Pengantar Analisis Survival

ANALISIS SURVIVAL PASIEN GAGAL JANTUNG PADA INSTITUT KARDIOLOGI FAISALABAD

Kelompok 8
Pengantar Analisis Survival D
2024

ANGGOTA KELOMPOK

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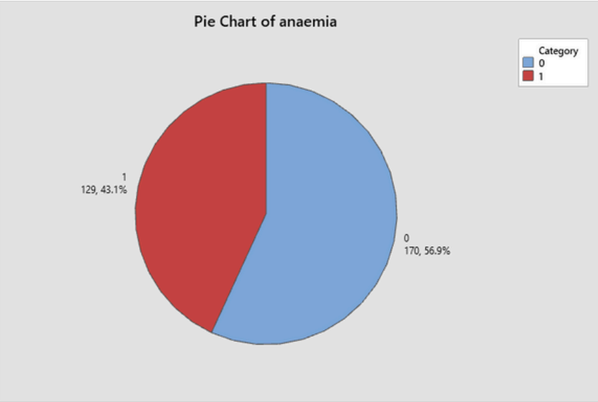
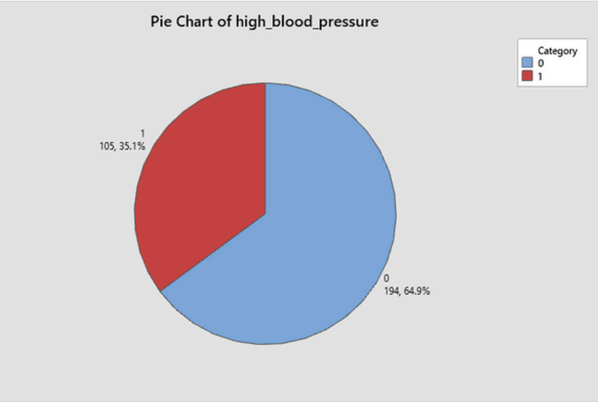
DATA DAN VARIABEL

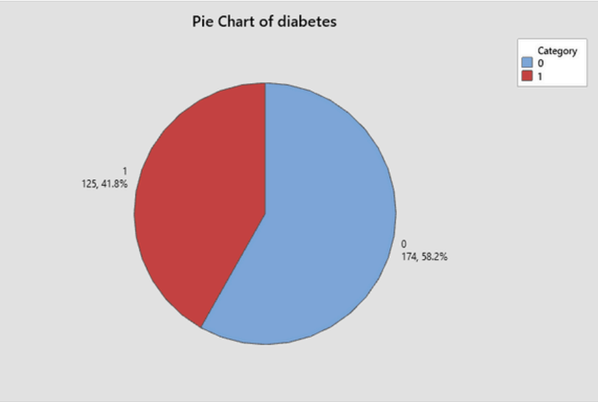
STATISTIKA DESKRIPTIF

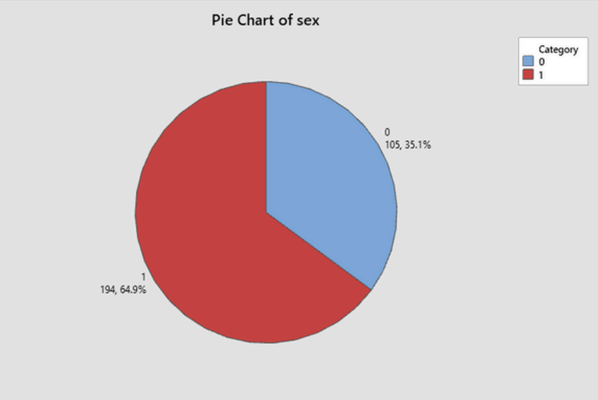
Variabel	N	Mean	SD	Median	Min	Max	Range	SE
Age	299	60.83	11.89	60	40	95	55	0.69
Creatinine_Phosphokinase	299	581.84	970.29	250	23	7861	7838	56.11
Ejection_Fraction	299	38.08	11.83	38	14	80	66	0.68
Platelets	299	263358	97804.24	262000	25100	850000	824900	5656.17
Serum_Creatinine	299	1.39	1.03	1.1	0.5	9.4	8.9	0.06
Serum_Sodium	299	136.63	4.41	137	113	148	35	0.26
Time	299	130.26	77.61	115	4	285	281	4.49

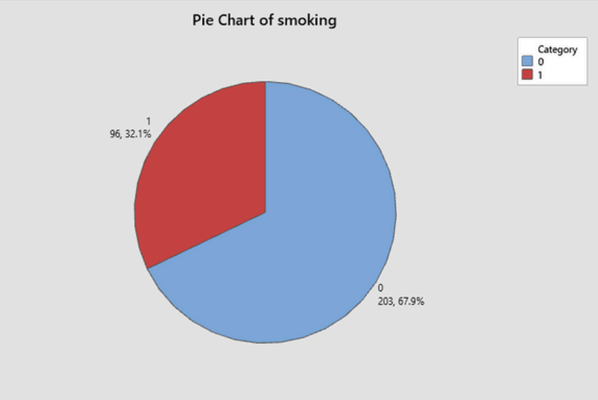
STATISTIKA DESKRIPTIF

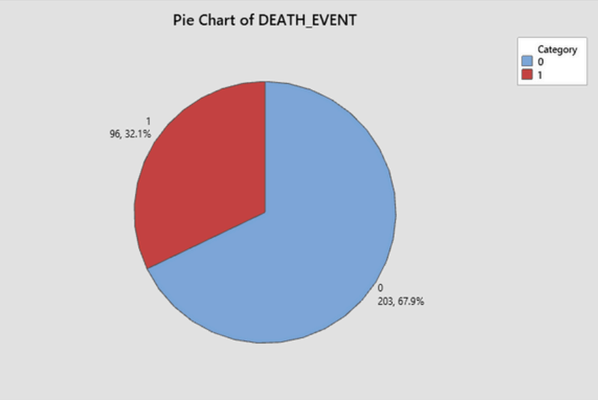












SUMBER DATA

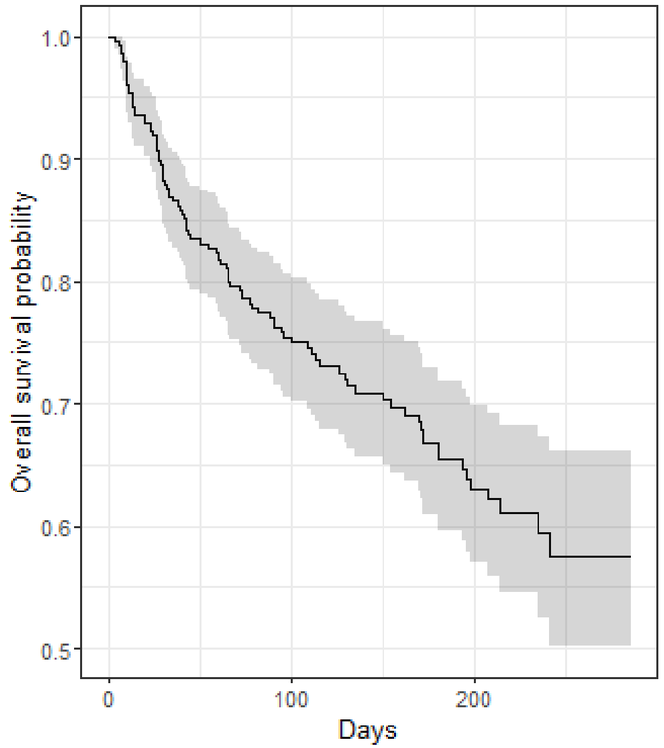
Dataset berasal dari Institut Kardiologi Faisalabad yang berisi rekam medis kardiovaskular dari 299 pasien. Pasien cohort terdiri atas 105 perempuan dan 194 laki-laki yang berumur 40-95 tahun. Seluruh pasien didiagnosa disfungsi sistolik pada ventrikel kiri dan pernah memiliki riwayat gagal jantung.

