCC (Not pretreated, Low risk)",
                              legend.pos = c(0.75,0.88),xlab="Months")
BJCH_data0 <- BJCH_data[which(BJCH_data$Preoperative_chemotherapy==0
                            & BJCH_data$riskgroup==0),]
labels <- factor(BJCH_data0$Adjuvant_chemotherapy,levels = c("0","1"),labels = c("No CTx","CTx"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(BJCH_data0$os.time,BJCH_data0$os.event))
input$V1 <- as.numeric(input$V1)
pre0SOFL_bj <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                            risk.table = T,risk.table.ratio = 0.4,
                          title = "BJCH (Not pretreated, Low risk)",
                            legend.pos = c(0.8,0.18),xlab="Months")

# figure--------------------------------
plot_grid(pre0_sysu,pre0SOFH_sysu,pre0SOFL_sysu,pre0_bj,pre0SOFH_bj,pre0SOFL_bj,ncol = 3,
                byrow = T,align = "v")
```



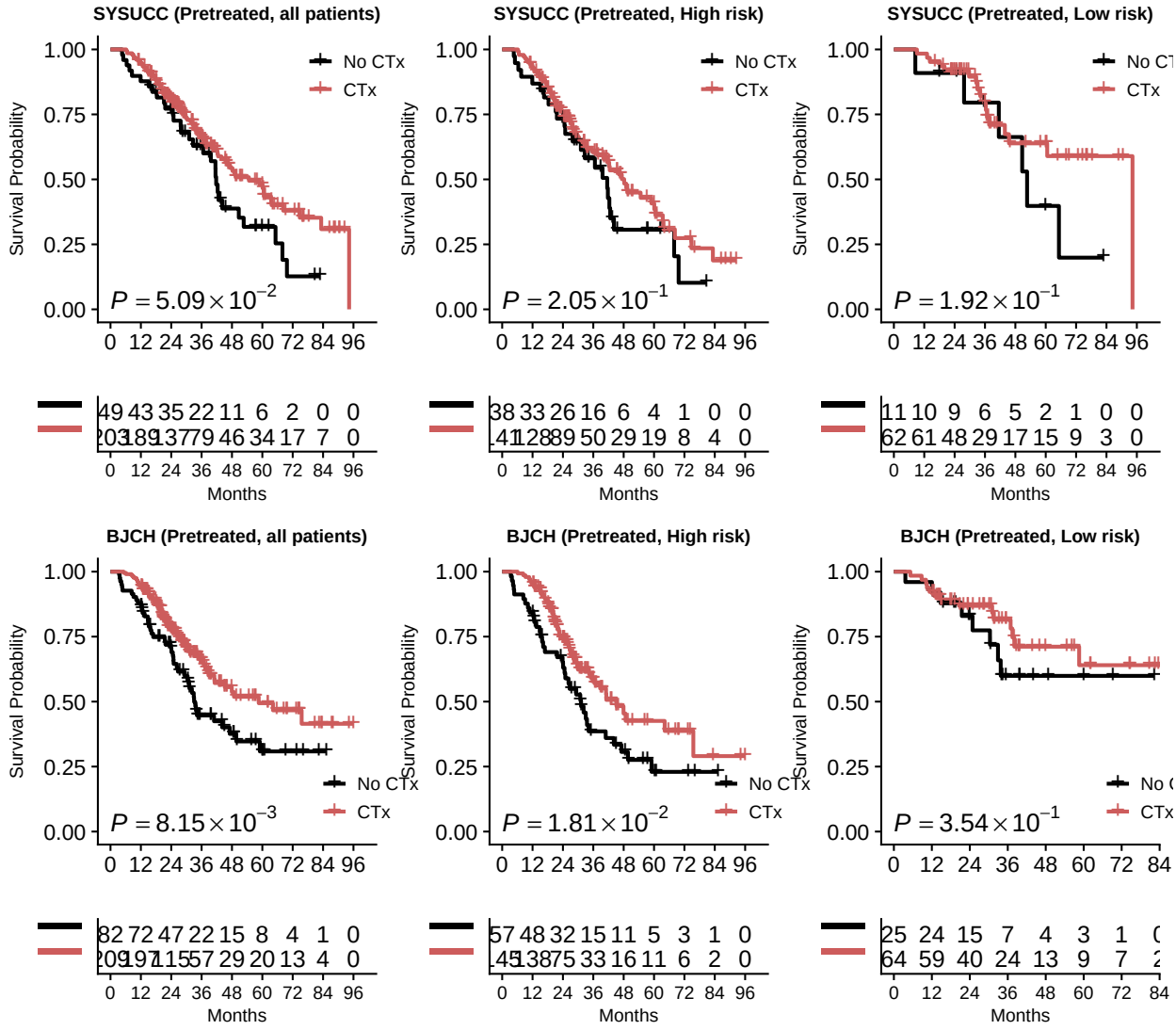
4 In patients with pretreatment

For patients who received preoperative CTx, the effectiveness of adjuvant CTx in improving OS did not achieve consistent results in the two cohorts even if stratified by the SOF risk scores.

