LDA_IGA-NTX

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§ 1

Load required packages:

```
#if (Sys.info()["sysname"] != "Darwin"){
#  default_theme <- theme_minimal() +
#  theme(text = element_text(family = "Decima WE", size = 15)) +
#  theme(panel.grid.major = element_line(color = "grey", size = 0.3)) +
#  theme(axis.line = element_line(color = "black", size = 0.4))
#
#} else {
#  default_theme <- theme_minimal()
#}
default_theme <- theme_minimal()
two_scale_fill <- scale_fill_manual(values=c("#69b3a2", "#404080"))
```

Read data using read_data.R scrip:

```
source("read_data.R")
```

§ 2 EDA

```
follow_up <- years(10)
```

§ 2.1 IGA

```
# follow-up (mean)
(interval(data_iga2$`T-date`, data_iga2$`T-dls`) / years(1)) %>%
  mean()
```

```
## [1] 7.728562
```

```
# patient death within follow up
nrow(data_iga2[(`T-dls` <= (`T-date` + follow_up)) & `Pat death (0=alive, 1= dead)` == 1])
```

```
## [1] 23
```

```
# patient drop out
nrow(data_iga2[(`T-dls` <= (`T-date` + follow_up)) & `Pat death (0=alive, 1= dead)` == 0])
```

