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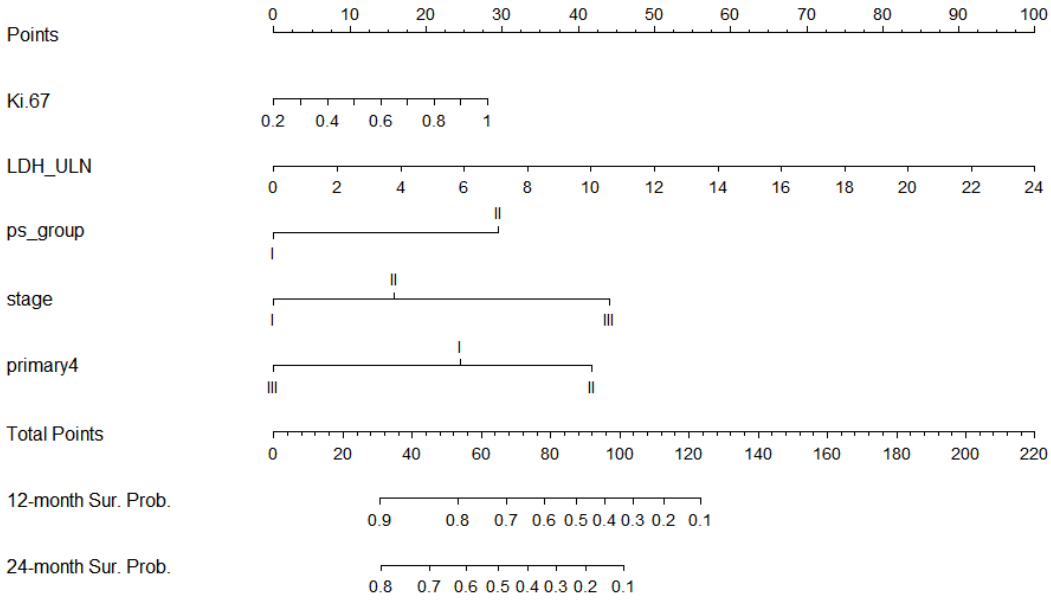
Supplemental Appendix for:
Development and validation of a prognostic nomogram to guide decision-making for high-grade digestive neuroendocrine neoplasms
Tao Zhanget al.

Supplementary Appendix

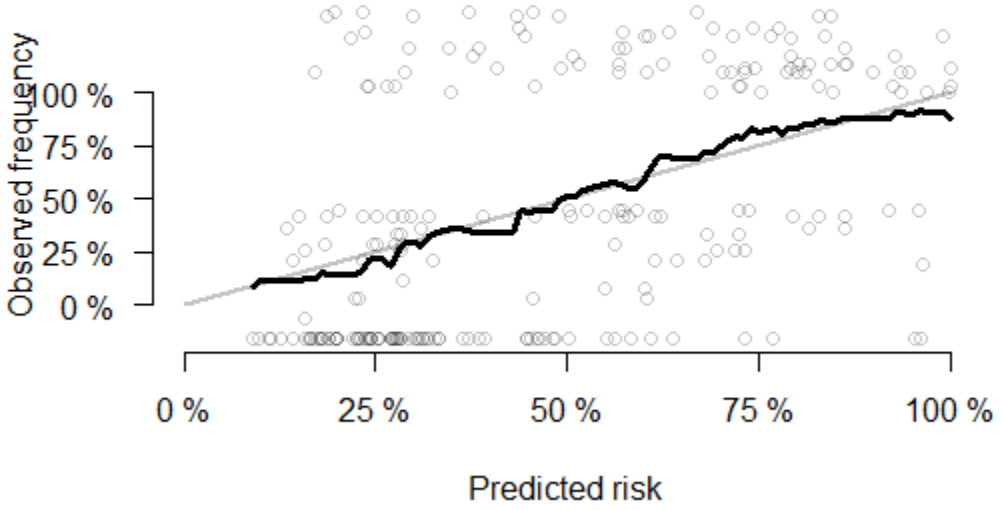
Repeated with a imputed dataset after multiple imputation

