

Survival Analysis: Ovarian Cancer

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October 18, 2019

Ovarian Cancer:

Survival in a randomised trial comparing two treatments for ovarian cancer. Format

Treatment of patients with advanced ovarian carcinoma (stages IIIB and IV) using either cyclophosphamide alone (1 g/m²) or cyclophosphamide (500 mg/m²) plus adriamycin (40 mg/m²) by iv injection every 3 weeks each produced partial regression in approximately one third of the patients.

```
data("ovarian")
attach(ovarian)

Status <- ifelse(fustat == 0, "Death", "Censored")
Progression <- ifelse(resid.ds == 1, "No Progression", "Progression")
Treatment <- ifelse(rx == 1, "Endoxan alone", "Endoxan + Adria")
Performance <- ifelse(ecog.ps == 1, "High", "Low")
dummy_Age <- ifelse(age >= 50, "Old", "Young")

ex <- data.frame(Status, Progression, Treatment, Performance, dummy_Age)

Ovarian <- cbind(ovarian, ex)

Ovarian$dummy_Age <- factor(Ovarian$dummy_Age)
Ovarian$Status <- factor(Ovarian$Status)
Ovarian$Progression <- factor(Ovarian$Progression)
Ovarian$Treatment <- factor(Ovarian$Treatment)
Ovarian$Performance <- factor(Ovarian$Performance)

write.csv(Ovarian, file="ovarian.csv")
ovarian <- read.csv(choose.files(), header = T)
attach(ovarian)
```

Description:

```
##              Description
## futime      Survival or Censoring time
## fustat      Censoring status
## age         Age in years
## resid.ds    Residual disease present
## rx          Treatment Group
## ecog.ps     ECOG Performance Status
```

```
summary(ovarian)
```

```
##      X      futime      fustat      age
## Min.   : 1.00   Min.    : 59.0   Min.    :0.0000   Min.    :38.89
```

```
## 1st Qu.: 7.25    1st Qu.: 368.0    1st Qu.:0.0000    1st Qu.:50.17
## Median :13.50    Median : 476.0    Median :0.0000    Median :56.85
## Mean   :13.50    Mean   : 599.5    Mean   :0.4615    Mean   :56.17
## 3rd Qu.:19.75    3rd Qu.: 794.8    3rd Qu.:1.0000    3rd Qu.:62.38
## Max.   :26.00    Max.   :1227.0    Max.   :1.0000    Max.   :74.50
##      resid.ds      rx      ecog.ps      Status
## Min.   :1.000    Min.   :1.0    Min.   :1.000    Censord:12
## 1st Qu.:1.000    1st Qu.:1.0    1st Qu.:1.000    Death  :14
## Median :2.000    Median :1.5    Median :1.000
## Mean   :1.577    Mean   :1.5    Mean   :1.462
## 3rd Qu.:2.000    3rd Qu.:2.0    3rd Qu.:2.000
## Max.   :2.000    Max.   :2.0    Max.   :2.000
##      Progression      Treatment      Performance      dummy_Age
## No Progression:11    Endoxan + Adria:13    High:14    Old :20
## Progression :15    Endoxan alone :13    Low :12    Young: 6
##
##
##
##
```

First, Analysis of Variance:

1- Age:

```
AGE_mean <- as.data.frame(ovarian %>%
  summarise(count = n(), mean = mean(age, na.rm = T), sd = sd(age, na.rm = T)))
AGE_mean
```

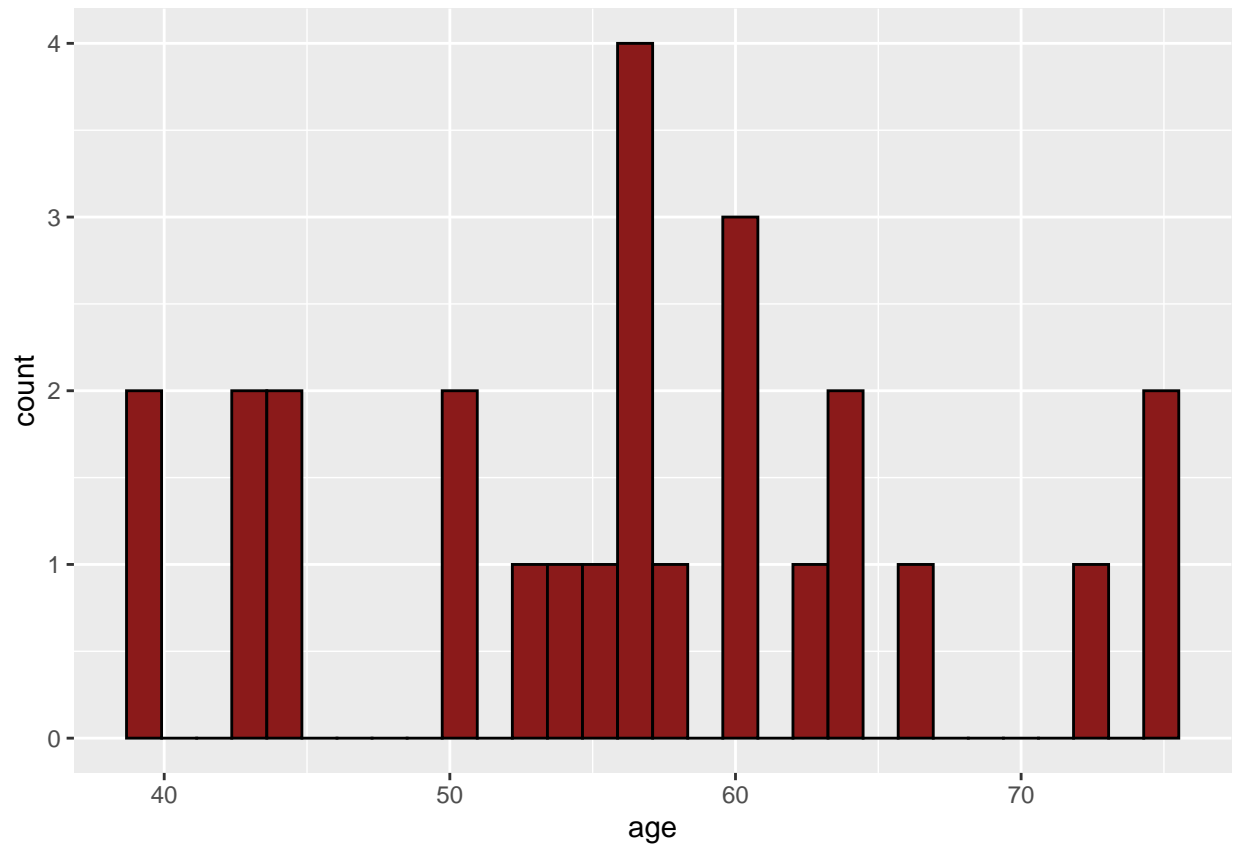
```
##      count      mean      sd
## 1      26 56.16544 10.10036
```

```
summary(ovarian$age)
```

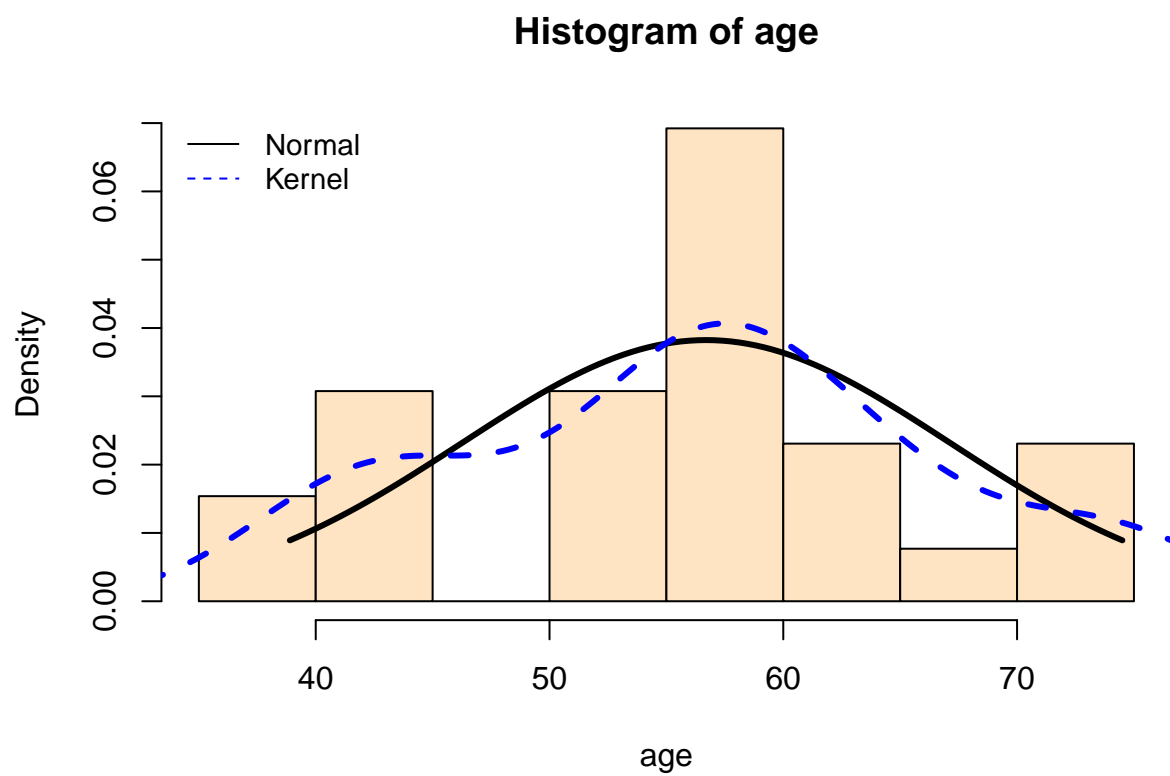
```
##      Min. 1st Qu.  Median      Mean 3rd Qu.      Max.
## 38.89   50.17   56.85   56.17   62.38   74.50
```

```
ggplot(ovarian, aes(x= age)) +
  geom_histogram(aes(y=..count..), color = "black", fill="firebrick4")
```