VARIABEL

Variabel	Penjelasan	Satuan	Jenis data	Range dan Keterangan
Age	Umur pasien	Tahun	Rasio	[40,95]
Anaemia	Kekurangan sel darah merah	-	Nominal	0: Tidak anemia 1: Anemia
High Blood Pressure	Indikasi pasien hipertensi	-	Nominal	0: Tidak hipertensi 1: Hipertensi
Creatinine Phosphokinase	Kadar enzim CPK dalam darah	mcg/L	Rasio	[23,7861]
Diabetes	Diabetes pada pasien	-	Nominal	0: Tidak diabetes 1: Diabetes
Ejection Fraction	Persentase darah keluar dari jantung tiap kontraksi	Persen	Rasio	[14,80]
Sex	Jenis kelamin pasien	-	Nominal	0: Perempuan 1: Laki-laki
Platelets	Sel darah merah dalam darah	kiloplatelets/mL	Rasio	[25.01,850.00]
Serum creatinine	Kasar kreatinin dalam darah	mg/dL	Rasio	[0.50,9.40]
Serum sodium	Kadar sodium dalam darah	mEq/L	Rasio	[114,148]
Smoking	Indikasi pasien merokok	-	Nominal	0: Tidak merokok 1: Merokok
Time	Waktu follow up untuk visitasi dokter	Hari	Rasio	[4,285]
Death Event	Pasien meninggal di rentang waktu follow up	-	Nominal	0: Tidak meninggal 1: Meninggal

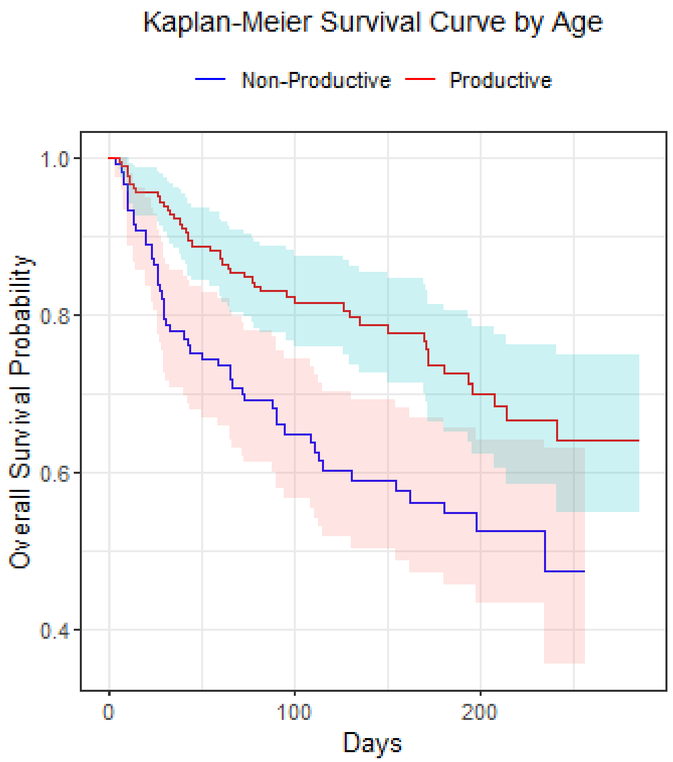
KURVA KAPLAN MEIER DAN UJI LOGRANK

KURVA KAPLAN-MEIER



Pasien gagal jantung secara keseluruhan memiliki peluang bertahan hingga hari ke-240 sebesar 58%.

KURVA KAPLAN-MEIER BERDASARKAN AGE



UJI LOG-RANK

Hipotesis:

$H_0: S_1(t) = S_2(t)$

$H_1: S_1(t) \neq S_2(t)$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $\mathrm{LR} = 10{,}9$

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
age1=Non-Productive	118	50	34.5	6.95	10.9
age1=Productive	181	46	61.5	3.90	10.9

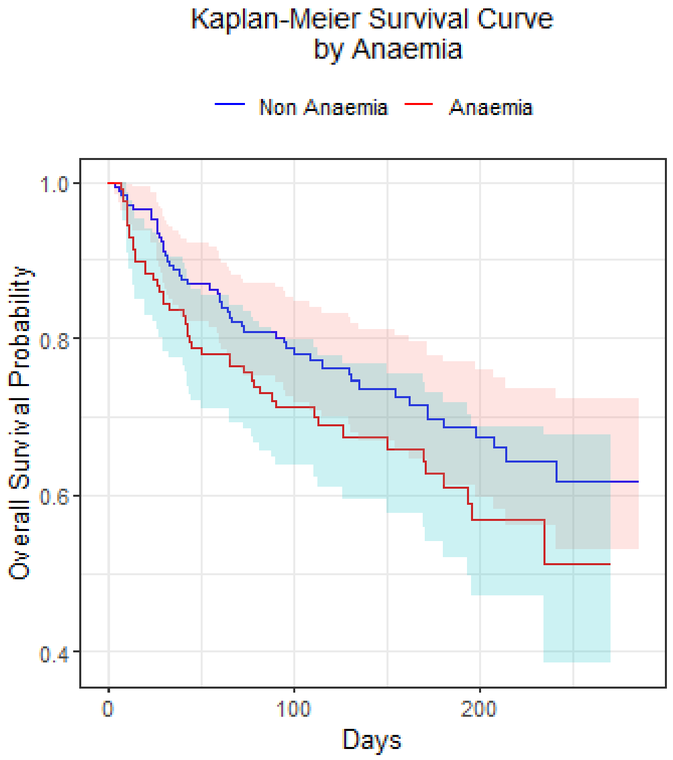
Chisq= 10.9 on 1 degrees of freedom, p= 0.001

Keputusan: Tolak H_0 karena $\mathrm{LR} > \chi^2_{crit} = 3{,}84$

Kesimpulan:

Probabilitas survival antara kelompok usia produktif dan tidak produktif berbeda.

KURVA KAPLAN-MEIER BERDASARKAN ANAEMIA



UJI LOG-RANK

Hipotesis:

$H_0: S_1(t) = S_2(t)$

$H_1: S_1(t) \neq S_2(t)$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $\mathrm{LR} = 2{,}73$

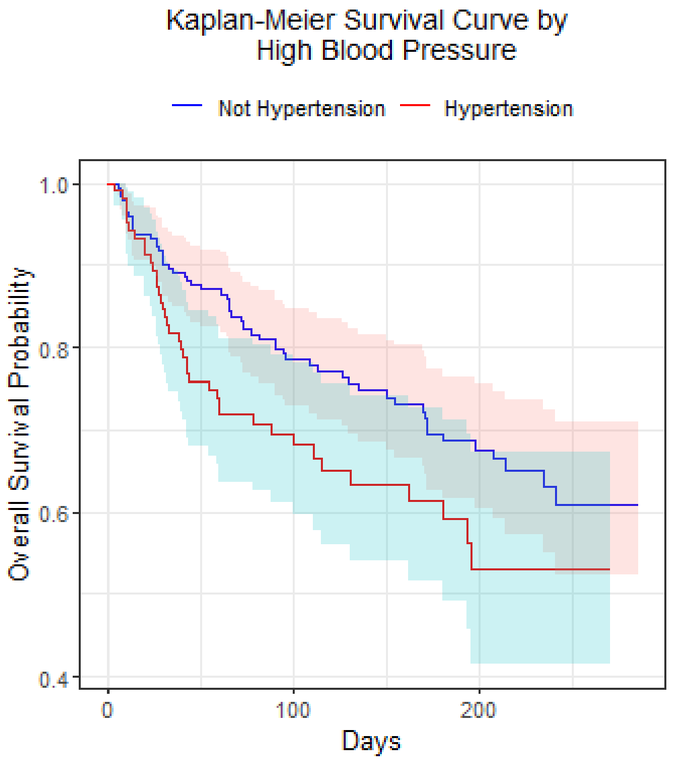
```
survdiff(formula = y ~ df$anaemia)

                N Observed Expected (O-E)^2/E (O-E)^2/V
df$anaemia=0 170       50     57.9      1.07      2.73
df$anaemia=1 129       46     38.1      1.63      2.73

 Chisq= 2.7  on 1 degrees of freedom, p= 0.1
```

Keputusan: Gagal tolak H_0 karena $\mathrm{LR} < \chi^2_{crit} = 3{,}84$

Kesimpulan:

Probabilitas survival antara orang yang anemia dan tidak, sama.