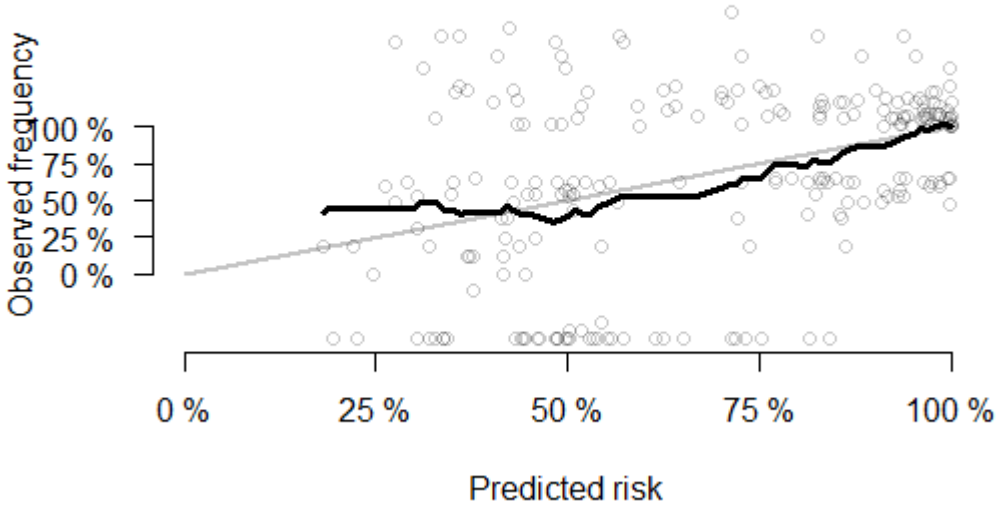
For nomogram after multiple imputation



Footnotes: LDH_UNL= Lactate dehydrogenase (upper normal limit); PS_GROUP= Performance status group (I: 0-1; II: ≥2); Stage: I=Localized, II=Regional, III=Distant; primary4 = site of primary tumor (I= Gastrointestinal tract, II= Hepato-biliary-pancreatic system, III=Unknown primary);

For calibration plot at 1 year in the development cohort





For calibration plot at 2 year in the development cohort

For AUC in the development cohort after multiple imputation

model times AUC se lower upper

1: coxph 6months 0.8032137 0.03497937 0.7346554 0.8717720

2: coxph 12months 0.8327024 0.03295456 0.7681127 0.8972922

3: coxph 24months 0.7856507 0.03880295 0.7095983 0.8617031

For AUC in the validation cohort after multiple imputation

model times AUC se lower upper

1: coxph 6 months 0.7474382 0.06881793 0.6125575 0.8823189

2: coxph 12months 0.7988768 0.06123301 0.6788623 0.9188913

3: coxph 24months 0.8284224 0.06383747 0.7033033 0.9535416

Supplementary R packages and related codes

The packages in R and the related codes that were used in this study are reported as follows:

>library(survival)

>library(riskRegression)

>library(table1)

>library(mice)

>library(QuantPsyc)

>library(rms)

#AIC for selecting Variables

>XHNO<-

coxph(Surv(os,mortality)~ps_group+stage+Ki.67+primary4+LDH_ULN+ALP_ULN+NLR+live

rM,xh, y=TRUE, x = TRUE)

>XHNO.backward=stepAIC(XHNO, direction="backward")