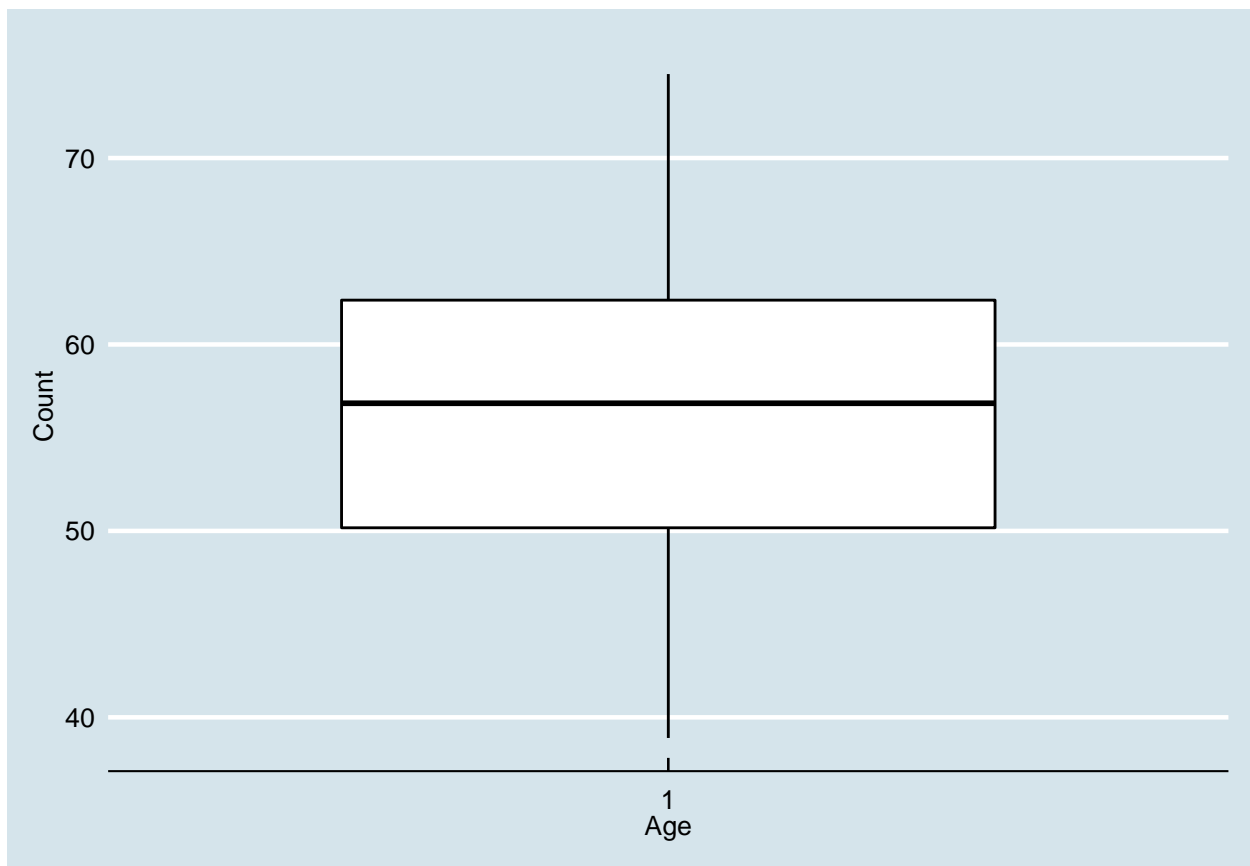
```
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```



```
hist (age , col="bisque" , freq=FALSE)
meanx <- mean( age )
sdx <- sd (age)
curve (dnorm(x , mean=mean(x) , sd=sd(x) ) ,
from=min(age ) , to=max(age) , add=TRUE,
lty=1, col="Black " , lwd=3)
kernel <- density (age)
points ( kernel$x , kernel$y , type="l " ,
lty=2, col="blue " , lwd=3)
legend ("topleft" , c ("Normal " , "Kernel") , lty=c (1 ,2) ,
bty="n" , cex=.9 , col=c (" black " , " blue "))
```



```
ggboxplot(age, xlab = "Age") +  
  labs(x = "Age", y = "Count", main = "Age Normality", fill = "age") +  
  theme_economist()
```



```
skewness(age)
```

```
## [1] 0.04340272
```

```
kurtosis(age)
```

```
## [1] -0.6562135
```

```
shapiro.test(age)
```

```
##  
## Shapiro-Wilk normality test  
##  
## data: age  
## W = 0.96169, p-value = 0.4259
```

```
t.test(age, mu=56.17, conf.level = 0.95)
```

```
##  
## One Sample t-test  
##  
## data: age  
## t = -0.0023009, df = 25, p-value = 0.9982
```

```
## alternative hypothesis: true mean is not equal to 56.17
## 95 percent confidence interval:
##  52.08582 60.24507
## sample estimates:
## mean of x
##  56.16544
```

Mean age of population of Intrest is 56.17 and standard Deviation is 10.1. Age of Patients: From 38.89 To 74.5 years.

The Distribution is moderatly Skewed & approximatly Symmetric, and Kurtosis is in acceptable range for bing normally distributed.

From the output, the p-values= 0.4259 > the significance level 0.05, implying that the distribution of the data are not significantly different from the normal distribution.

In other words, we can assume the normality, Normally Distributed.

The p-value of one sample t.test is 0.9982, which is greater than the significance level $\alpha = 0.05$. We can conclude that average Ages is not significantly different from there mean with a p-value = 0.9982.

=====

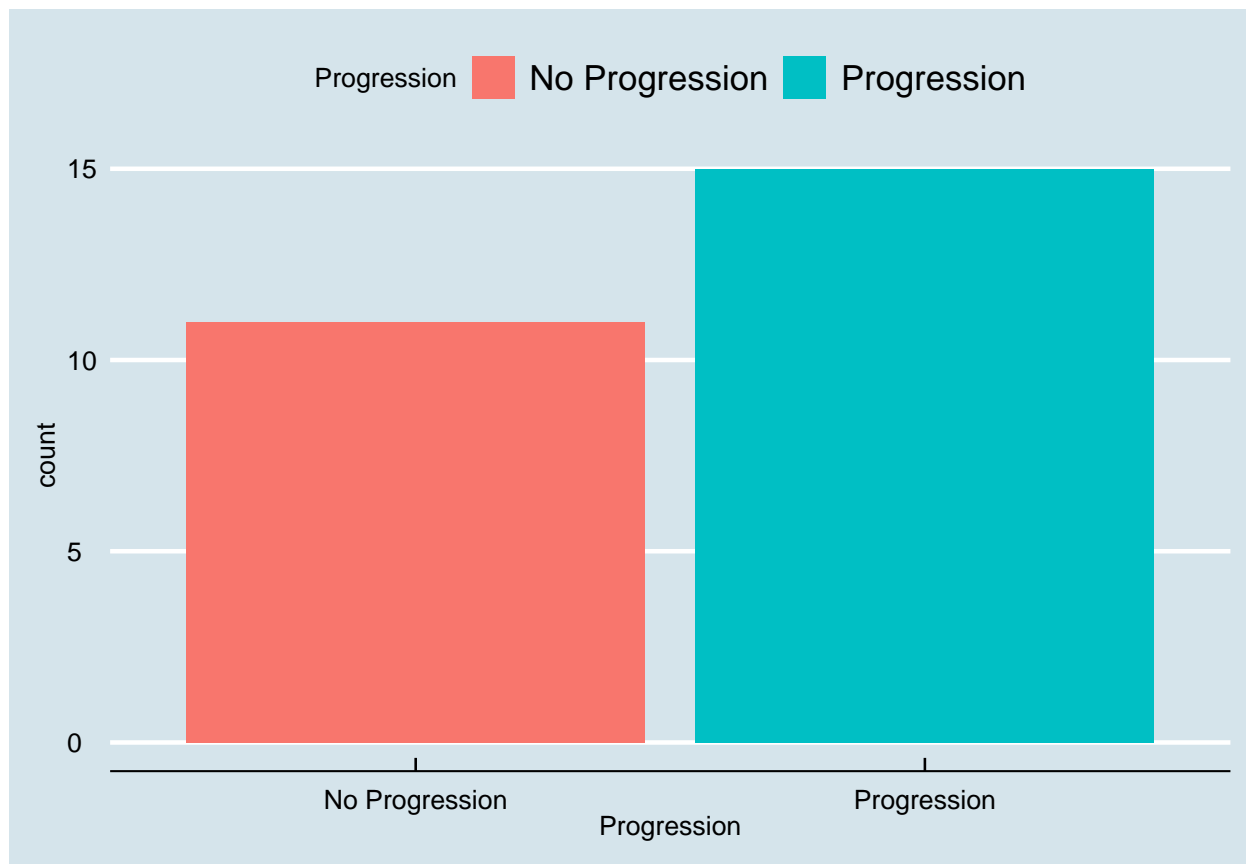
2- Progression:

```
Count_Prog <- table(ovarian$Progression)
Percent_Prog <- prop.table(Count_Prog)*100

Prog_persent <- as.data.frame(cbind(Count_Prog, Percent_Prog))
Prog_persent
```

```
##           Count_Prog Percent_Prog
## No Progression      11    42.30769
## Progression         15    57.69231
```

```
ggplot(ovarian,aes(Progression, fill= Progression)) +
  geom_bar(stat="count") +
  theme_economist()
```



```
chisq.test(Count_Prog)
```

```
##
## Chi-squared test for given probabilities
##
## data: Count_Prog
## X-squared = 0.61538, df = 1, p-value = 0.4328
```

The p-value of the Chi.Square test is 0.4328, which is greater than the significance level $\alpha = 0.05$. We can conclude that Progression is significantly commonly distributed with a p-value = 0.4328.

=====

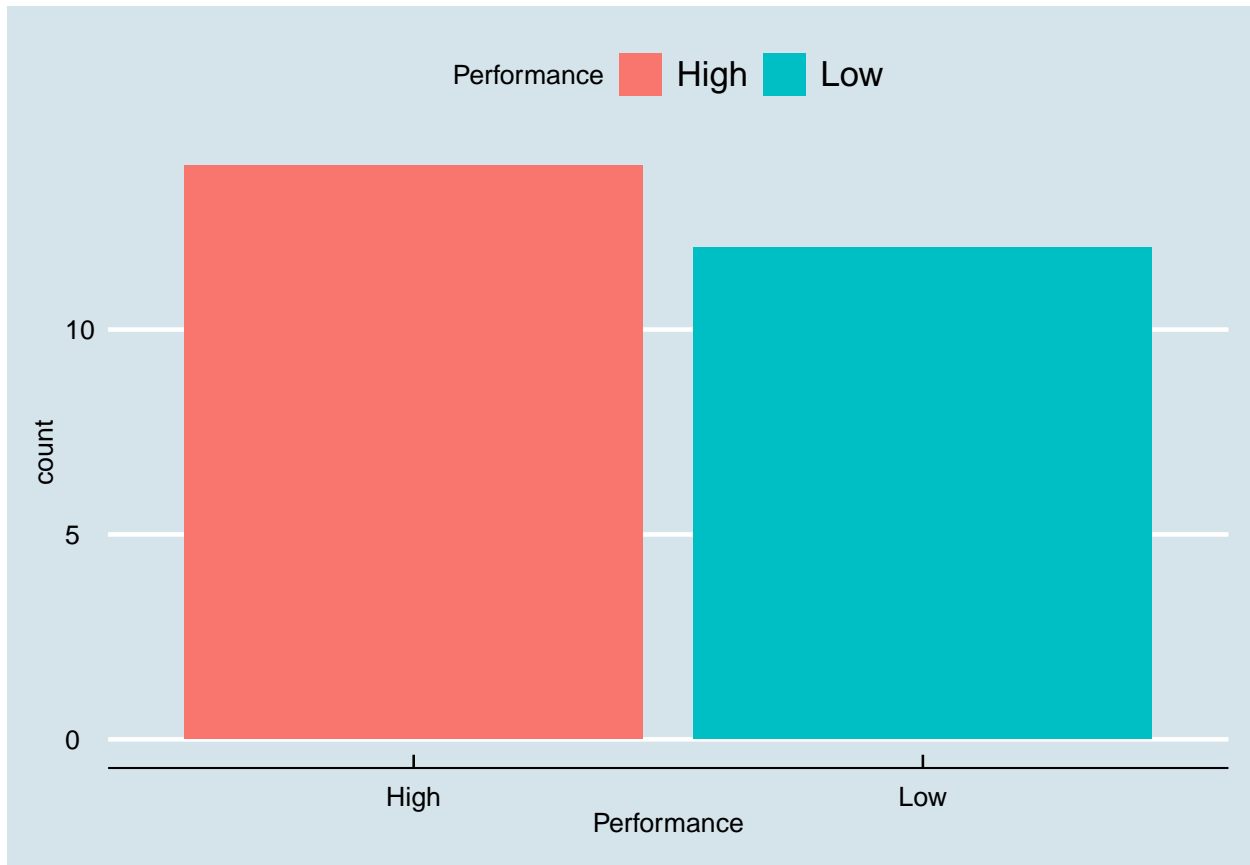
3- ECOG Performance Status:

```
Count_per <- table(ovarian$Performance)
Percent_per <- prop.table(Count_per)*100

per_persent <- as.data.frame(cbind(Count_per, Percent_per))
per_persent
```

```
##      Count_per Percent_per
## High         14    53.84615
## Low          12    46.15385
```

```
ggplot(ovarian, aes(Performance, fill= Performance)) +
  geom_bar(stat="count") +
  theme_economist()
```



```
chisq.test(Count_per)
```

```
##
## Chi-squared test for given probabilities
##
## data: Count_per
## X-squared = 0.15385, df = 1, p-value = 0.6949
```

The p-value of the Chi.Square test is 0.6949, which is greater than the significance level $\alpha = 0.05$. We can conclude that ECOG Performance Status is significantly commonly distributed with a p-value = 0.6949.

Second, Survival Analysis:

Kaplan-Meier Estimator:

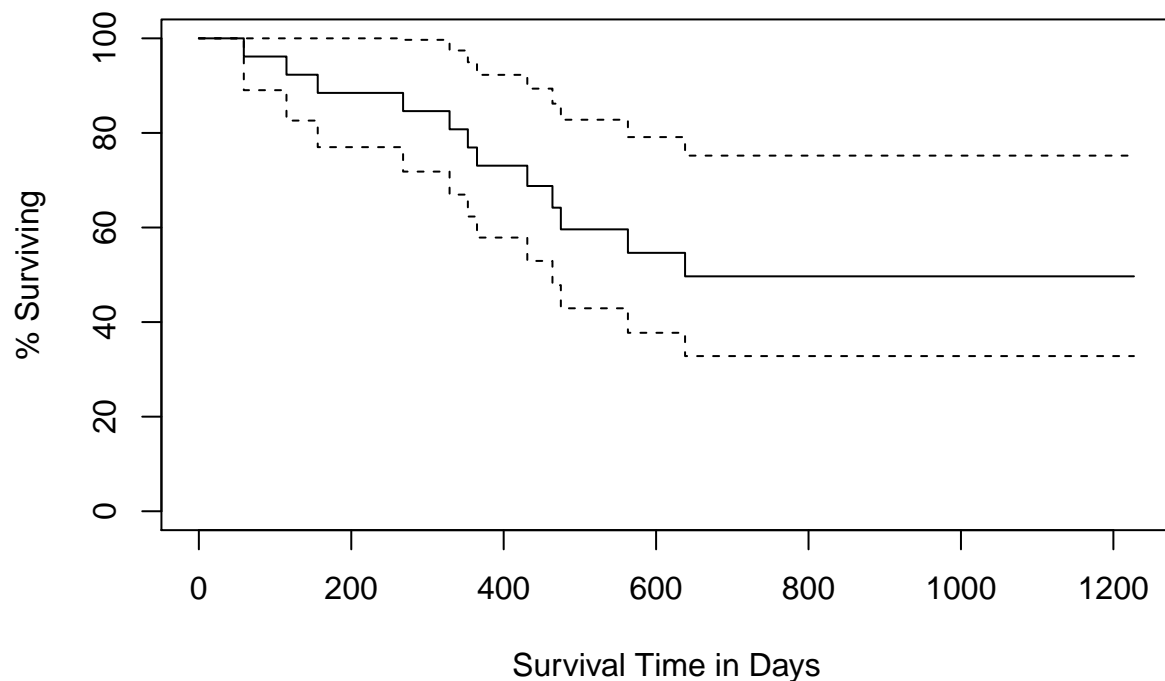

```
survobj <- with(ovarian, Surv(futime, fustat))

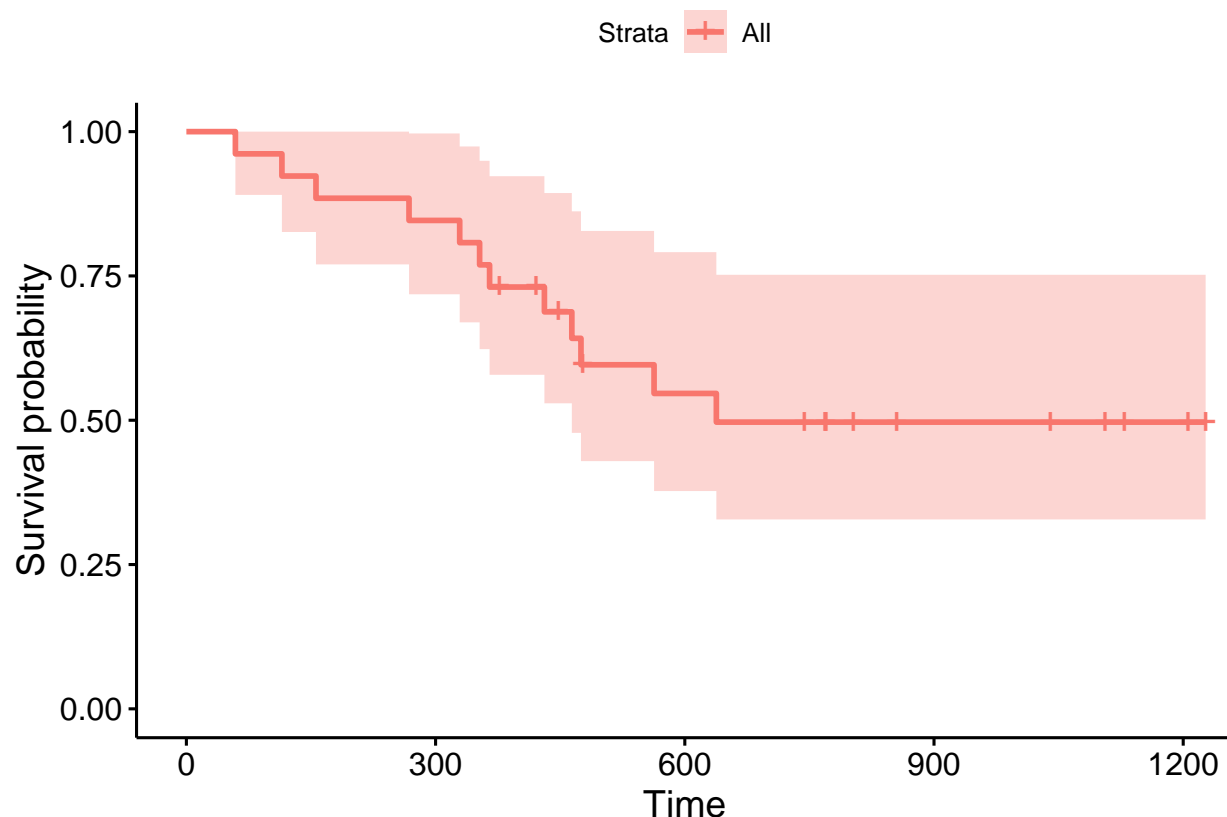
surviv <- survfit(survobj ~ 1, data = ovarian)
summary(surviv)
```

```
## Call: survfit(formula = survobj ~ 1, data = ovarian)
##
##   time n.risk n.event survival std.err lower 95% CI upper 95% CI
##    59     26      1   0.962  0.0377    0.890    1.000
##   115     25      1   0.923  0.0523    0.826    1.000
##   156     24      1   0.885  0.0627    0.770    1.000
##   268     23      1   0.846  0.0708    0.718    0.997
##   329     22      1   0.808  0.0773    0.670    0.974
##   353     21      1   0.769  0.0826    0.623    0.949
##   365     20      1   0.731  0.0870    0.579    0.923
##   431     17      1   0.688  0.0919    0.529    0.894
##   464     15      1   0.642  0.0965    0.478    0.862
##   475     14      1   0.596  0.0999    0.429    0.828
##   563     12      1   0.546  0.1032    0.377    0.791
##   638     11      1   0.497  0.1051    0.328    0.752
```

```
plot(surviv, xlab = "Survival Time in Days", ylab = "% Surviving", yscale = 100, main = "Survival Distr
ggsurvplot(surviv, data = ovarian, pval = TRUE)
```

Survival Distribution (Overall)





1- Compare the Survival Distribution Between Old and Young Female Patients (Survival Curves):