KURVA KAPLAN-MEIER BERDASARKAN HIGH BLOOD PRESSURE



UJI LOG-RANK

Hipotesis:

$H_0: S_1(t) = S_2(t)$

$H_1: S_1(t) \neq S_2(t)$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $\mathrm{LR} = 4{,}41$

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
df$high_blood_pressure=0	194	57	66.4	1.34	4.41
df$high_blood_pressure=1	105	39	29.6	3.00	4.41

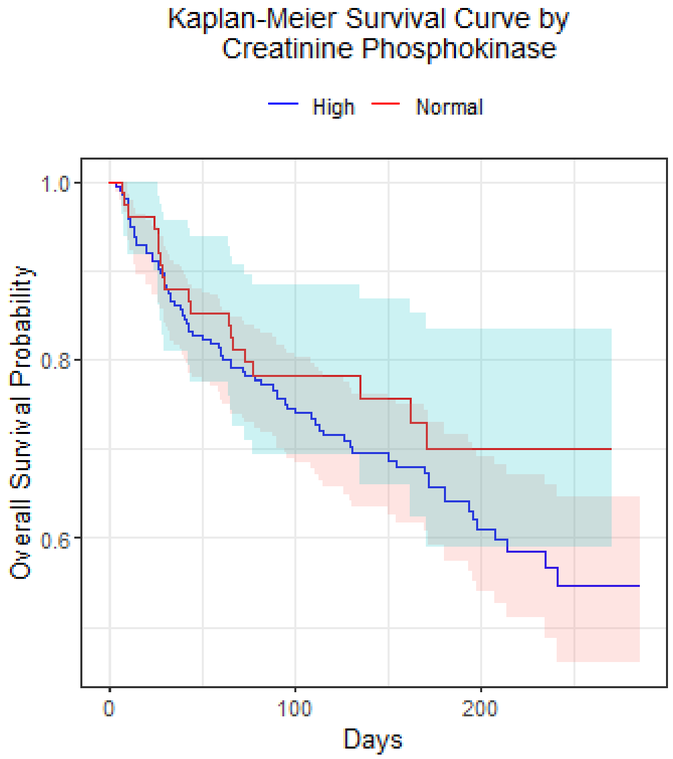
Chisq= 4.4 on 1 degrees of freedom, p= 0.04

Keputusan: Tolak H_0 karena $\mathrm{LR} > \chi^2_{crit} = 3{,}84$

Kesimpulan:

Probabilitas survival antara kelompok orang dengan hipertensi dan tidak hipertensi berbeda.

KURVA KAPLAN-MEIER BERDASARKAN CREATININE PHOSPHOKINASE



UJI LOG-RANK

Hipotesis:

$H_0: S_1(t) = S_2(t)$

$H_1: S_1(t) \neq S_2(t)$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $\mathrm{LR} = 1{,}19$

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
creatinine=High	222	77	72.4	0.292	1.19
creatinine=Normal	77	19	23.6	0.895	1.19

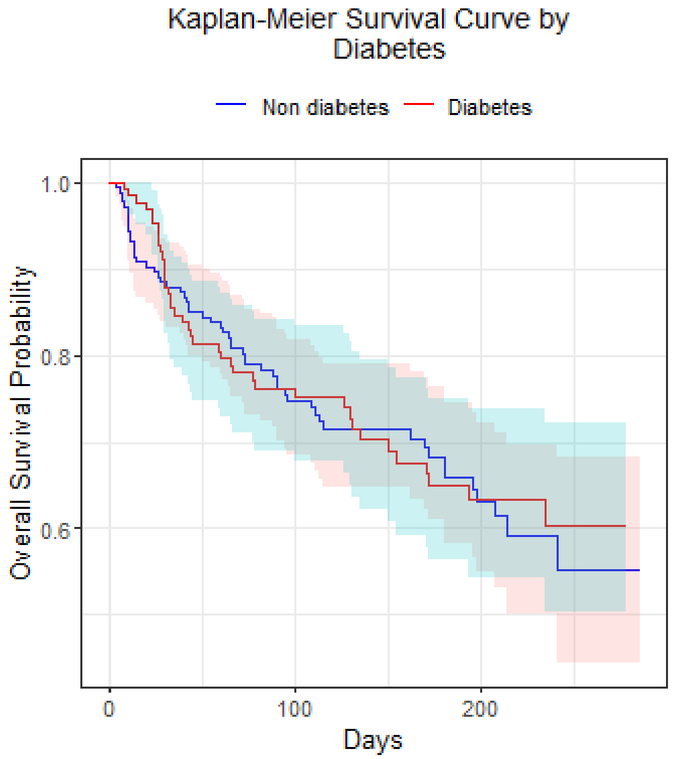
Chisq= 1.2 on 1 degrees of freedom, p= 0.3

Keputusan: Gagal tolak H_0 karena $\mathrm{LR} < \chi^2_{crit} = 3{,}84$

Kesimpulan:

Probabilitas survival antara kelompok orang dengan kadar enzim CPK dalam darah yang tinggi dan normal sama.

KURVA KAPLAN-MEIER BERDASARKAN DIABETES



UJI LOG-RANK

Hipotesis:

$H_0: S_1(t) = S_2(t)$

$H_1: S_1(t) \neq S_2(t)$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $\mathrm{LR} = 0{,}0405$

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
df$diabetes=0	174	56	55	0.0172	0.0405
df$diabetes=1	125	40	41	0.0231	0.0405

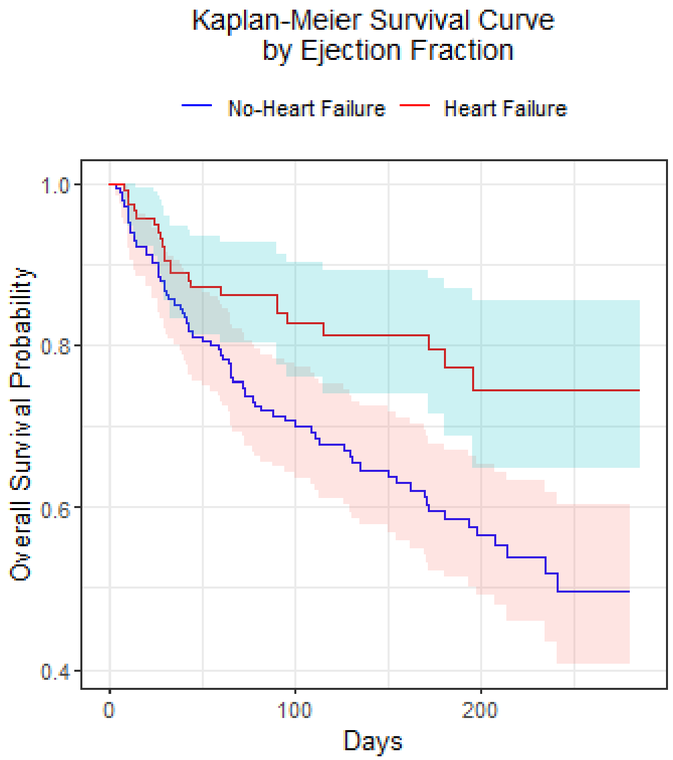
Chisq= 0 on 1 degrees of freedom, p= 0.8

Keputusan: Gagal tolak H_0 karena $\mathrm{LR} < \chi^2_{crit} = 3{,}84$

Kesimpulan:

Probabilitas survival antara kelompok orang diabetes dan tidak diabetes sama.

KURVA KAPLAN-MEIER BERDASARKAN EJECTION FRACTION



UJI LOG-RANK

Hipotesis:

$H_0: S_1(t) = S_2(t)$

$H_1: S_1(t) \neq S_2(t)$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $\text{LR} = 9{,}47$

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
ef=Heart Failure	182	73	58.3	3.69	9.47
ef=No-Heart Failure	117	23	37.7	5.72	9.47

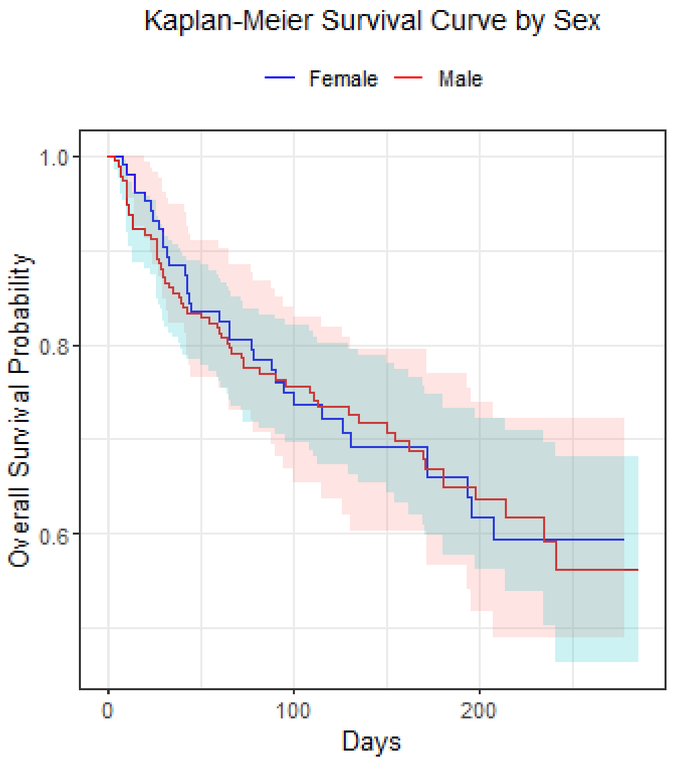
Chisq= 9.5 on 1 degrees of freedom, p= 0.002

Keputusan: Tolak H_0 karena $\text{LR} > \chi^2_{crit} = 3{,}84$

Kesimpulan:

Probabilitas survival antara kelompok orang dengan risiko gagal jantung dan tidak berisiko berbeda.