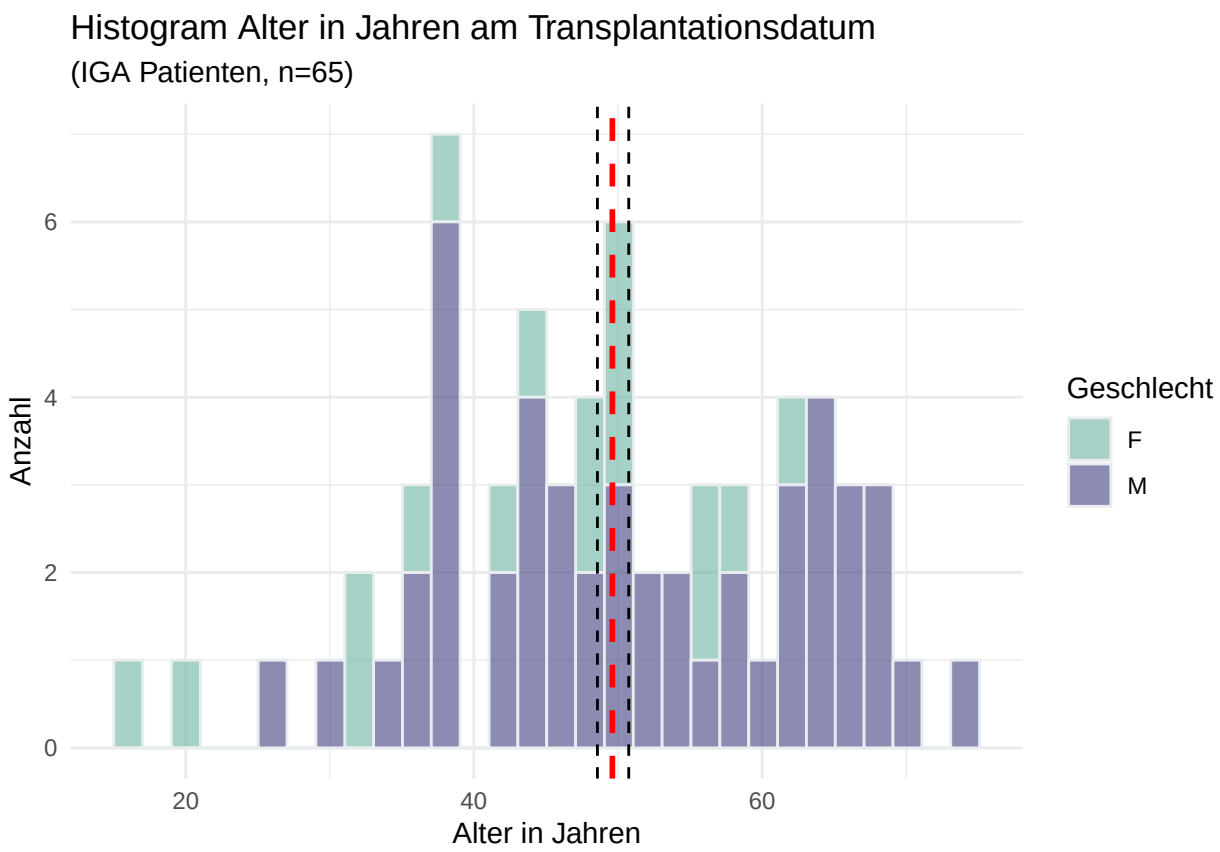
```
## [1] 27
```

```
# patients with graft loss
nrow(data_iga2[`graft loss (0=functial, 1=loss)` == 1])
```

```
## [1] 15
```

```
# age patients (yrs.)
ggplot(data = data_iga2) +
  geom_histogram(mapping = aes(x = interval(`Date of birth`,`T-date`) / years(1),
                               fill = `R-sex`),
                 color="#e9ecef",
                 alpha=0.6) +
  two_scale_fill +
  # median age total
  geom_vline(aes(xintercept = median(
    interval(`Date of birth`,`T-date`) / years(1))
    ), size = 1.0, color = "red", linetype = "dashed") +
  # median age F
  geom_vline(aes(xintercept = median(