```
surviv1 <- survfit(survobj ~ dummy_Age, data = ovarian)
surviv1
```

```
## Call: survfit(formula = survobj ~ dummy_Age, data = ovarian)
```

```
##
```

```
##           n events median 0.95LCL 0.95UCL
```

```
## dummy_Age=Old  20    11   563    431    NA
```

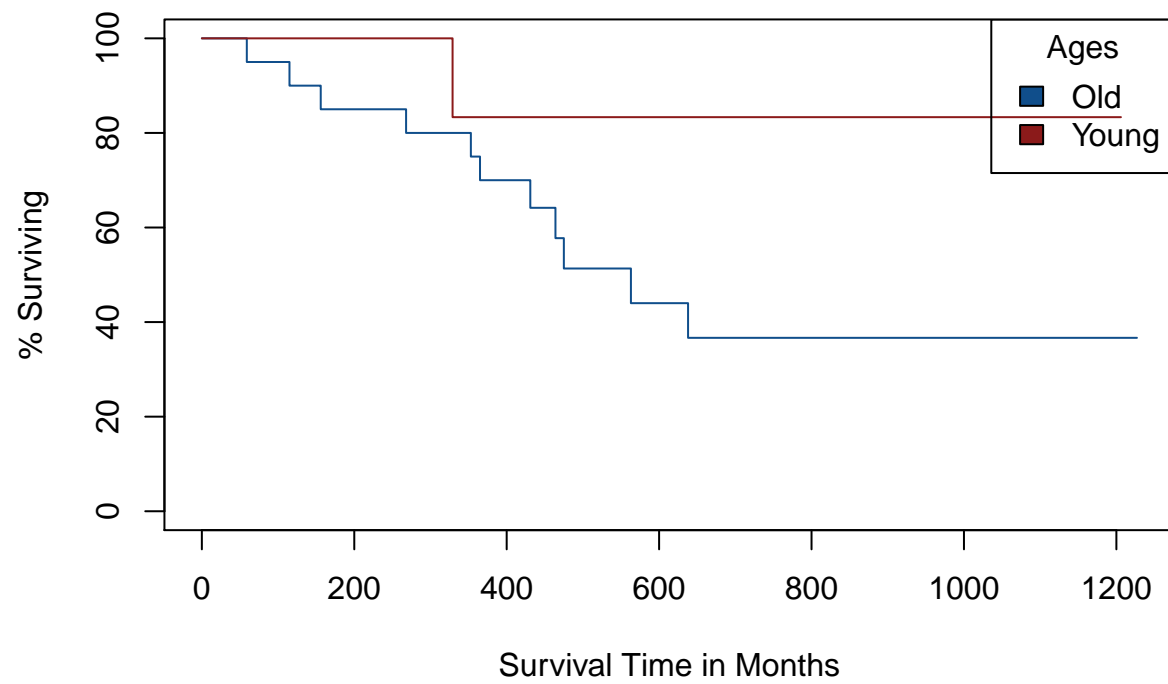
```
## dummy_Age=Young  6     1    NA     NA     NA
```

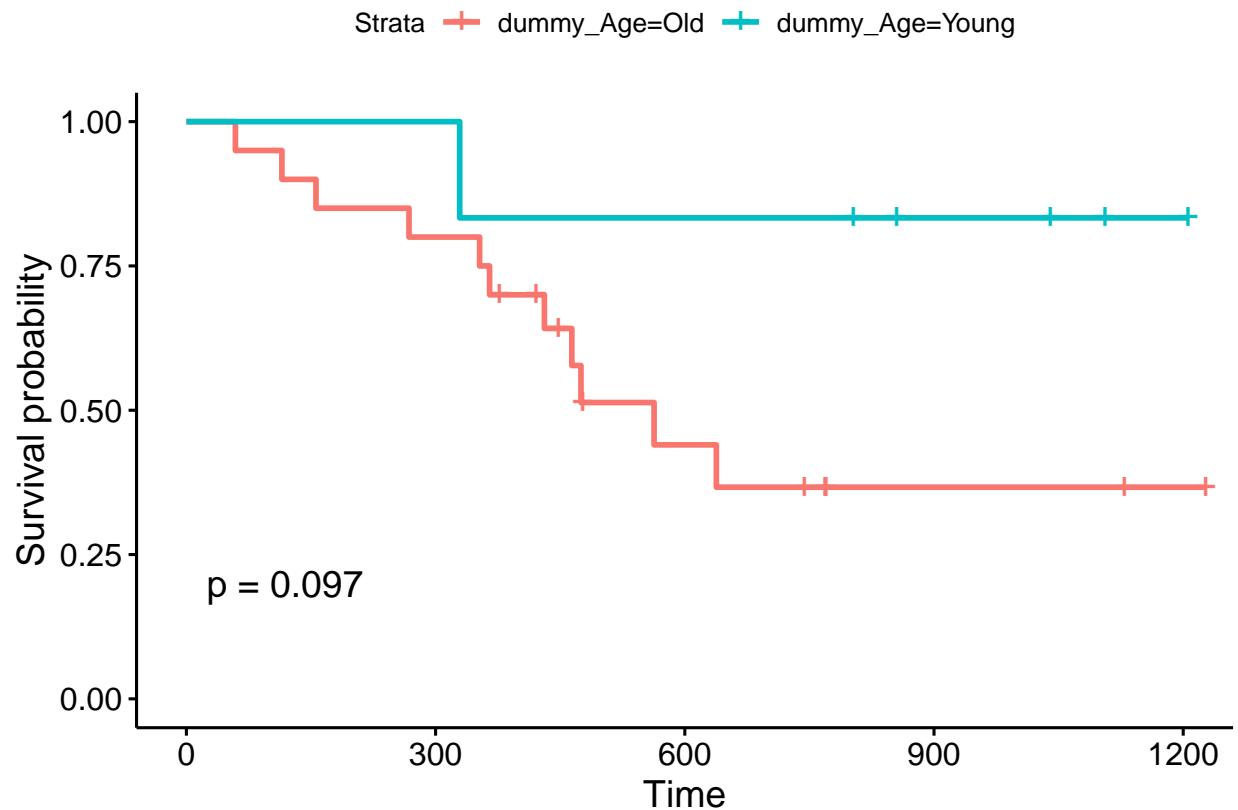
```
plot(surviv1, xlab = "Survival Time in Months", ylab = "% Surviving", yscale = 100,
     col = c("dodgerblue4", "firebrick4"),
     main = "Survival Distribution Between Different ages")
```

```
legend("topright", title = "Ages", c("Old", "Young"),
     fill = c("dodgerblue4", "firebrick4"))
```

```
ggsurvplot(surviv1, data = ovarian, pval = TRUE)
```

Survival Distribution Between Different ages





```
survdifftime(survobj ~ dummy_Age, data = ovarian)
```

```
## Call:
## survdiff(formula = survobj ~ dummy_Age, data = ovarian)
##
##              N Observed Expected (O-E)^2/E (O-E)^2/V
## dummy_Age=Old 20      11      8.4    0.804    2.75
## dummy_Age=Young 6       1      3.6    1.876    2.75
##
## Chisq= 2.7  on 1 degrees of freedom, p= 0.1
```

p-value = 0.1, This means Median Survival Time of old and young patients is not Significantly different.

=====

2- Compare the Survival Distribution of Different Progression Status (Survival Curves):

```
surviv2 <- survfit(survobj ~ ovarian$Progression, data = ovarian)
surviv2
```

```
## Call: survfit(formula = survobj ~ ovarian$Progression, data = ovarian)
##
```

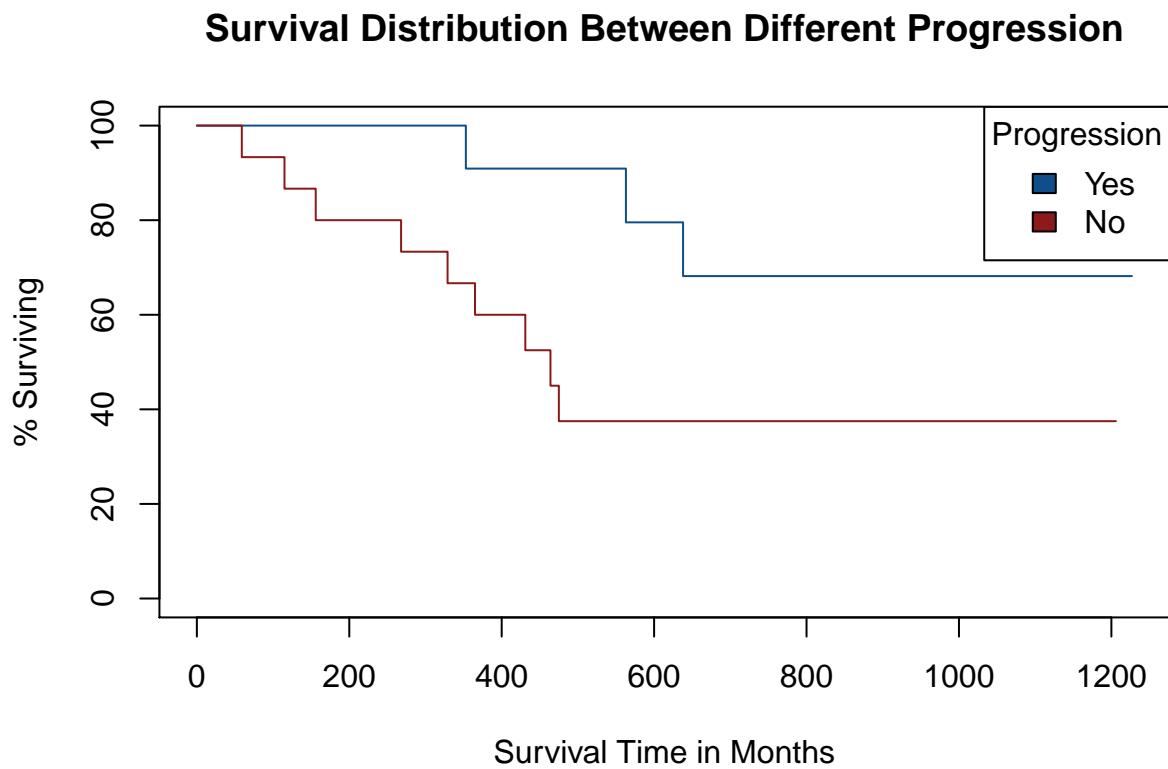
	n	events	median	0.95LCL	0.95UCL
ovarian\$Progression=No Progression	11	3	NA	638	NA
ovarian\$Progression=Progression	15	9	464	329	NA

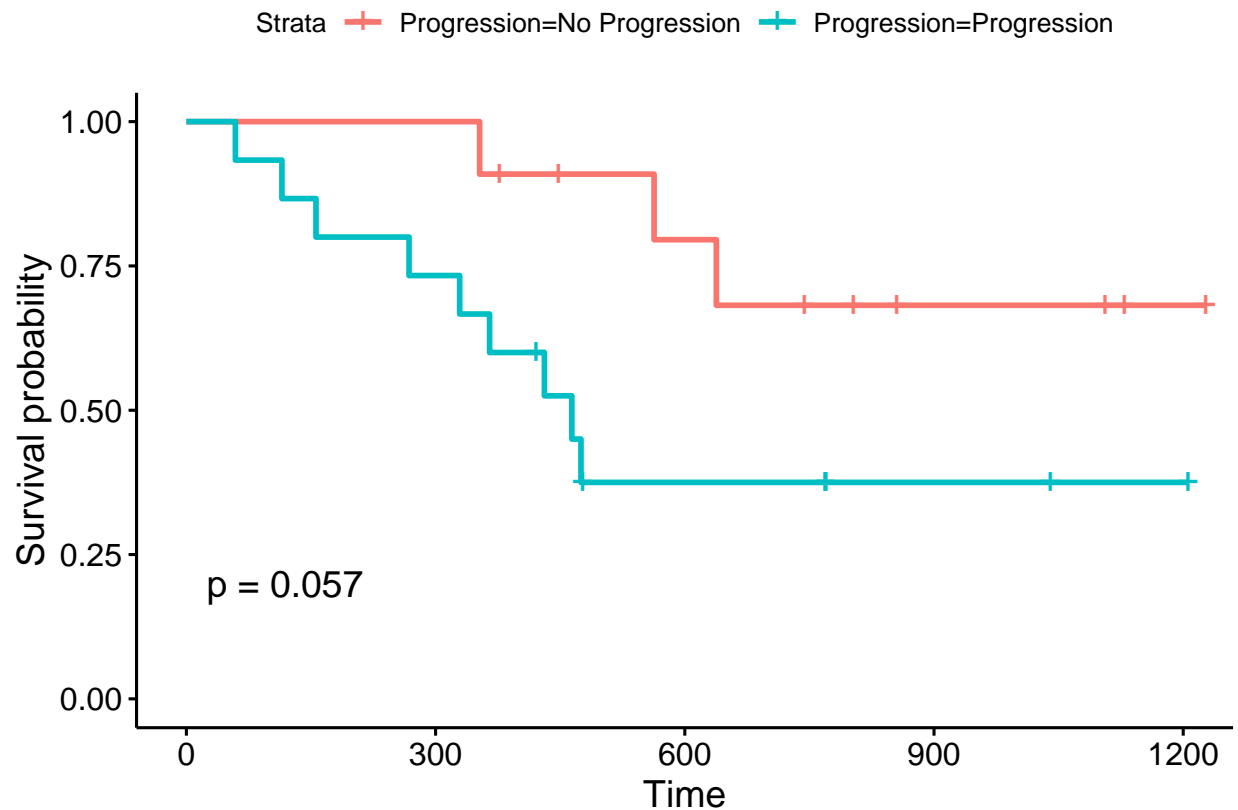
```