KURVA KAPLAN-MEIER BERDASARKAN SEX



UJI LOG-RANK

Hipotesis:

$H_0: S_1(t) = S_2(t)$

$H_1: S_1(t) \neq S_2(t)$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $\mathrm{LR} = 0{,}00397$

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
df$sex=0	105	34	34.3	0.00254	0.00397
df$sex=1	194	62	61.7	0.00141	0.00397

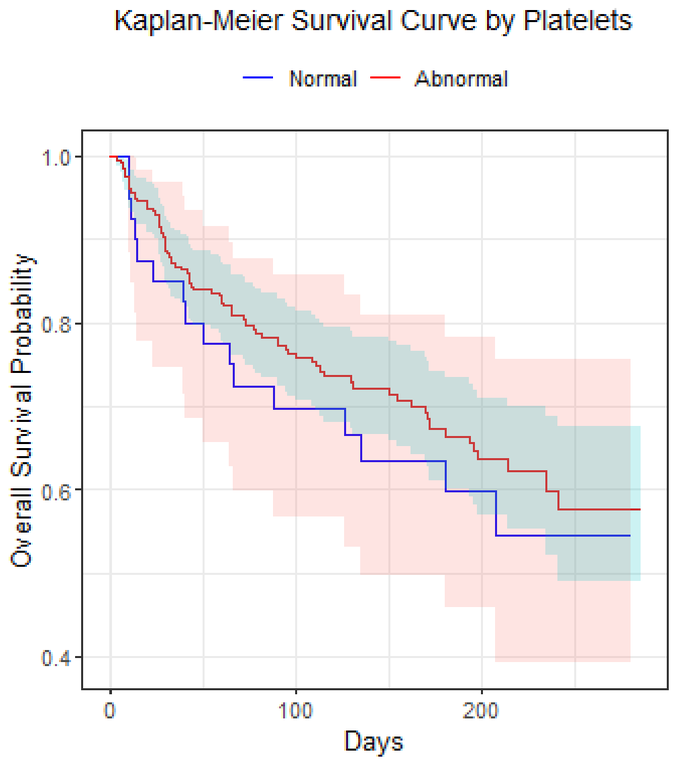
Chisq= 0 on 1 degrees of freedom, p= 0.9

Keputusan: Tolak H_0 karena $\mathrm{LR} > \chi^2_{crit} = 3{,}84$

Kesimpulan:

Probabilitas survival antara perempuan dan laki-laki berbeda.

KURVA KAPLAN-MEIER BERDASARKAN PLATELETS



UJI LOG-RANK

Hipotesis:

$H_0: S_1(t) = S_2(t)$

$H_1: S_1(t) \neq S_2(t)$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $\mathrm{LR} = 0{,}641$

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
platelets1=Abnormal	40	16	13.3	0.5486	0.641
platelets1=Normal	259	80	82.7	0.0882	0.641

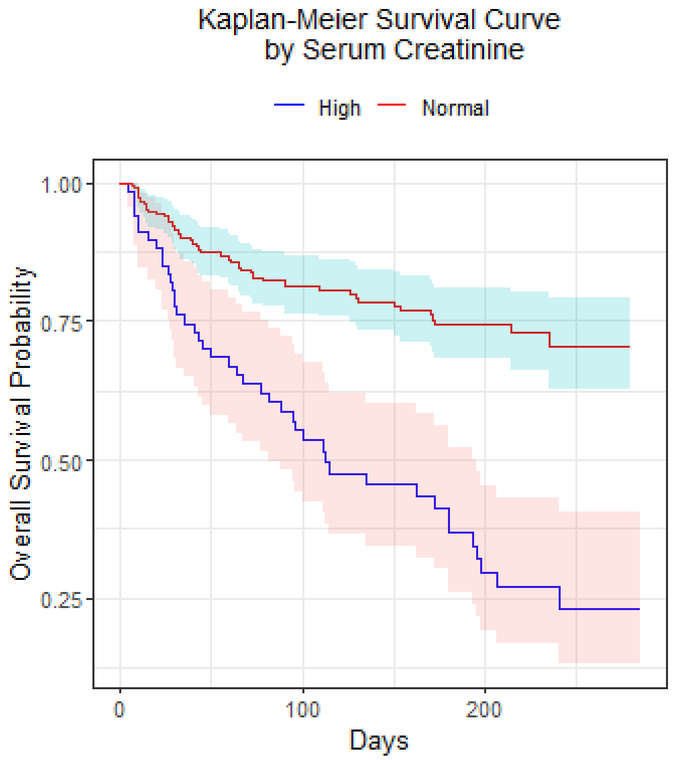
Chisq= 0.6 on 1 degrees of freedom, p= 0.4

Keputusan: Gagal tolak H_0 karena $\mathrm{LR} < \chi^2_{crit} = 3{,}84$

Kesimpulan:

Probabilitas survival antara kelompok orang dengan platelets normal dan tidak normal sama.

KURVA KAPLAN-MEIER BERDASARKAN SERUM CREATININE



UJI LOG-RANK

Hipotesis:

$H_0: S_1(t) = S_2(t)$

$H_1: S_1(t) \neq S_2(t)$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $\mathrm{LR} = 39{,}6$

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
ser_creatinine=High	67	43	18.7	31.74	39.6
ser_creatinine=Normal	232	53	77.3	7.66	39.6

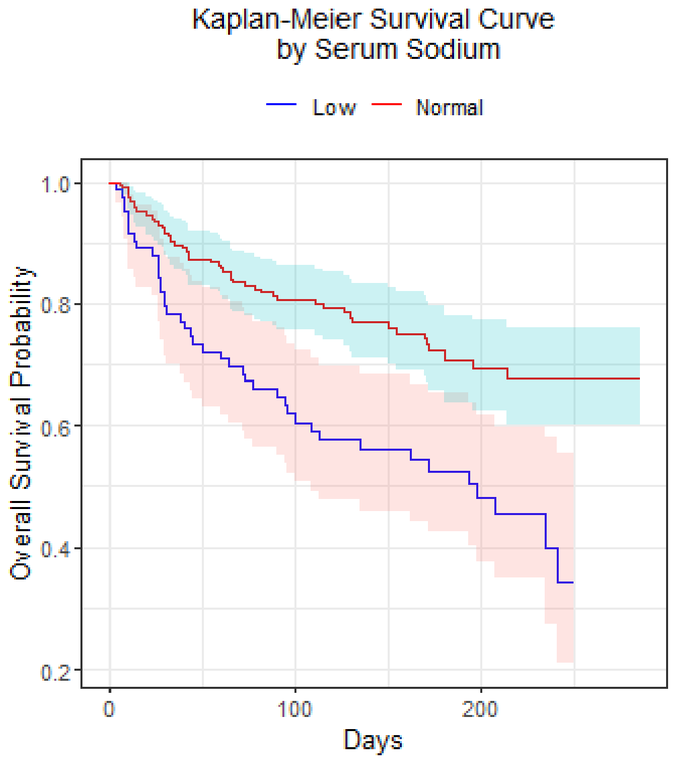
Chisq= 39.6 on 1 degrees of freedom, p= 3e-10

Keputusan: Tolak H_0 karena $\mathrm{LR} > \chi^2_{crit} = 3{,}84$

Kesimpulan:

Probabilitas survival antara kelompok orang dengan kadar kreatinin tinggi dan normal berbeda.