    interval(`Date of birth`,`T-date`) / years(1))
    ), data = data_iga2[`R-sex` == "F"], linetype = "dashed") +
  # median M
  geom_vline(aes(xintercept = median(
    interval(`Date of birth`,`T-date`) / years(1))
    ), data = data_iga2[`R-sex` == "M"], linetype = "dashed") +
  ylab("Anzahl") +
  xlab("Alter in Jahren") +
  ggtitle("Histogram Alter in Jahren am Transplantationsdatum",
          subtitle =  paste0("(IGA Patienten, n=",
          sum(!is.na(data_iga2$`Date of birth`)),
          ")", collapse = "")) +
  labs(fill = "Geschlecht") +
  default_theme
```

```
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```

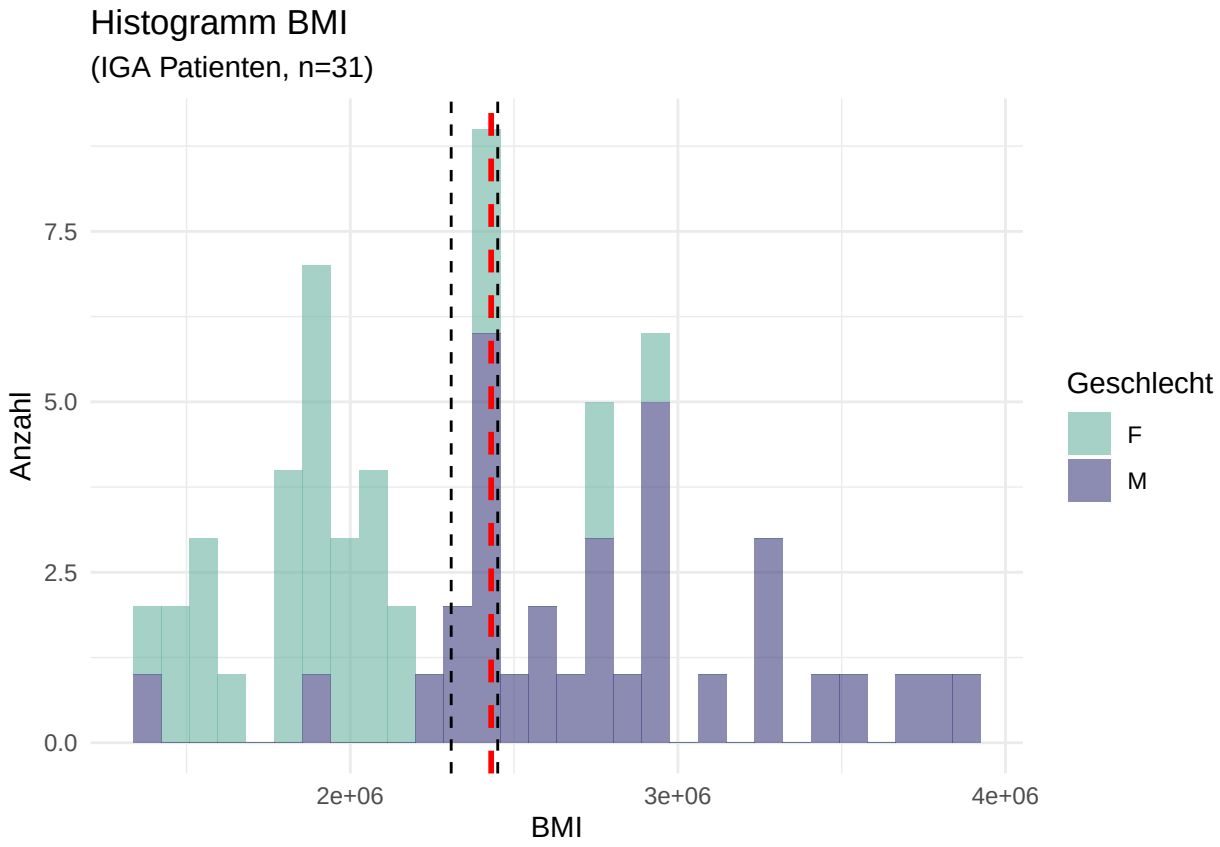