plot(surviv2, xlab = "Survival Time in Months", ylab = "% Surviving", yscale = 100,
     col = c("dodgerblue4", "firebrick4"),
     main = "Survival Distribution Between Different Progression")
legend("topright", title = "Progression", c("Yes", "No"),
     fill= c("dodgerblue4", "firebrick4"))

ggsurvplot(surviv2, data = ovarian, pval = TRUE)

```





```
survdifftime(survobj ~ ovarian$Progression, data = ovarian)
```

```
## Call:
## survdiff(formula = survobj ~ ovarian$Progression, data = ovarian)
##
##
##          N Observed Expected (O-E)^2/E
## ovarian$Progression=No Progression 11      3      6.26      1.70
## ovarian$Progression=Progression    15      9      5.74      1.85
##
##          (O-E)^2/V
## ovarian$Progression=No Progression      3.62
## ovarian$Progression=Progression        3.62
##
## Chisq= 3.6  on 1 degrees of freedom, p= 0.06
```

p-value = 0.06, This means Median Survival Time between different progression status is not Significantly different.

3- Compare the Survival Distribution of Different Performance Status (Survival Curves):

```
surviv3 <- survfit(survobj ~ ovarian$Performance, data = ovarian)
surviv3
```

```
## Call: survfit(formula = survobj ~ ovarian$Performance, data = ovarian)
```

```
##
```

```
##               n events median 0.95LCL 0.95UCL
```

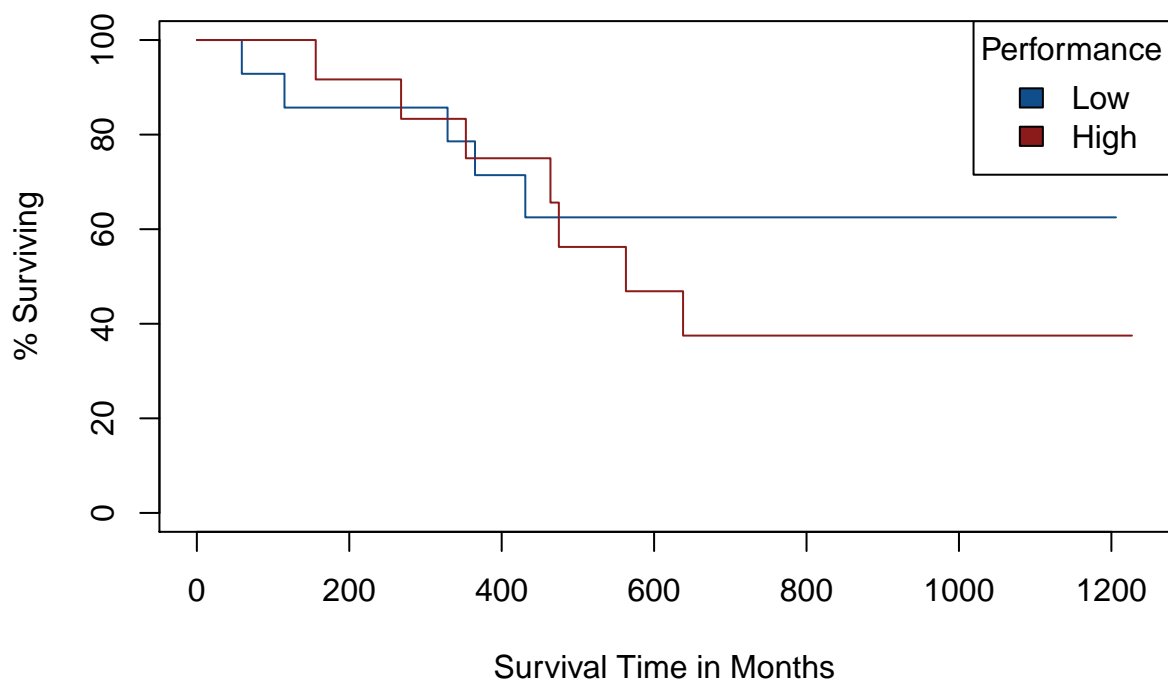
```
## ovarian$Performance=High 14      5      NA      431      NA
```

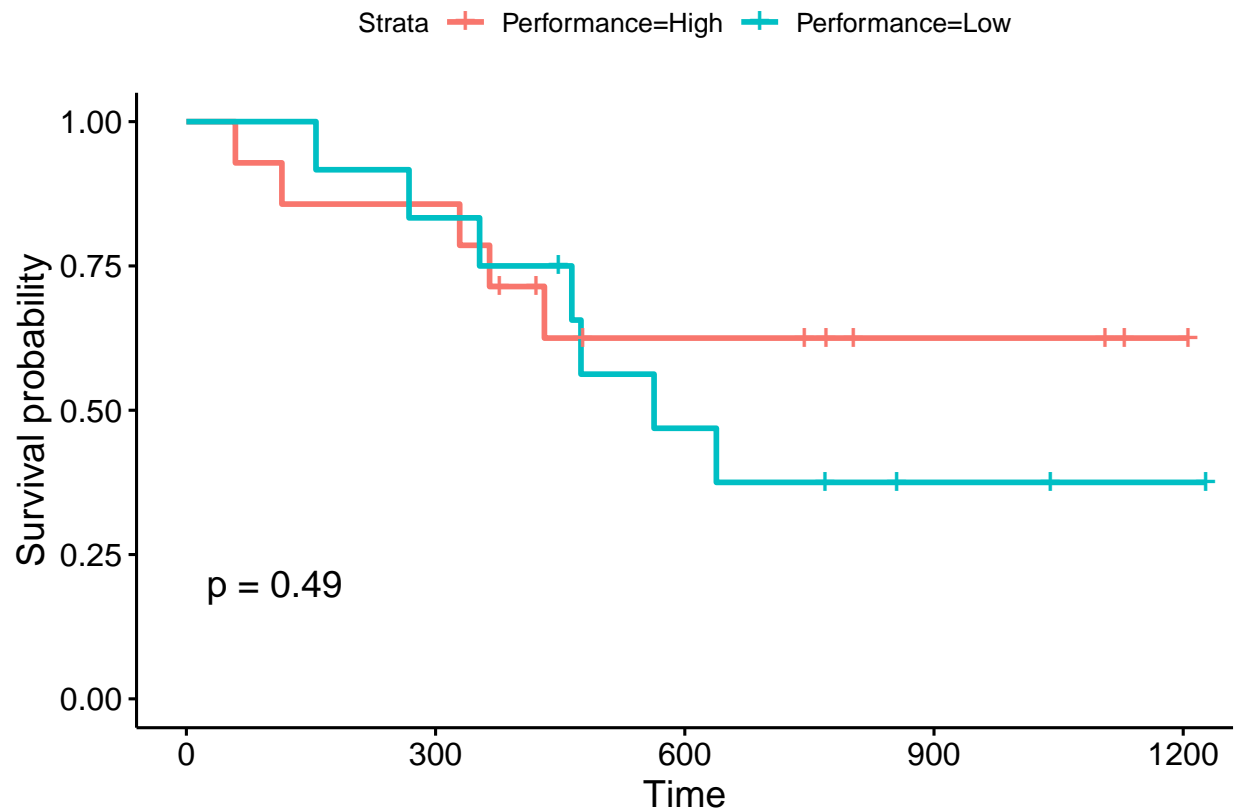
```
## ovarian$Performance=Low  12      7     563     464      NA
```

```
plot(surviv3, xlab = "Survival Time in Months", ylab = "% Surviving", yscale = 100,
     col = c("dodgerblue4", "firebrick4"),
     main = "Survival Distribution Between Different Performance")
legend("topright", title = "Performance", c("Low", "High"),
     fill = c("dodgerblue4", "firebrick4"))
```

```
ggsurvplot(surviv3, data = ovarian, pval = TRUE)
```

Survival Distribution Between Different Performance





```
survdifftime(survobj ~ ovarian$Performance, data = ovarian)
```

```
## Call:
## survdiff(formula = survobj ~ ovarian$Performance, data = ovarian)
##
##               N Observed Expected (O-E)^2/E (O-E)^2/V
## ovarian$Performance=High 14      5      6.18    0.226    0.468
## ovarian$Performance=Low  12      7      5.82    0.240    0.468
##
## Chisq= 0.5  on 1 degrees of freedom, p= 0.5
```

p-value = 0.5, This means Median Survival Time between different performance status is not Significantly different.

=====

4- Compare the Survival Distribution of Different Treatments (Survival Curves):

```
surviv4 <- survfit(survobj ~ ovarian$Treatment, data = ovarian)
surviv4
```

```
## Call: survfit(formula = survobj ~ ovarian$Treatment, data = ovarian)
##
```



```
##                                n events median 0.95LCL 0.95UCL
## ovarian$Treatment=Endoxan + Adria 13      5      NA      475      NA
## ovarian$Treatment=Endoxan alone   13      7     638     268     NA
```