KURVA KAPLAN-MEIER BERDASARKAN SERUM SODIUM



UJI LOG-RANK

Hipotesis:

$H_0: S_1(t) = S_2(t)$

$H_1: S_1(t) \neq S_2(t)$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $\mathrm{LR} = 15{,}6$

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
ser_sodium=Low	83	42	25	11.52	15.6
ser_sodium=Normal	216	54	71	4.06	15.6

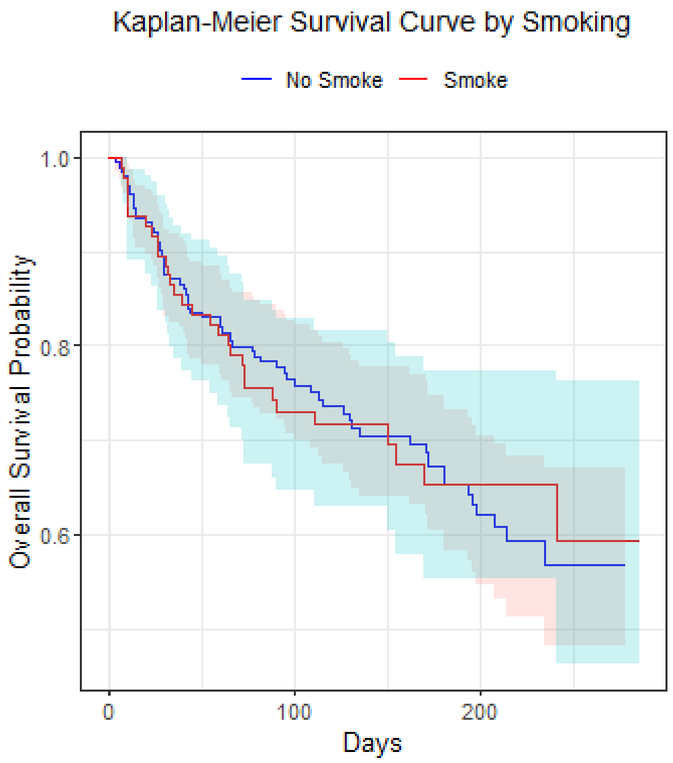
Chisq= 15.6 on 1 degrees of freedom, p= 8e-05

Keputusan: Tolak H_0 karena $\mathrm{LR} > \chi^2_{crit} = 3{,}84$

Kesimpulan:

Probabilitas survival antara kelompok orang dengan kadar sodium rendah dan normal berbeda

KURVA KAPLAN-MEIER BERDASARKAN SMOKING



UJI LOG-RANK

Hipotesis:

$H_0: S_1(t) = S_2(t)$

$H_1: S_1(t) \neq S_2(t)$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $\mathrm{LR} = 0{,}00204$

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
df$smoking=0	203	66	65.8	0.00064	0.00204
df$smoking=1	96	30	30.2	0.00139	0.00204

Chisq= 0 on 1 degrees of freedom, p= 1

Keputusan: Gagal tolak H_0 karena $\mathrm{LR} < \chi^2_{crit} = 3{,}84$

Kesimpulan:

Probabilitas survival antara kelompok orang yang merokok dan tidak merokok sama.

MODEL COX PH

MODEL COX PH DENGAN SELURUH VARIABEL PREDIKTOR

```
coxph(formula = y ~ age + anaemia + creatinine_phosphokinase +
    diabetes + ejection_fraction + high_blood_pressure + platelets +
    serum_creatinine + serum_sodium + sex + smoking, data = df)

  n= 299, number of events= 96

                             coef  exp(coef)   se(coef)      z Pr(>|z|)
age                      4.641e-02  1.048e+00  9.324e-03  4.977 6.45e-07 ***
anaemia                  4.601e-01  1.584e+00  2.168e-01  2.122   0.0338 *
creatinine_phosphokinase 2.207e-04  1.000e+00  9.919e-05  2.225   0.0260 *
diabetes                 1.399e-01  1.150e+00  2.231e-01  0.627   0.5307
ejection_fraction       -4.894e-02  9.522e-01  1.048e-02 -4.672 2.98e-06 ***
high_blood_pressure      4.757e-01  1.609e+00  2.162e-01  2.201   0.0278 *
platelets               -4.635e-07  1.000e+00  1.126e-06 -0.412   0.6806
serum_creatinine         3.210e-01  1.379e+00  7.017e-02  4.575 4.76e-06 ***
serum_sodium            -4.419e-02  9.568e-01  2.327e-02 -1.899   0.0575 .
sex                     -2.375e-01  7.886e-01  2.516e-01 -0.944   0.3452
smoking                  1.289e-01  1.138e+00  2.512e-01  0.513   0.6078
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

                        exp(coef) exp(-coef) lower .95 upper .95
age                        1.0475     0.9547    1.0285     1.067
anaemia                    1.5843     0.6312    1.0358     2.423
creatinine_phosphokinase   1.0002     0.9998    1.0000     1.000
diabetes                   1.1501     0.8695    0.7427     1.781
ejection_fraction          0.9522     1.0502    0.9329     0.972
high_blood_pressure        1.6092     0.6214    1.0534     2.458
platelets                  1.0000     1.0000    1.0000     1.000
serum_creatinine           1.3786     0.7254    1.2014     1.582
serum_sodium               0.9568     1.0452    0.9141     1.001
sex                        0.7886     1.2681    0.4816     1.291
smoking                    1.1376     0.8790    0.6953     1.861

Concordance= 0.741  (se = 0.027 )
Likelihood ratio test= 81.95  on 11 df,   p=6e-13
Wald test            = 87.27  on 11 df,   p=6e-14
Score (logrank) test = 88.39  on 11 df,   p=3e-14
```

UJI SIMULTAN

Hipotesis:

$H_0: \beta_1 = \beta_2 = \beta_3 = \beta_4 = \beta_5 = \beta_6 = \beta_7 = \beta_8 = \beta_9 = \beta_{10} = \beta_{11}$

H_1: Minimal ada satu $\beta_j \neq 0,\ j = 1,2,3,4,5,6,7,8,9,10,11$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: Likelihood ratio test = 81,95 ($p\text{-}value = 6 \times 10^{-14}$)

Daerah penolakan: Tolak H_0 jika Likelihood Ratio $> \chi^2_{\alpha,p}$ atau $P - value < \alpha$

Keputusan dan Kesimpulan:

Tolak H_0 karena $p\text{-}value < \alpha$ ($6 \times 10^{-14} < 0{,}05$) sehingga minimal terdapat 1 $\beta_j \neq 0$ dengan j = 1,2,3,4,5,6,7,8,9,10,11

MODEL COX PH DENGAN SELURUH VARIABEL PREDIKTOR

```
coxph(formula = y ~ age + anaemia + creatinine_phosphokinase +
    diabetes + ejection_fraction + high_blood_pressure + platelets +
    serum_creatinine + serum_sodium + sex + smoking, data = df)

  n= 299, number of events= 96

                             coef  exp(coef)   se(coef)      z Pr(>|z|)
age                      4.641e-02  1.048e+00  9.324e-03  4.977 6.45e-07 ***
anaemia                  4.601e-01  1.584e+00  2.168e-01  2.122   0.0338 *
creatinine_phosphokinase 2.207e-04  1.000e+00  9.919e-05  2.225   0.0260 *
diabetes                 1.399e-01  1.150e+00  2.231e-01  0.627   0.5307
ejection_fraction       -4.894e-02  9.522e-01  1.048e-02 -4.672 2.98e-06 ***
high_blood_pressure      4.757e-01  1.609e+00  2.162e-01  2.201   0.0278 *
platelets               -4.635e-07  1.000e+00  1.126e-06 -0.412   0.6806
serum_creatinine         3.210e-01  1.379e+00  7.017e-02  4.575 4.76e-06 ***
serum_sodium            -4.419e-02  9.568e-01  2.327e-02 -1.899   0.0575 .
sex                     -2.375e-01  7.886e-01  2.516e-01 -0.944   0.3452
smoking                  1.289e-01  1.138e+00  2.512e-01  0.513   0.6078
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

                        exp(coef) exp(-coef) lower .95 upper .95
age                        1.0475     0.9547    1.0285     1.067
anaemia                    1.5843     0.6312    1.0358     2.423
creatinine_phosphokinase   1.0002     0.9998    1.0000     1.000
diabetes                   1.1501     0.8695    0.7427     1.781
ejection_fraction          0.9522     1.0502    0.9329     0.972
high_blood_pressure        1.6092     0.6214    1.0534     2.458
platelets                  1.0000     1.0000    1.0000     1.000
serum_creatinine           1.3786     0.7254    1.2014     1.582
serum_sodium               0.9568     1.0452    0.9141     1.001
sex                        0.7886     1.2681    0.4816     1.291
smoking                    1.1376     0.8790    0.6953     1.861

Concordance= 0.741  (se = 0.027 )
Likelihood ratio test= 81.95  on 11 df,   p=6e-13
Wald test            = 87.27  on 11 df,   p=6e-14
Score (logrank) test = 88.39  on 11 df,   p=3e-14
```