```
# male sex
summary(data_iga2$`R-sex`)
```

```
##  F  M
## 17 48
```

```
# BMI (mean.)
ggplot(data = data_iga2) +
  geom_histogram(mapping = aes(`D-weight` * (`D-height`)^2,
                               fill = `D-sex`),
                 alpha = 0.6) +
  two_scale_fill +
  # median BMI total
  geom_vline(aes(xintercept = median(`D-weight` * (`D-height`)^2)),
             size = 1.0, color = "red", linetype = "dashed") +
  # median BMI F
  geom_vline(aes(xintercept = median(`D-weight` * (`D-height`)^2)),
             data = data_iga2[`R-sex` == "F"], linetype = "dashed") +
  # median BMI M
  geom_vline(aes(xintercept = median(`D-weight` * (`D-height`)^2)),
             data = data_iga2[`R-sex` == "M"], linetype = "dashed") +
  ylab("Anzahl") +
  xlab("BMI") + # Einheit???
  ggtitle("Histogramm BMI", subtitle = paste0("(IGA Patienten, n=",
                                              sum(!is.na(data_iga2$`R-height`)),
                                              ")", collapse = "")) +
  labs(fill = "Geschlecht") +
  default_theme
```

```
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```




```
# deceased D.
# living D.
tbl_1 <- summary(data_iga2[`graft loss (0=functial, 1=loss)` == 1]$`D-type`)
tbl_1 <- round(tbl_1 / sum(tbl_1), 3)
tbl_2 <- summary(data_iga2[`graft loss (0=functial, 1=loss)` == 0]$`D-type`)
tbl_2 <- round(tbl_2 / sum(tbl_2),3)  # in %
rbind("loss" = tbl_1, "functional" = tbl_2)
```

```
##            Cadaver Living
## loss         0.867  0.133
## functional   0.740  0.260
```

```
tbl_1 <- summary(data_iga2[`Pat death (0=alive, 1= dead)` == 1]$`D-type`)
tbl_1 <- round(tbl_1 / sum(tbl_1), 3)
tbl_2<- summary(data_iga2[`Pat death (0=alive, 1= dead)` == 0]$`D-type`)
tbl_2 <-  round(tbl_2 / sum(tbl_2),3)  # in %
rbind("dead" = tbl_1, "alive" = tbl_2)
```

```
##       Cadaver Living
## dead    0.917  0.083
## alive   0.683  0.317
```

```
# BMI (mean.)
mean(data_iga2$`D-weight` * (data_iga2$`D-height`)^2)
```

```
## [1] 2393290
```

```r
# HLA-mm (0-6)
## data.table of mm-A, mm-B and mm-DR
tbl_1 <- as.data.table(lapply(data_iga2[, c("mm-A", "mm-B", "mm-DR")],
                              as.numeric))
## calculate mean for each column
tbl_2 <- apply(X = tbl_1,
               MARGIN = 2,
               FUN = mean, na.rm = TRUE)
round(tbl_2, 3)
```

```
##  mm-A  mm-B mm-DR
## 1.776 2.143 1.918
```

```r
# mean of means
round(mean(tbl_2),3)
```

```
## [1] 1.946
```

```r
## sum of mm-A, mm-B and mm-DR
tbl_3 <- apply(X = tbl_1,
               MARGIN = 1,
               FUN = sum, na.rm = TRUE)
# mean value
mean(tbl_3)
```

```
## [1] 4.4
```

```r
# median value
sd(tbl_3)
```

```
## [1] 2.691422
```

```r
# PRA current (mean)
# PRA highest (mean)
data_iga2[, c("Current PRA%", "Highest PRA%")] %>%
  apply(MARGIN = 2,
        FUN = mean, na.rm = TRUE)
```

```
## Current PRA% Highest PRA%
##     5.163934    10.786885
```

```r
# age donor (mean.)
mean(data_iga2$`D-age`)
```

```
## [1] 50.33846
```

```r
# cold-ischemia time (hours)
# mean
mean(data_iga2$`Cold ischaemic period hours`, na.rm = TRUE)
```

```
## [1] 11.61224
```

```r
# median
median(data_iga2$`Cold ischaemic period hours`, na.rm = TRUE)
```

```
## [1] 12
```

```r
# standard error
sd(data_iga2$`Cold ischaemic period hours`, na.rm = TRUE)
```

```
## [1] 6.330536
```

```
# living vs dead donator
cbind("Living" = nrow(data_iga2[`D-type` == "Living"]),
      "Cadaver" = nrow(data_iga2[`D-type` == "Cadaver"])
)
```

```
##      Living Cadaver
## [1,]     15      50
```

§ 2.2 NTX

§ 3 Kaplan-Meier

§ 3.1 IGA

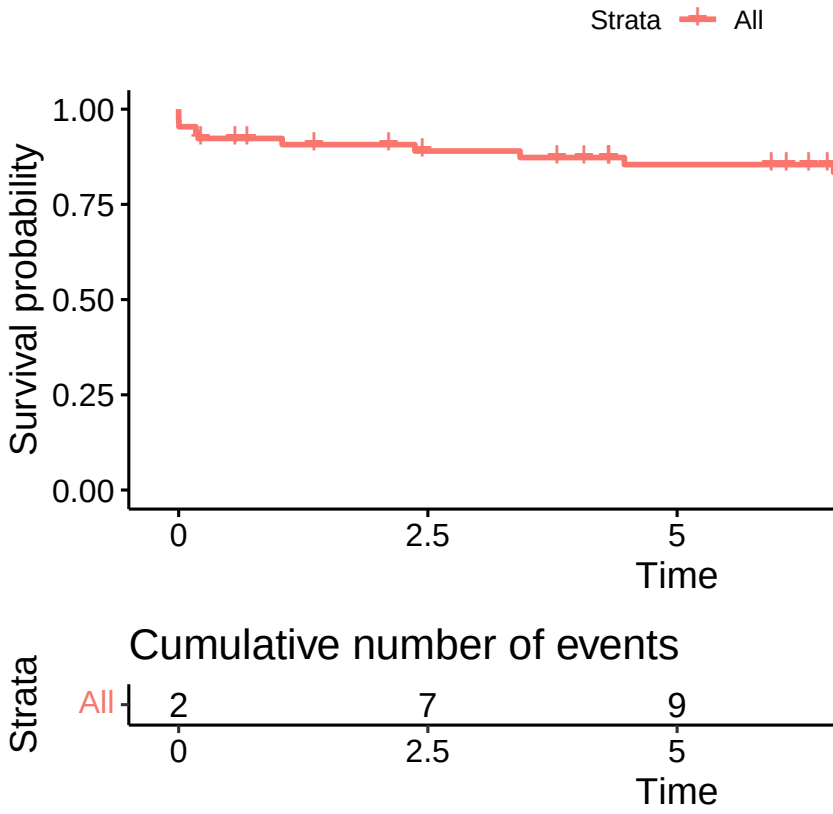
```
#  functions in survival and survminer package need numeric-type input
data_iga2[, time_date_biopsy := interval(`T-date`, `date of biopsy`) / years(1)]
data_iga2[, time_t_dls := interval(`T-date`, `T-dls`) / years(1)]
data_iga2[, time_date_birth := interval(`T-date`, `Date of birth`) / years(1)]
data_iga2[, time_graft_loss := interval(`T-date`, `graft loss date`) / years(1)]
data_iga2[, time_date_follow_up := interval(`T-date`,`T-date` + follow_up) / years(1)]
```