```
summary(surviv4)
```

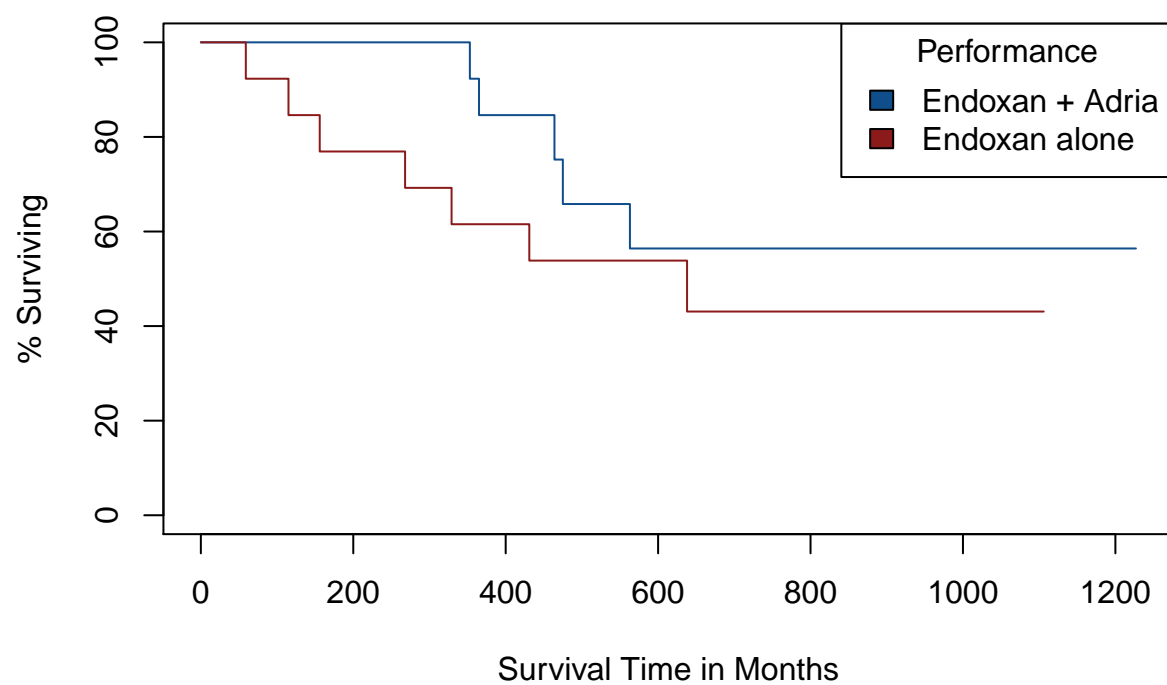
```
## Call: survfit(formula = survobj ~ ovarian$Treatment, data = ovarian)
```

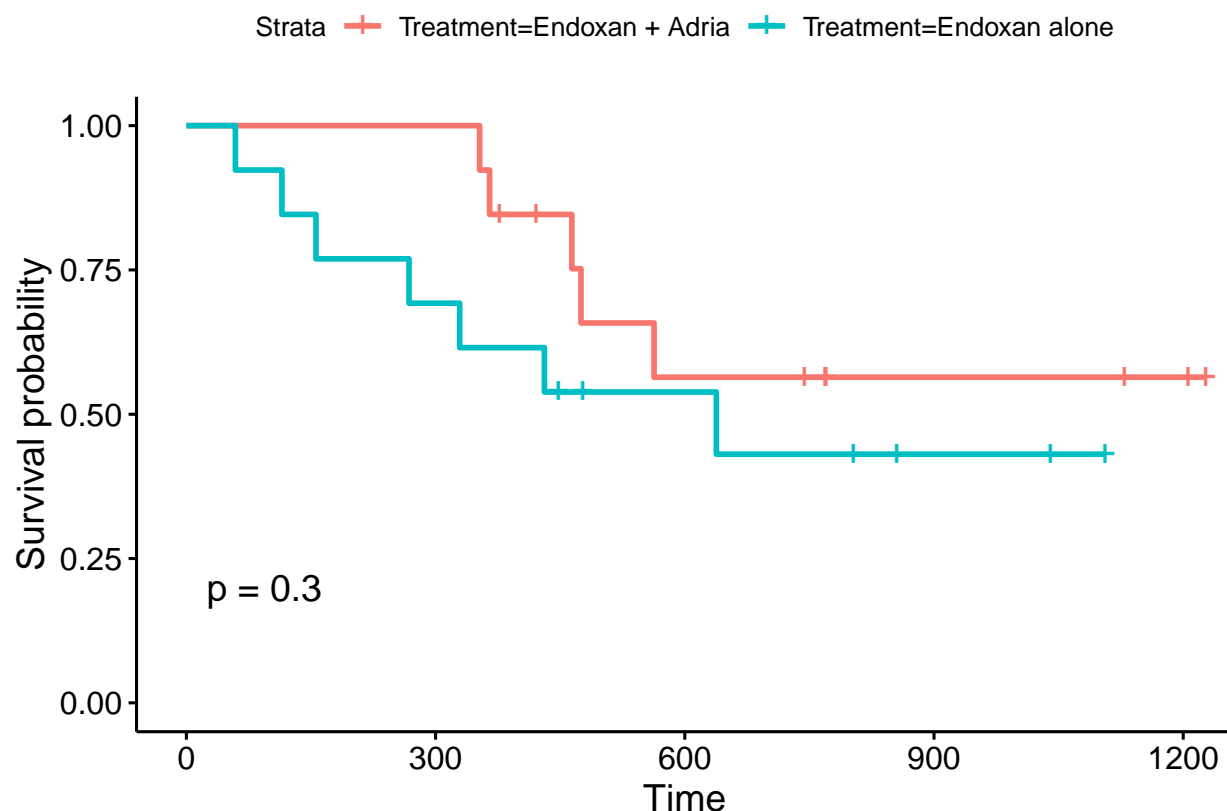
```
##
##               ovarian$Treatment=Endoxan + Adria
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##   353    13      1   0.923  0.0739    0.789    1.000
##   365    12      1   0.846  0.1001    0.671    1.000
##   464     9      1   0.752  0.1256    0.542    1.000
##   475     8      1   0.658  0.1407    0.433    1.000
##   563     7      1   0.564  0.1488    0.336    0.946
##
##               ovarian$Treatment=Endoxan alone
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##    59    13      1   0.923  0.0739    0.789    1.000
##   115    12      1   0.846  0.1001    0.671    1.000
##   156    11      1   0.769  0.1169    0.571    1.000
##   268    10      1   0.692  0.1280    0.482    0.995
##   329     9      1   0.615  0.1349    0.400    0.946
##   431     8      1   0.538  0.1383    0.326    0.891
##   638     5      1   0.431  0.1467    0.221    0.840
```

```
plot(surviv4, xlab = "Survival Time in Months", ylab = "% Surviving", yscale = 100,
     col = c("dodgerblue4", "firebrick4"),
     main = "Survival Distribution Between Treatments")
legend("topright", title = "Performance", c("Endoxan + Adria", "Endoxan alone"),
     fill= c("dodgerblue4", "firebrick4"))
```

```
ggsurvplot(surviv4, data = ovarian, pval = TRUE)
```

Survival Distribution Between Treatments





```
survdif(survobj ~ ovarian$Treatment, data = ovarian)
```

```
## Call:
## survdiff(formula = survobj ~ ovarian$Treatment, data = ovarian)
##
##               N Observed Expected (O-E)^2/E (O-E)^2/V
## ovarian$Treatment=Endoxan + Adria 13      5      6.77    0.461    1.06
## ovarian$Treatment=Endoxan alone  13      7      5.23    0.596    1.06
##
## Chisq= 1.1  on 1 degrees of freedom, p= 0.3
```

p-value = 0.3, This means Median Survival Time after using different Treatment Regimens is not Significantly different. Though, patients receiving Cyclophosphamide alone are doing better in the first month of follow-up.

=====

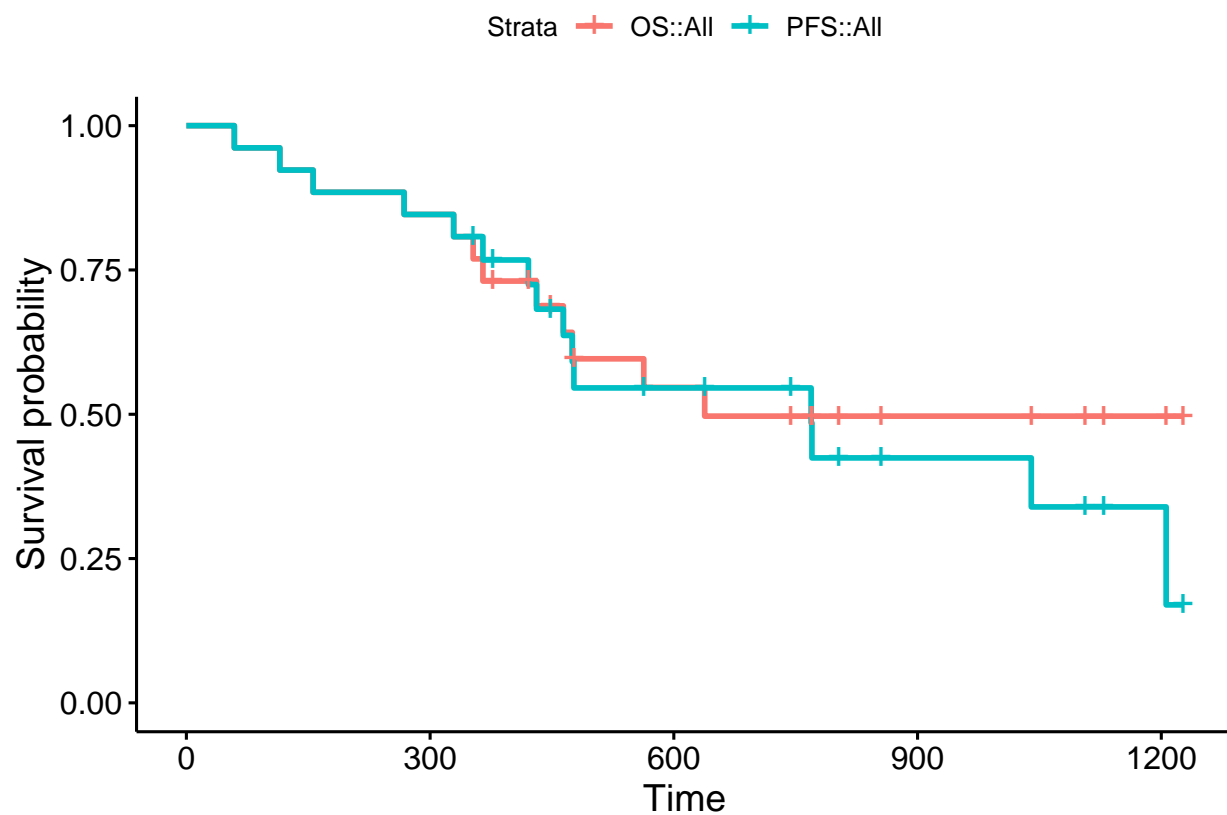
4- Progression Free Survival:

```
stat1 <- survfit(Surv(futime, fustat) ~ 1, data = ovarian)
Prog1 <- survfit(Surv(futime, resid.ds) ~ 1, data = ovarian)