UJI PARSIAL

Hipotesis:

$H_0: \beta_j = 0$

$H_1: \beta_j \neq 0$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $W_{hit}^2 = \dfrac{(\hat{\beta}_j)^2}{(SE(\hat{\beta}_j))^2}$

Daerah penolakan: Tolak H_0 jika $W_{hit}^2 > \chi_{\alpha,p}^2$ atau $P - value < \alpha$

Keputusan dan Kesimpulan:

Variabel yang berpengaruh signifikan terhadap model adalah age, anaemia, creatinine phosphokinase, ejection fraction, high blood pressure, dan serum creatinine.

MODEL COX PH DENGAN SELURUH VARIABEL PREDIKTOR

```
coxph(formula = y ~ age + anaemia + creatinine_phosphokinase +
    diabetes + ejection_fraction + high_blood_pressure + platelets +
    serum_creatinine + serum_sodium + sex + smoking, data = df)

  n= 299, number of events= 96

                             coef  exp(coef)   se(coef)      z Pr(>|z|)
age                      4.641e-02  1.048e+00  9.324e-03  4.977 6.45e-07 ***
anaemia                  4.601e-01  1.584e+00  2.168e-01  2.122   0.0338 *
creatinine_phosphokinase 2.207e-04  1.000e+00  9.919e-05  2.225   0.0260 *
diabetes                 1.399e-01  1.150e+00  2.231e-01  0.627   0.5307
ejection_fraction       -4.894e-02  9.522e-01  1.048e-02 -4.672 2.98e-06 ***
high_blood_pressure      4.757e-01  1.609e+00  2.162e-01  2.201   0.0278 *
platelets               -4.635e-07  1.000e+00  1.126e-06 -0.412   0.6806
serum_creatinine         3.210e-01  1.379e+00  7.017e-02  4.575 4.76e-06 ***
serum_sodium            -4.419e-02  9.568e-01  2.327e-02 -1.899   0.0575 .
sex                     -2.375e-01  7.886e-01  2.516e-01 -0.944   0.3452
smoking                  1.289e-01  1.138e+00  2.512e-01  0.513   0.6078
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                        exp(coef) exp(-coef) lower .95 upper .95
age                        1.0475     0.9547    1.0285     1.067
anaemia                    1.5843     0.6312    1.0358     2.423
creatinine_phosphokinase   1.0002     0.9998    1.0000     1.000
diabetes                   1.1501     0.8695    0.7427     1.781
ejection_fraction          0.9522     1.0502    0.9329     0.972
high_blood_pressure        1.6092     0.6214    1.0534     2.458
platelets                  1.0000     1.0000    1.0000     1.000
serum_creatinine           1.3786     0.7254    1.2014     1.582
serum_sodium               0.9568     1.0452    0.9141     1.001
sex                        0.7886     1.2681    0.4816     1.291
smoking                    1.1376     0.8790    0.6953     1.861

Concordance= 0.741  (se = 0.027 )
Likelihood ratio test= 81.95  on 11 df,   p=6e-13
Wald test            = 87.27  on 11 df,   p=6e-14
Score (logrank) test = 88.39  on 11 df,   p=3e-14
```

MODEL COX PH

$$h(t,\boldsymbol{X}) = h_0(t)exp[\beta_1 age + \beta_2 anameia + \beta_3 creatinine\ phosphokinase + \beta_4 diabetes + \beta_5 ejection\ fraction + \beta_6 high\ blood\ pressure + \beta_7 platelets + \beta_8 serum\ creatinine + \beta_9 serum\ sodium + \beta_{10} sex + \beta_{11} smoking]$$

$$\hat{h}(t,\boldsymbol{X}) = \widehat{h_0}(t)exp[\widehat{\beta_1} age + \widehat{\beta_2} anameia + \widehat{\beta_3} creatinine\ phosphokinase + \widehat{\beta_4} diabetes + \widehat{\beta_5} ejection\ fraction + \widehat{\beta_6} high\ blood\ pressure + \widehat{\beta_7} platelets + \widehat{\beta_8} serum\ creatinine + \widehat{\beta_9} serum\ sodium + \widehat{\beta_{10}} sex + \widehat{\beta_{11}} smoking]$$

$$\hat{h}(t,\boldsymbol{X}) = \widehat{h_0}(t)exp[0{,}046\ age + 0{,}460\ anameia + 0{,}000\ creatinine\ phosphokinase + 0{,}139\ diabetes - 0{,}049\ ejection\ fraction + 0{,}476\ high\ blood\ pressure - 0{,}000\ platelets + 0{,}321\ serum\ creatinine - 0{,}044\ serum\ sodium - 0{,}238\ sex + 0{,}129 smoking]$$

HAZARD RATIO

$$\widehat{HR}_{age} = \exp(\widehat{\beta_1}) = \exp(0{,}046) = 1{,}048$$

$$\widehat{HR}_{anaemia} = \exp(\widehat{\beta_2}) = \exp(0{,}460) = 1{,}584$$

$$\widehat{HR}_{creatinine\ phosphokinase} = \exp(\widehat{\beta_3}) = \exp(0{,}000) = 1{,}000$$

$$\widehat{HR}_{diabetes} = \exp(\widehat{\beta_4}) = \exp(0{,}139) = 1{,}15$$

$$\widehat{HR}_{ejection\ fraction} = \exp(\widehat{\beta_5}) = \exp(0{,}049) = 0{,}952$$

$$\widehat{HR}_{high\ blod\ pressure} = \exp(\widehat{\beta_6}) = \exp(0{,}476) = 1{,}609$$

$$\widehat{HR}_{platelets} = \exp(\widehat{\beta_7}) = \exp(0{,}000) = 1{,}000$$

$$\widehat{HR}_{serum\ creatinine} = \exp(\widehat{\beta_8}) = \exp(0{,}321) = 1{,}379$$

$$\widehat{HR}_{serum\ sodium} = \exp(\widehat{\beta_9}) = \exp(0{,}044) = 0{,}957$$

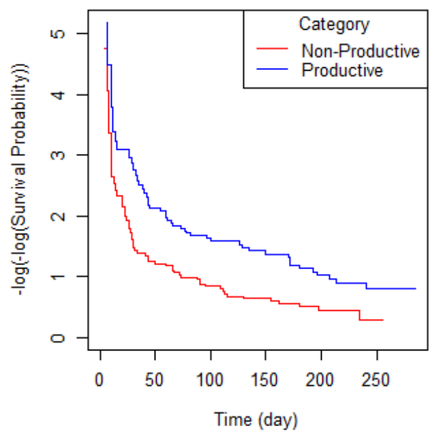
$$\widehat{HR}_{sex} = \exp(\widehat{\beta_{10}}) = \exp(0{,}238) = 0{,}789$$

$$\widehat{HR}_{smoking} = \exp(\widehat{\beta_{11}}) = \exp(0{,}129) = 1{,}138$$

CEK ASUMSI (PENDEKATAN GRAFIK)

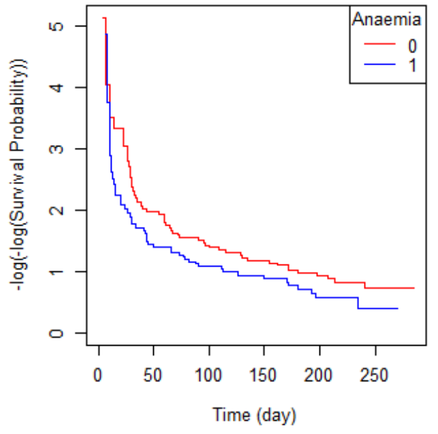
Grafik -log(-log(S(t))

Age



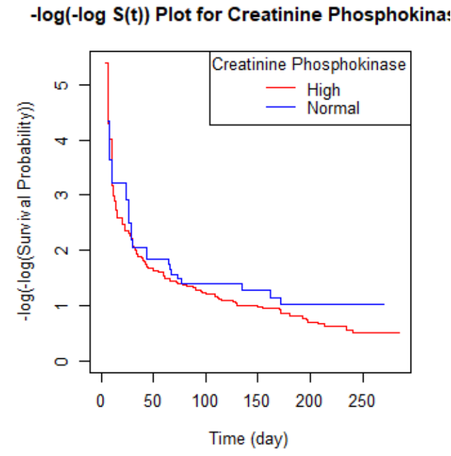
Secara visual, variabel Age memenuhi asumsi PH karena kurva paralel.