```
# Figure S5: Patients with pretreatment

# 1. all having pre patients
SYSUCC_data0 <- SYSUCC_data[which(SYSUCC_data$Preoperative_chemotherapy==1),]
labels <- factor(SYSUCC_data0$Adjuvant_chemotherapy,levels = c("0","1"),labels = c("No CTx","CTx"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(SYSUCC_data0$os.time,SYSUCC_data0$os.event))
input$V1 <- as.numeric(input$V1)
pre1_sysu <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                                  risk.table = T,risk.table.ratio = 0.4,
                          title = "SYSUCC (Pretreated, all patients)",
                                  legend.pos = c(0.75,0.88),xlab="Months")
```

```r
BJCH_data0 <- BJCH_data[which(BJCH_data$Preoperative_chemotherapy==1),]
labels <- factor(BJCH_data0$Adjuvant_chemotherapy,levels = c("0","1"),labels = c("No CTx","CTx"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(BJCH_data0$os.time,BJCH_data0$os.event))
input$V1 <- as.numeric(input$V1)
pre1_bj <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                                risk.table = T,risk.table.ratio = 0.4,
                        title = "BJCH (Pretreated, all patients)",
                                legend.pos = c(0.8,0.18),xlab="Months")
# 2. all having pre + SOFs high patients
SYSUCC_data0 <- SYSUCC_data[which(SYSUCC_data$Preoperative_chemotherapy==1
                                  & SYSUCC_data$riskgroup==1),]
labels <- factor(SYSUCC_data0$Adjuvant_chemotherapy,levels = c("0","1"),labels = c("No CTx","CTx"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(SYSUCC_data0$os.time,SYSUCC_data0$os.event))
input$V1 <- as.numeric(input$V1)
pre1SOFH_sysu <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                                risk.table = T,risk.table.ratio = 0.4,
                              title = "SYSUCC (Pretreated, High risk)",
                                legend.pos = c(0.75,0.88),xlab="Months")
BJCH_data0 <- BJCH_data[which(BJCH_data$Preoperative_chemotherapy==1
                              & BJCH_data$riskgroup==1),]
labels <- factor(BJCH_data0$Adjuvant_chemotherapy,levels = c("0","1"),labels = c("No CTx","CTx"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(BJCH_data0$os.time,BJCH_data0$os.event))
input$V1 <- as.numeric(input$V1)
pre1SOFH_bj <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                                risk.table = T,risk.table.ratio = 0.4,
                            title = "BJCH (Pretreated, High risk)",
                                legend.pos = c(0.8,0.18),xlab="Months")

# 3. all having pre + SOFs low patients
SYSUCC_data0 <- SYSUCC_data[which(SYSUCC_data$Preoperative_chemotherapy==1
                                  & SYSUCC_data$riskgroup==0),]
labels <- factor(SYSUCC_data0$Adjuvant_chemotherapy,levels = c("0","1"),labels = c("No CTx","CTx"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(SYSUCC_data0$os.time,SYSUCC_data0$os.event))
input$V1 <- as.numeric(input$V1)
pre1SOFL_sysu <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                                risk.table = T,risk.table.ratio = 0.4,
                              title = "SYSUCC (Pretreated, Low risk)",
                                legend.pos = c(0.75,0.88),xlab="Months")
BJCH_data0 <- BJCH_data[which(BJCH_data$Preoperative_chemotherapy==1
                              & BJCH_data$riskgroup==0),]
labels <- factor(BJCH_data0$Adjuvant_chemotherapy,levels = c("0","1"),labels = c("No CTx","CTx"))
legend.labs <- as.vector(na.omit(unique(labels)))
input <- as.data.frame( cbind(BJCH_data0$os.time,BJCH_data0$os.event))
input$V1 <- as.numeric(input$V1)
pre1SOFL_bj <- plot_KMCurve(input,labels,font = "sans",color = c("black","indianred"),
                                risk.table = T,risk.table.ratio = 0.4,
                            title = "BJCH (Pretreated, Low risk)",
                                legend.pos = c(0.8,0.18),xlab="Months")
```

```
# figure--------------------------------
plot_grid(pre1_sysu,pre1SOFH_sysu,pre1SOFL_sysu,pre1_bj,pre1SOFH_bj,pre1SOFL_bj,ncol = 3,
                byrow = T,align = "v")
```



In summary, our data showed that patients who did not receive preoperative CTx and were assigned to the SOFs high-risk group are most likely to benefit from adjuvant CTx after resection of CRLM.