Fitting <- list(OS = stat1, PFS = Prog1)
Fitting
```

```
## $OS
## Call: survfit(formula = Surv(futime, fustat) ~ 1, data = ovarian)
##
##      n  events  median 0.95LCL 0.95UCL
##    26     12    638    464     NA
##
## $PFS
## Call: survfit(formula = Surv(futime, resid.ds) ~ 1, data = ovarian)
##
##      n  events  median 0.95LCL 0.95UCL
##    26     15    769    464     NA
```

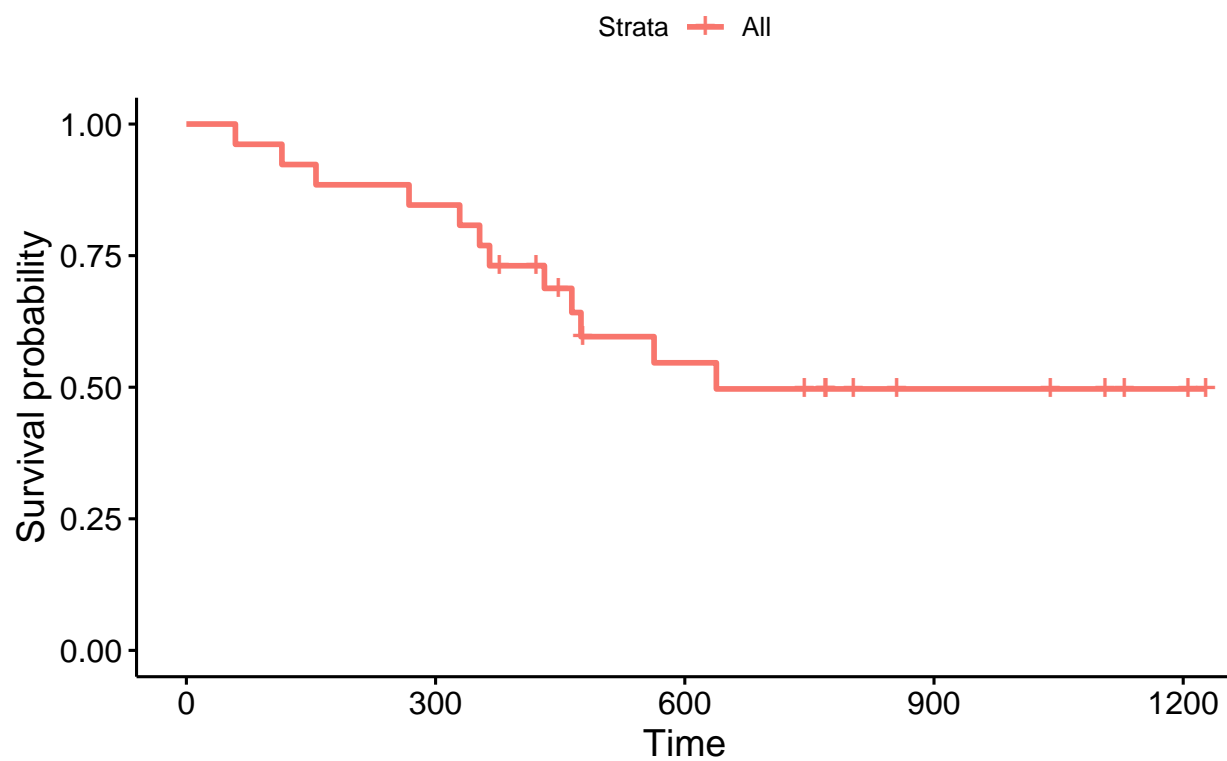
```
ggsurvplot_combine(Fitting, ovarian)
```



```
ggsurvplot(Fitting, data = ovarian, pval = TRUE)
```

```
## $OS
```

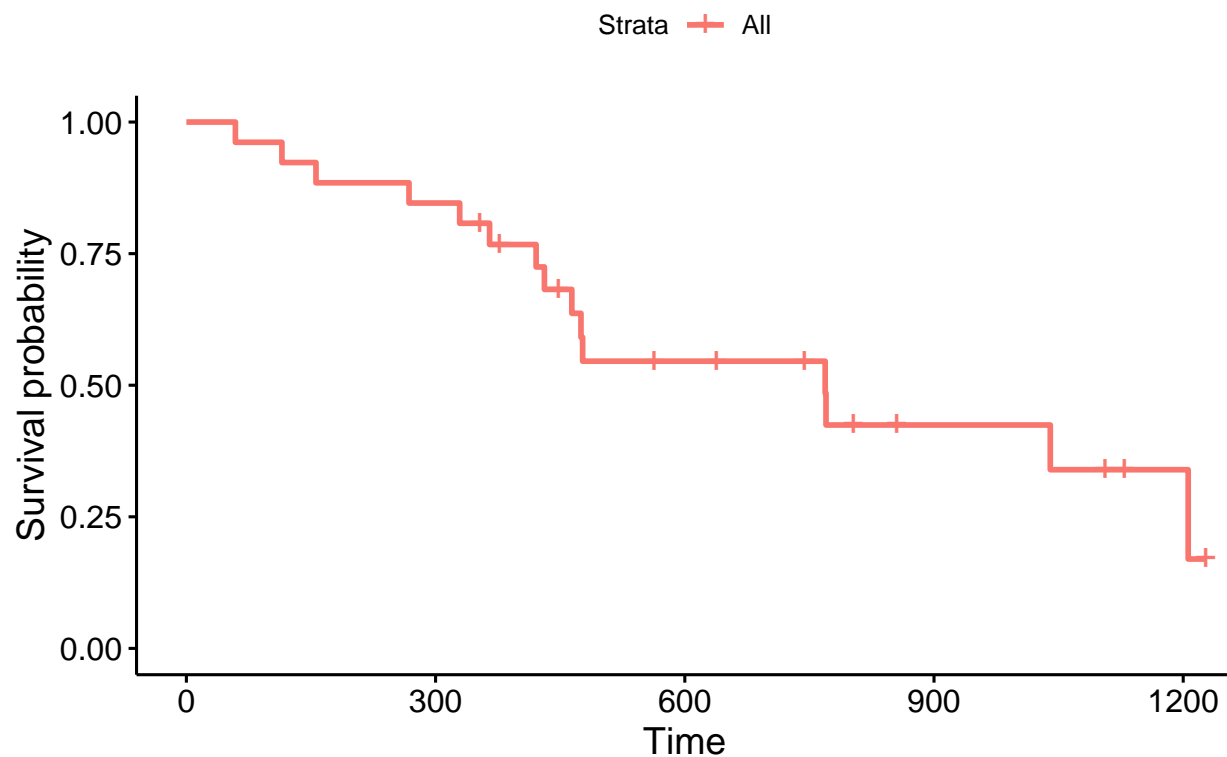
OS



##

\$PFS

PFS



```
##
## attr("class")
## [1] "list"          "ggsurvplot_list"
```

Third, Cox Regression:

reference = Endoxan alone:

```
survobj <- with(ovarian, Surv(futime, fustat))
```

```
Model1 <- coxph(survobj ~ rx, data = ovarian)
summary(Model1)
```

```
## Call:
## coxph(formula = survobj ~ rx, data = ovarian)
##
##   n= 26, number of events= 12
##
##           coef exp(coef) se(coef)      z Pr(>|z|)
## rx -0.5964    0.5508    0.5870 -1.016    0.31
```

```
##
##      exp(coef) exp(-coef) lower .95 upper .95
## rx      0.5508      1.816      0.1743      1.74
##
## Concordance= 0.608 (se = 0.07 )
## Likelihood ratio test= 1.05 on 1 df,  p=0.3
## Wald test              = 1.03 on 1 df,  p=0.3
## Score (logrank) test = 1.06 on 1 df,  p=0.3
```

1- Regression Coefficient = -0.5964, Negative sign means Risk of Death is lower when using Cyclophosphamide alone. 2- Patients using Cyclophosphamide alone has lower risk of death than using Cyclophosphamide & Adriamycin. 3- The effect size of age as a covariate = 0.55, This mean: Taking Cyclophosphamide alone reduce hazard of death by 45%.

```
progobj <- with(ovarian, Surv(futime, resid.ds))

Model11 <- coxph(progobj ~ rx, data = ovarian)
summary(Model11)
```

```
## Call:
## coxph(formula = progobj ~ rx, data = ovarian)
##
##      n= 26, number of events= 15
##
##      coef exp(coef) se(coef)      z Pr(>|z|)
## rx -0.5104      0.6002      0.5413 -0.943      0.346
##
##      exp(coef) exp(-coef) lower .95 upper .95
## rx      0.6002      1.666      0.2078      1.734
##
## Concordance= 0.606 (se = 0.068 )
## Likelihood ratio test= 0.9 on 1 df,  p=0.3
## Wald test              = 0.89 on 1 df,  p=0.3
## Score (logrank) test = 0.91 on 1 df,  p=0.3
```

1- Regression Coefficient = -0.5104, Negative sign means Risk of Progression is lower when using Cyclophosphamide alone. 2- Patients using Cyclophosphamide alone has lower risk of Progression than using Cyclophosphamide & Adriamycin. 3- The effect size of age as a covariate = 0.6, This mean: Taking Cyclophosphamide alone reduce hazard of Progression by 40%.

=====

Survival per Treatment from other variables:

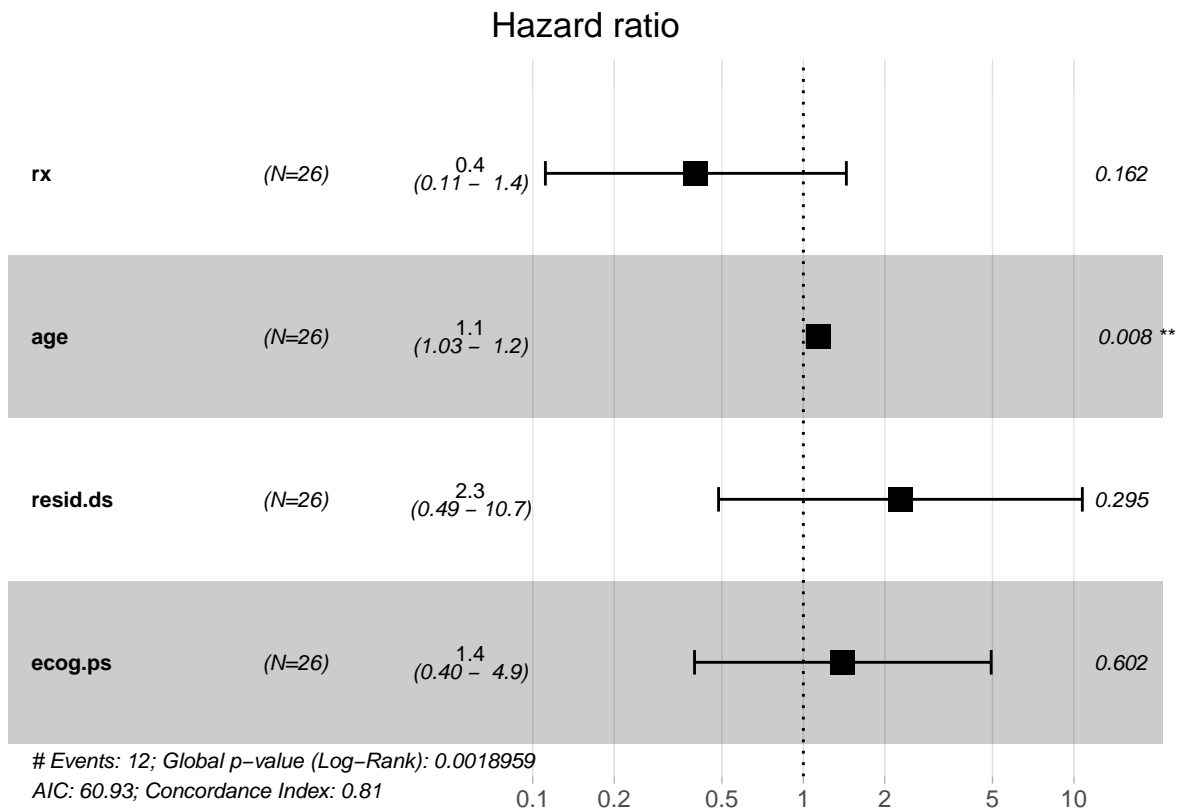
- Hazard of Death from ovarian cancer considering the Covariate:

```
Model2 <- coxph(survobj ~ rx + age + resid.ds + ecog.ps, data = ovarian)
summary(Model2)
```

```
## Call:
## coxph(formula = survobj ~ rx + age + resid.ds + ecog.ps, data = ovarian)
```

```
##
## n= 26, number of events= 12
##
##      coef exp(coef) se(coef)      z Pr(>|z|)
## rx      -0.91450   0.40072  0.65332 -1.400  0.16158
## age       0.12481   1.13294  0.04689  2.662  0.00777 **
## resid.ds  0.82619   2.28459  0.78961  1.046  0.29541
## ecog.ps   0.33621   1.39964  0.64392  0.522  0.60158
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##      exp(coef) exp(-coef) lower .95 upper .95
## rx           0.4007     2.4955   0.1114   1.442
## age          1.1329     0.8827   1.0335   1.242
## resid.ds     2.2846     0.4377   0.4861  10.738
## ecog.ps      1.3996     0.7145   0.3962   4.945
##
## Concordance= 0.807 (se = 0.068 )
## Likelihood ratio test= 17.04 on 4 df,  p=0.002
## Wald test              = 14.25 on 4 df,  p=0.007
## Score (logrank) test = 20.81 on 4 df,  p=3e-04
```

```
ggforest(Model2, data = ovarian)
```



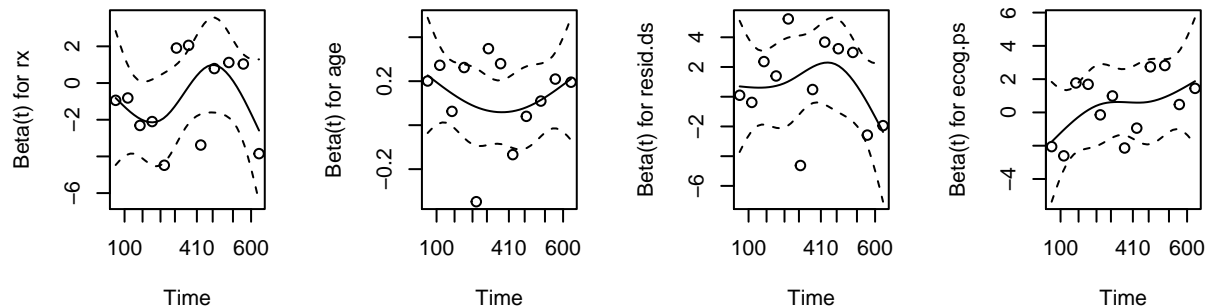
1- Older Patients has higher risk of death, this risk is significant (p-value = 0.00777) 2- likelihood ratio test Significance decreased from 0.3 to 0.002.

Evaluate Proportional Hazard Assumption:

```
cox.zph(Model2)
```

```
##           rho  chisq    p
## rx          0.1325 0.2001 0.655
## age         -0.0399 0.0262 0.871
## resid.ds    -0.1417 0.2463 0.620
## ecog.ps      0.4845 1.8819 0.170
## GLOBAL              NA 3.3609 0.499
```

```
par(mfrow = c(2, 4))
plot(cox.zph(Model2), data = ovarian)
```



By using the Schoenfeld residuals against the transformed time:

From the output above, the test is not statistically significant for each of the covariates, and the global test is also not statistically significant. Therefore, we can assume the proportional hazards.

1- rho: Pearson's correlation between the scaled Schoenfeld residuals and Time. The value of ecog.ps has higher correlation (0.4845) from over covariate, and resid.ds has the least correlation (-0.1417). All in positive direction except age and resid.ds in Negative direction.

2- chisq: The correlation coefficient follows a chi-square distribution and the statistic is present in the second column.

3- p-value: P value is given for each covariate.

4- For the global test there is no correlation and NA is entered into the cell.

Progression Free Survival per Treatment from other variables:

- Hazard of Progression from ovarian cancer considering th Covariences:

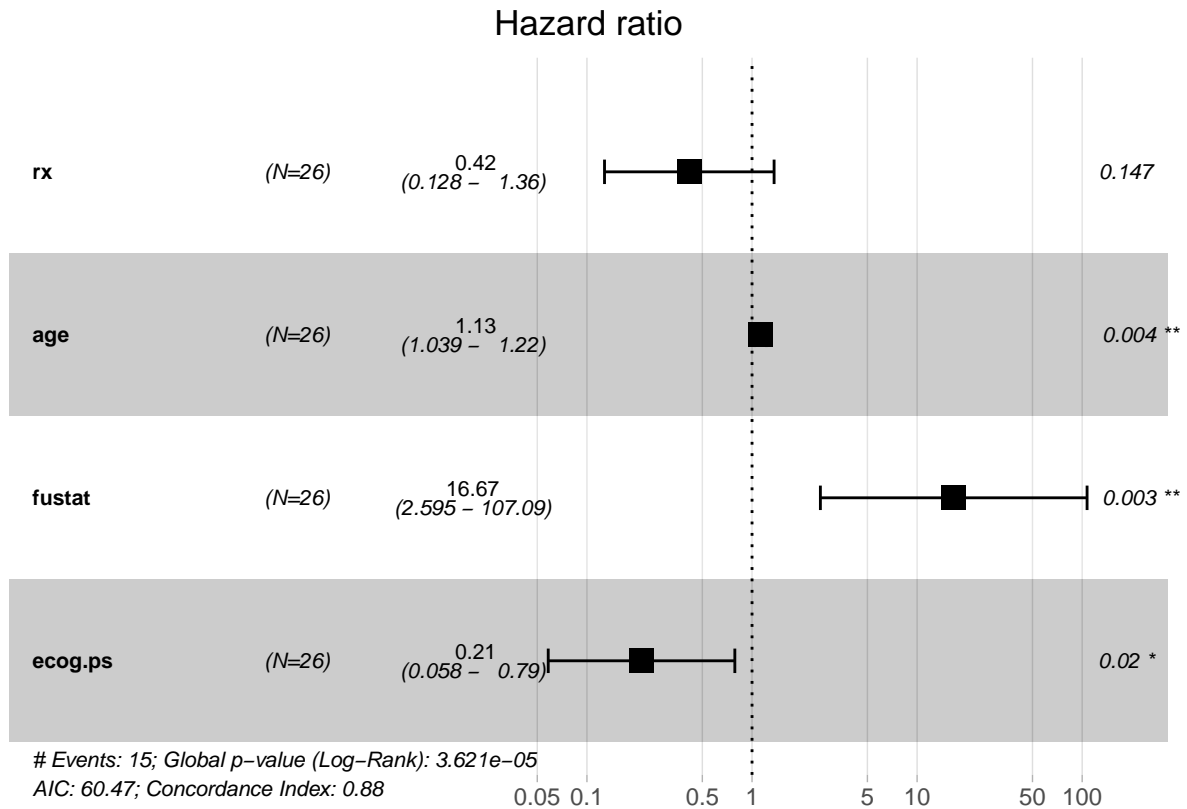
```
progobj <- with(ovarian, Surv(futime, resid.ds))

Model22 <- coxph(progobj ~ rx + age + fustat + ecog.ps, data = ovarian)

summary(Model22)

## Call:
## coxph(formula = progobj ~ rx + age + fustat + ecog.ps, data = ovarian)
##
##      n= 26, number of events= 15
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## rx           -0.87491   0.41690  0.60341 -1.450  0.14708
## age            0.11938   1.12679  0.04151  2.876  0.00403 **
## fustat         2.81365  16.67057  0.94903  2.965  0.00303 **
## ecog.ps       -1.54115   0.21413  0.66405 -2.321  0.02030 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##              exp(coef) exp(-coef) lower .95 upper .95
## rx                0.4169      2.39865    0.12776    1.3604
## age                1.1268      0.88747    1.03875    1.2223
## fustat            16.6706      0.05999    2.59497   107.0948
## ecog.ps           0.2141      4.66997    0.05827    0.7869
##
## Concordance= 0.876  (se = 0.038 )
## Likelihood ratio test= 25.71  on 4 df,   p=4e-05
## Wald test               = 15.51  on 4 df,   p=0.004
## Score (logrank) test = 25.95  on 4 df,   p=3e-05

ggforest(Model22, data = ovarian)
```



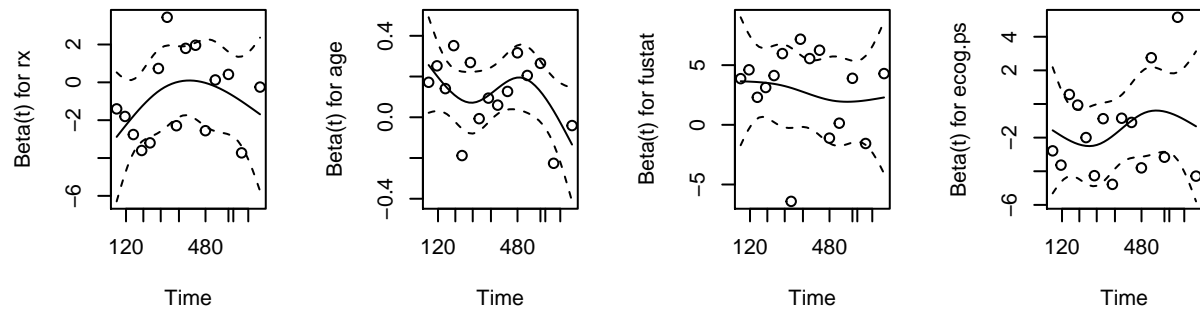
1- Older Patients has higher risk of Progression, this risk is significant (p-value = 0.00403) 2- Different in Status has higher risk of Progression, this risk is significant (p-value = 0.00303) 3- High Performance Status has Lower risk of Progression, this risk is significant (p-value = 0.02030)

Evaluate Proportional Hazard Assumption:

```
cox.zph(Model122)
```

```
##          rho chisq    p
## rx         0.182 0.425 0.514
## age        -0.300 1.478 0.224
## fustat     -0.171 0.402 0.526
## ecog.ps    0.194 0.625 0.429
## GLOBAL      NA 1.951 0.745
```

```
par(mfrow = c(2, 4))
plot(cox.zph(Model122), data = ovarian)
```



By using the Schoenfeld residuals against the transformed time:

From the output above, the test is not statistically significant for each of the covariates, and the global test is also not statistically significant. Therefore, we can assume the proportional hazards.

1- rho: Pearson's correlation between the scaled Schoenfeld residuals and Time. The value of ecog.ps has higher correlation (0.194) from over covariate, and age has the least correlation (-0.300). All in positive direction except age and fustat in Negative direction.

2- chisq: The correlation coefficient follows a chi-square distribution and the statistic is present in the second column.

3- p-value: P value is given for each covariate.

4- For the global test there is no correlation and NA is entered into the cell.