§ 3.1.1

- Event:
  - graft-loss within the follow up period.
- Censoring scheme:
  - if `graft loss date` after follow up period, censored by end of follow up.
  - if `T-dls` (date last seen) within follow up period, censored by `T-dls`.
- Time period:
  - 10 years after `T-date` (kidney transplantaion).

```
data_iga2 <- data_iga2 %>%
  mutate(status_date = case_when(
    ## graft-loss within follow up period
    !is.na(`graft loss date`) & `graft loss date` <  `T-date` + follow_up ~ time_graft_loss,
    ## graft-loss after follow up period
    !is.na(`graft loss date`) & `graft loss date` >  `T-date` + follow_up ~ time_date_follow_up,
    ## no graft-loss and last seen within follow up
    is.na(`graft loss date`) & !is.na(`T-dls`) & `T-dls` < `T-date` + follow_up ~ time_t_dls,
    ## no graft-loss and last seen after follow up
    is.na(`graft loss date`) & !is.na(`T-dls`) & `T-dls` > `T-date` + follow_up ~ time_date_follow_up,
    ## no graft loss and no last seen
    is.na(`graft loss date`) & is.na(`T-dls`) ~ time_date_follow_up
                                  )
  )
data_iga2 <- data_iga2 %>%
  mutate(status = case_when(
    ## graft-loss within follow up period
    !is.na(`graft loss date`) & `graft loss date` <  `T-date` + follow_up ~ 1,
    ## else censored
    TRUE ~ 0,
                                  )
  )
```

```
model_iga_1 <- survfit(formula = Surv(time = status_date,
                                      event = status, type = "right")~ 1,
                       data = data_iga2)
ggsurvplot(model_iga_1,
           conf.int = FALSE,
           cumevents = TRUE)
```