Anaemia



Secara visual, variabel Anaemia memenuhi asumsi PH karena kurva paralel.

Creatinine Phosphokinase

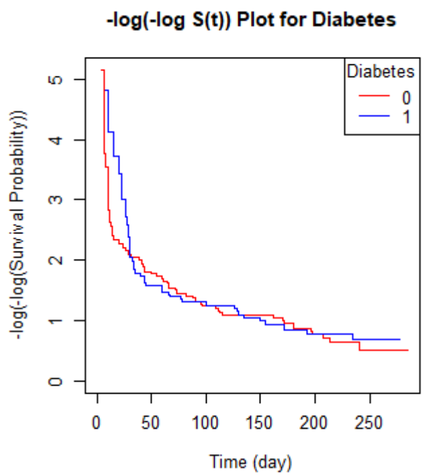


Secara visual, variabel Creatinine Phosphokinase memenuhi asumsi PH meski banyak perpotongan tapi tetap berusaha paralel.

CEK ASUMSI (PENDEKATAN GRAFIK)

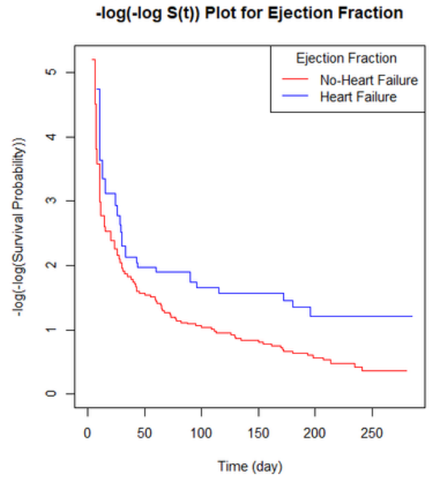
Grafik -log(-log(S(t))

Diabetes



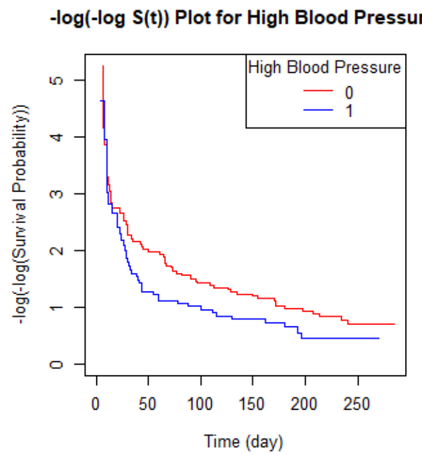
Secara visual, variabel Diabetes memenuhi asumsi PH karena kurva paralel meski banyak perpotongan.

Ejection Fraction



Secara visual, variabel Ejection Fraction tidak memenuhi asumsi PH karena tidak paralel.

High Blood Pressure

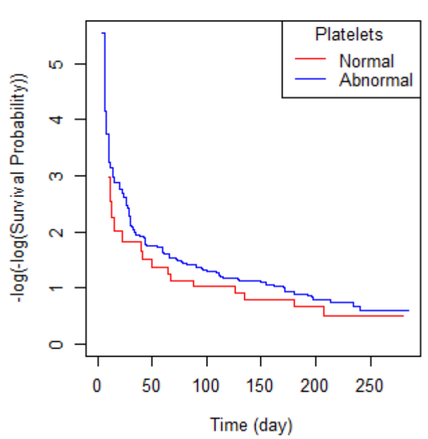


Secara visual, variabel High Blood Pressure memenuhi asumsi PH karena kurva paralel.

CEK ASUMSI (PENDEKATAN GRAFIK)

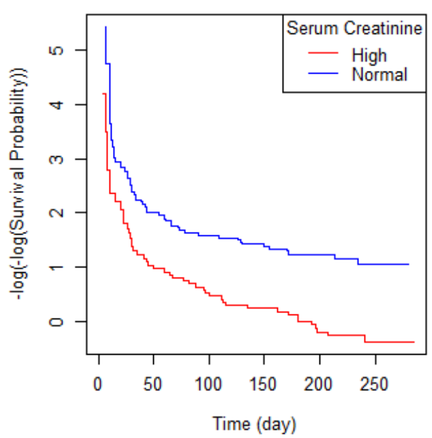
Grafik -log(-log(S(t))

Platelets



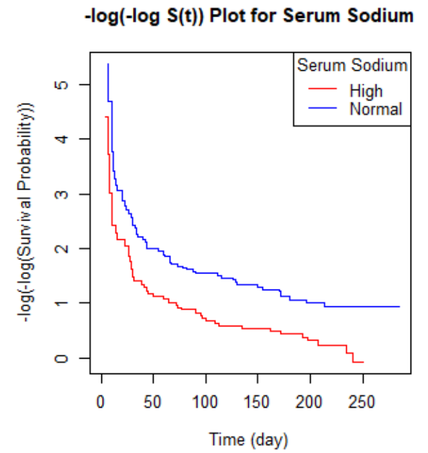
Secara visual, variabel Platelets memenuhi asumsi PH karena kurva paralel.

Serum Creatinine



Secara visual, variabel Serum Creatinine memenuhi asumsi PH karena kurva paralel.

Serum Sodium

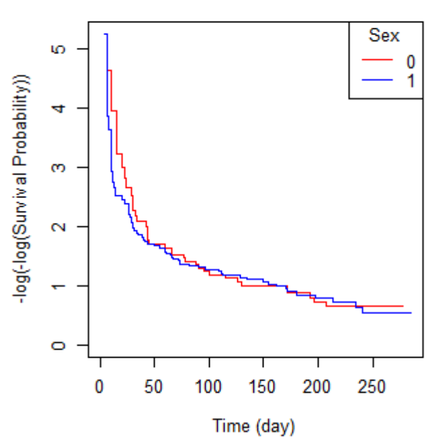


Secara visual, variabel Serum Sodium memenuhi asumsi PH karena kurva paralel.

CEK ASUMSI (PENDEKATAN GRAFIK)

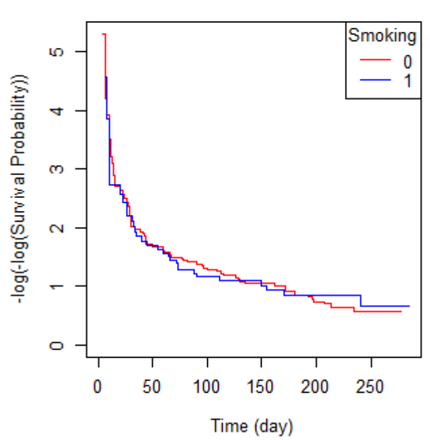
Grafik -log(-log(S(t))

Sex



Secara visual, variabel Sex memenuhi asumsi PH karena kurva paralel.

Smoking



Secara visual, variabel Smoking memenuhi asumsi PH karena kurva paralel meski banyak perpotongan.