Start: AIC=727.38

Surv(os, mortality) ~ ps_group + stage + Ki.67 + primary4 + LDH_ULN +

ALP_ULN + NLR + liverM

Df AIC

- liverM 1 725.45

- ALP_ULN 1 726.42

- NLR 1 727.32

<none> 727.38

- primary4 2 729.65

- stage 2 731.85

- Ki.67 1 733.24

- LDH_ULN 1 733.51

- ps_group 1 734.75

Step: AIC=725.45

Surv(os, mortality) ~ ps_group + stage + Ki.67 + primary4 + LDH_ULN +

ALP_ULN + NLR

Df AIC

- ALP_ULN 1 724.51

- NLR 1 725.32

<none> 725.45

- primary4 2 727.71

- Ki.67 1 731.26

- LDH_ULN 1 731.81

- ps_group 1 732.77

- stage   2 738.18

Step: AIC=724.51

Surv(os, mortality) ~ ps_group + stage + Ki.67 + primary4 + LDH_ULN +

    NLR

           Df   AIC

- NLR   1 724.46

<none>   724.51

- primary4 2 727.37

- Ki.67   1 730.37

- LDH_ULN   1 730.82

- ps_group 1 731.87

- stage   2 737.59

Step: AIC=724.46

Surv(os, mortality) ~ ps_group + stage + Ki.67 + primary4 + LDH_ULN

           Df   AIC

<none>   724.46

- primary4 2 727.96

- Ki.67   1 731.28

- LDH_ULN   1 732.30

- ps_group 1 733.98

- stage   2 739.04

For Nomogram

```
>noldh=cph(Surv(os,mortality)~Ki.67 + LDH_ULN + ps_group +
        stage + primary4, xh, surv=TRUE)
>ddist <- datadist(xh)
>options(datadist='ddist')
>surv.cox <- Survival(noldh)
>nom.cox <- nomogram(noldh, fun=list(function(x) surv.cox(12, x), function(x) surv.cox(24,
x)), funlabel=c("12-month Sur. Prob.","24-month Sur. Prob."),lp=F)
>nom.cox
>plot(nom.cox )
```

For Computing the C-Index and 95% CI

```
>v=validate(XH2, method="boot",dxy=TRUE, B=1000)
>Dxy = v[rownames(v)=="Dxy", colnames(v)=="index.corrected"]
>orig_Dxy = v[rownames(v)=="Dxy", colnames(v)=="index.orig"]
>bias_corrected_c_index  <- abs(Dxy)/2+0.5
>orig_c_index <- abs(orig_Dxy)/2+0.5
```

For Calibration Curve and AUC

```
>score=Score(list(XH2),formula=Surv(os,mortality)~1,data=xh,
        plot=c("calibration","ROC"), summary = "risks",times=c(6,12,24))
>plotCalibration(score,times = 12)
>score$AUC$score
>ggplot(data = score$AUC$score, aes(x=times,y=AUC,colour=model))+
  geom_point()+  geom_line()
```

For Calibration with internally cross validation method

>score.cv=Score(list(XH2),formula=Surv(os,mortality)~1,data=xh,plot=c("calibration","ROC"),

split.method="bootcv", B=1000,plots = "calibration",

summary = "risks", times=c(6,12,24))

 # For External Validation of Nomogram and Calibration Curve for Validation Cohort

>PNI<-coxph(Surv(os,mortality)~ score, zs4,y=TRUE, x = TRUE)

>summary(PNI) , 95%CI, 1.96 × se; se = S.D./2

>v=validate(PNI, method="boot",dxy=TRUE, B=1000)

>Score.ex=Score(list(PNI),formula=Surv(os,mortality)~1,data=zs4,

plot=c("calibration","ROC"),

summary = "risks",times=c(6,12,24))

 # For multiple imputation

>imp <- mice(cb, seed=12345)

>cb2<-with(imp,coxph(Surv(os,mortality)~ps_group+stage+Ki.67+primary4+LDH_ULN,

y=TRUE, x = TRUE))

> dt5<-complete(imp2, action=5)

> cb5<-coxph(Surv(os,mortality)~ps_group+stage+Ki.67+primary4+LDH_ULN,dt5, y=TRUE,

x = TRUE)

coef exp(coef) se(coef) z Pr(>|z|)

ps_groupII 0.97656 2.65531 0.25631 3.810 0.000139 ***

stageII 0.52596 1.69208 0.44962 1.170 0.242091

stageIII 1.46565 4.33035 0.44340 3.305 0.000948 ***

Ki.67 1.16505 3.20608 0.50036 2.328 0.019890 *

primary4II 0.57247 1.77264 0.22000 2.602 0.009263 **

primary4III -0.81284 0.44359 0.49305 -1.649 0.099228 .

LDH_ULN 0.13835 1.14838 0.03223 4.293 1.76e-05 ***