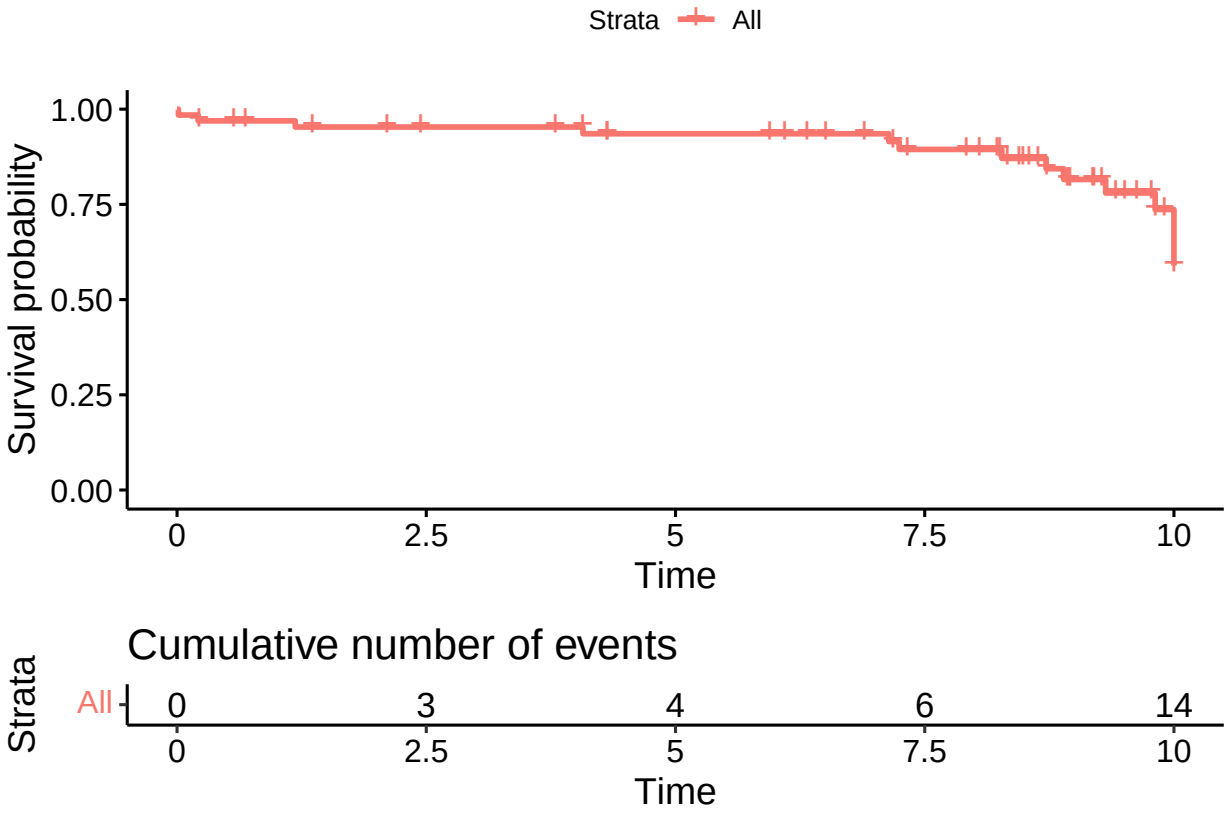
Overall kaplan-Meier curve (no stratification)

§ 3.1.2

- Event:
  - `T-dls` & '`Pat death (0=alive, 1= dead)` (patient death).
- Censoring scheme:
  - `T-dls` (date last seen) within follow up period.
- Time period:
  - 10 years after `T-date` (kidney transplantaion).

```
data_iga2 <- data_iga2 %>%
  mutate(status_date = case_when(
    ## patient death and death date within follow up
    (`Pat death (0=alive, 1= dead)` == 1) & `T-dls` < `T-date` + follow_up ~ time_t_dls,
    ## patient dead but after follow up
    (`Pat death (0=alive, 1= dead)` == 1) & `T-dls` > `T-date` + follow_up ~ time_date_follow_up,
    ## patient not death but dropped within follow up
    (`Pat death (0=alive, 1= dead)` == 0) & `T-dls` < `T-date` + follow_up ~ time_t_dls,
    ## patient not death but dropped after follow up
    (`Pat death (0=alive, 1= dead)` == 0) & `T-dls` > `T-date` + follow_up ~ time_date_follow_up,
    ## NOTE: T-dls never NA
  )
)
```

```
model_iga_2 <- survfit(formula = Surv(time = status_date,
                                      event = status, type = "right")~ 1,
                       data = data_iga2)
ggsurvplot(model_iga_2,
           conf.int = FALSE,
           cumevents = TRUE)
```



§ 3.1.3

- Event: graft loss and death
- Censoring scheme:
- Time period:

§ 4 Cox regression

§ 4.1 IGA

```
data_iga2 <- data_iga2 %>%
  ## censor/event date
  mutate(status_date = case_when(
    ## patient dropped during follow up
    (`T-dls` <= `T-date` + follow_up) ~ `T-dls`,
    ## patient experienced graft loss but after follow up
    ((!is.na(`graft loss date`)) &  (`graft loss date` > `T-date` + follow_up)) ~ `T-date` + follow_up,
    ## patient experienced graft loss within follow up
    ((!is.na(`graft loss date`)) &  (`graft loss date` <= `T-date` + follow_up)) ~ `graft loss date`,
    ## patient experienced no graft loss within follow up, neither dropped
    (is.na(`graft loss date`) & (`T-dls` > `T-date` + follow_up)) ~ `T-date` + follow_up
  )) %>%
  ## status indicator
  mutate(status = case_when(
    ## patient dropped during follow up
    (`T-dls` <= `T-date` + follow_up) ~ 0,
    ## patient experienced graft loss but after follow up
```

```
    ((!is.na(`graft loss date`)) &  (`graft loss date` > `T-date` + follow_up)) ~ 0,
    ## patient experienced graft loss within follow up
    ((!is.na(`graft loss date`)) &  (`graft loss date` <= `T-date` + follow_up)) ~ 1,
    ## patient experienced no graft loss within follow up, neither dropped
    (is.na(`graft loss date`) & (`T-dls` > `T-date` + follow_up)) ~ 0
  ))
```

```
data_iga2 <- data_iga2 %>%
  ## censor/event date
  mutate(status_date = case_when(
    ## if graft loss within follow up
    `graft loss date` <= `T-date` + follow_up ~ `graft loss date`,
    ## else
    TRUE ~ `T-dls`
  )) %>%
  ## censor/event indicator
  mutate(status = case_when(
    ## if graft loss within follow up
    data_iga2$`graft loss date` <= data_iga2$`T-date` + follow_up ~ 1,
    ## else
    TRUE ~ 0
  ))
```

```
model_iga_cox <- coxph(formula = Surv(time = as.numeric(status_date),
                                      event = status) ~ R_age_Tdate +
                         ##
                         data_iga2$`D-age` +
                         data_iga2$`D-sex` +
                         data_iga2$`R-sex`,
                         data = data_iga2)
summary(model_iga_cox)
```

```
## Call:
## coxph(formula = Surv(time = as.numeric(status_date), event = status) ~
##     R_age_Tdate + data_iga2$`D-age` + data_iga2$`D-sex` + data_iga2$`R-sex`,
##     data = data_iga2)
##
##   n= 65, number of events= 14
##
##                          coef exp(coef)  se(coef)      z Pr(>|z|)
## R_age_Tdate        -0.009528  0.990517  0.023006 -0.414    0.679
## data_iga2$`D-age`   0.044603  1.045613  0.030033  1.485    0.138
## data_iga2$`D-sex`M -1.566856  0.208700  0.656309 -2.387    0.017 *
## data_iga2$`R-sex`M -0.239641  0.786911  0.624461 -0.384    0.701
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                    exp(coef) exp(-coef) lower .95 upper .95
## R_age_Tdate           0.9905     1.0096   0.94685    1.0362
## data_iga2$`D-age`     1.0456     0.9564   0.98584    1.1090
## data_iga2$`D-sex`M    0.2087     4.7916   0.05766    0.7554
## data_iga2$`R-sex`M    0.7869     1.2708   0.23141    2.6759
##
## Concordance= 0.75  (se = 0.062 )
```

```
## Likelihood ratio test= 10.34  on 4 df,   p=0.04
## Wald test            = 7.53  on 4 df,   p=0.1
## Score (logrank) test = 9.2  on 4 df,   p=0.06
```

```
## check prop. hazard assumptions
```