CEK ASUMSI (GOODNESS OF FIT)

```
> gof1 <- cox.zph(model, transform = "identity")
> gof1
                            chisq df     p
age                       0.22543  1 0.635
anaemia                   0.00479  1 0.945
creatinine_phosphokinase  1.35159  1 0.245
diabetes                  0.58638  1 0.444
ejection_fraction         4.66861  1 0.031
high_blood_pressure       0.07043  1 0.791
platelets                 0.29627  1 0.586
serum_creatinine          1.75892  1 0.185
serum_sodium              0.03032  1 0.862
sex                       0.03416  1 0.853
smoking                   0.64081  1 0.423
GLOBAL                   12.51231 11 0.326
```

Uji Goodness of Fit

Hipotesis:

$H_0: \rho = 0$

$H_1: \rho \neq 0$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: χ^2

Daerah penolakan: Tolak H_0 jika $p\text{-}value < \alpha$

Keputusan dan Kesimpulan:

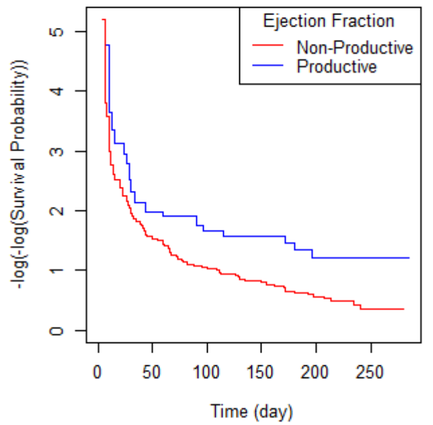
Variabel	Keputusan	Kesimpulan
age	Gagal Tolak H_0	$\rho = 0$, asumsi PH terpenuhi
anaemia	Gagal Tolak H_0	$\rho = 0$, asumsi PH terpenuhi
creatinine phosphokinase	Gagal Tolak H_0	$\rho = 0$, asumsi PH terpenuhi
diabetes	Gagal Tolak H_0	$\rho = 0$, asumsi PH terpenuhi
ejection fraction	Tolak H_0	$\rho \neq 0$, asumsi PH tidak terpenuhi
high blood pressure	Gagal Tolak H_0	$\rho = 0$, asumsi PH terpenuhi
platelets	Gagal Tolak H_0	$\rho = 0$, asumsi PH terpenuhi
serum creatinine	Gagal Tolak H_0	$\rho = 0$, asumsi PH terpenuhi
serum sodium	Gagal Tolak H_0	$\rho = 0$, asumsi PH terpenuhi
sex	Gagal Tolak H_0	$\rho = 0$, asumsi PH terpenuhi
smoking	Gagal Tolak H_0	$\rho = 0$, asumsi PH terpenuhi

Variabel ejection fraction tidak memenuhi asumsi PH sehingga analisis dilanjutkan dengan pembuatan model *Stratified Cox* atau *Extended Cox*.

MODEL STRATIFIED COX

MODEL STRATIFIED COX

Ejection Fraction



Secara visual, variabel Ejection Fraction tidak memenuhi asumsi PH karena tidak paralel.

```
> gof1 <- cox.zph(model, transform = "identity")
> gof1
                            chisq df     p
age                       0.22543  1 0.635
anaemia                   0.00479  1 0.945
creatinine_phosphokinase  1.35159  1 0.245
diabetes                  0.58638  1 0.444
ejection_fraction         4.66861  1 0.031
high_blood_pressure       0.07043  1 0.791
platelets                 0.29627  1 0.586
serum_creatinine          1.75892  1 0.185
serum_sodium              0.03032  1 0.862
sex                       0.03416  1 0.853
smoking                   0.64081  1 0.423
GLOBAL                   12.51231 11 0.326
```

Variabel **ejection fraction tidak memenuhi asumsi PH**, sehingga pada model stratified Cox dilakukan strata pada pemodelannya.

MODEL STRATIFIED COX 1

```
Call:
coxph(formula = y ~ age1 + anaemia + creatinine + diabetes +
    high_blood_pressure + platelets1 + ser_creatinine + ser_sodium +
    sex + smoking + strata(ef), data = df)

  n= 299, number of events= 96

                       coef exp(coef) se(coef)      z Pr(>|z|)
age1Productive      -0.61928   0.53833  0.21520 -2.878  0.00401 **
anaemia              0.54266   1.72058  0.21023  2.581  0.00984 **
creatinineNormal    -0.26639   0.76614  0.26049 -1.023  0.30648
diabetes             0.05973   1.06155  0.22174  0.269  0.78764
high_blood_pressure  0.44280   1.55706  0.21419  2.067  0.03871 *
platelets1Normal    -0.21559   0.80607  0.28483 -0.757  0.44911
ser_creatinineNormal -1.01460   0.36255  0.22543 -4.501 6.77e-06 ***
ser_sodiumNormal    -0.44546   0.64053  0.23107 -1.928  0.05388 .
sex                 -0.09558   0.90885  0.23655 -0.404  0.68617
smoking              0.21163   1.23569  0.24635  0.859  0.39030
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                    exp(coef) exp(-coef) lower .95 upper .95
age1Productive         0.5383     1.8576    0.3531    0.8208
anaemia                1.7206     0.5812    1.1395    2.5979
creatinineNormal       0.7661     1.3052    0.4598    1.2766
diabetes               1.0616     0.9420    0.6874    1.6394
high_blood_pressure    1.5571     0.6422    1.0233    2.3693
platelets1Normal       0.8061     1.2406    0.4612    1.4087
ser_creatinineNormal   0.3625     2.7583    0.2331    0.5640
ser_sodiumNormal       0.6405     1.5612    0.4072    1.0075
sex                    0.9088     1.1003    0.5717    1.4449
smoking                1.2357     0.8093    0.7625    2.0026

Concordance= 0.691  (se = 0.029 )
Likelihood ratio test= 52.13  on 10 df,   p=1e-07
Wald test            = 54.82  on 10 df,   p=3e-08
Score (logrank) test = 59.3  on 10 df,   p=5e-09
```

UJI SIMULTAN

Hipotesis:

$H_0 : \beta_1 = \beta_2 = \beta_3 = \beta_4 = \beta_6 = \beta_7 = \beta_8 = \beta_9 = \beta_{10} = \beta_{11}$

$H_1 : Minimal\ ada\ satu\ \beta_j \neq 0, \quad j = 1,2,3,4,6,7,8,9,10,11$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: Likelihood ratio test = 52.13 ($p - value = 1\ x\ 10^{-7}$)

Daerah penolakan: Tolak H_0 jika Likelihood Ratio $> \chi^2_{\alpha,p}$ atau $P - value < \alpha$

Keputusan dan Kesimpulan:

Tolak Ho karena $p - value < \alpha$ ($1\ x\ 10^{-7} < 0.05$) sehingga minimal terdapat 1 $\beta_j \neq 0$ dengan j = 1,2,3,4,6,7,8,9,10,11

MODEL STRATIFIED COX 1

```
Call:
coxph(formula = y ~ age1 + anaemia + creatinine + diabetes +
    high_blood_pressure + platelets1 + ser_creatinine + ser_sodium +
    sex + smoking + strata(ef), data = df)

  n= 299, number of events= 96

                        coef exp(coef) se(coef)      z Pr(>|z|)
age1Productive       -0.61928   0.53833  0.21520 -2.878  0.00401 **
anaemia               0.54266   1.72058  0.21023  2.581  0.00984 **
creatinineNormal     -0.26639   0.76614  0.26049 -1.023  0.30648
diabetes              0.05973   1.06155  0.22174  0.269  0.78764
high_blood_pressure   0.44280   1.55706  0.21419  2.067  0.03871 *
platelets1Normal     -0.21559   0.80607  0.28483 -0.757  0.44911
ser_creatinineNormal -1.01460   0.36255  0.22543 -4.501 6.77e-06 ***
ser_sodiumNormal     -0.44546   0.64053  0.23107 -1.928  0.05388 .
sex                  -0.09558   0.90885  0.23655 -0.404  0.68617
smoking               0.21163   1.23569  0.24635  0.859  0.39030
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                     exp(coef) exp(-coef) lower .95 upper .95
age1Productive          0.5383     1.8576    0.3531    0.8208
anaemia                 1.7206     0.5812    1.1395    2.5979
creatinineNormal        0.7661     1.3052    0.4598    1.2766
diabetes                1.0616     0.9420    0.6874    1.6394
high_blood_pressure     1.5571     0.6422    1.0233    2.3693
platelets1Normal        0.8061     1.2406    0.4612    1.4087
ser_creatinineNormal    0.3625     2.7583    0.2331    0.5640
ser_sodiumNormal        0.6405     1.5612    0.4072    1.0075
sex                     0.9088     1.1003    0.5717    1.4449
smoking                 1.2357     0.8093    0.7625    2.0026

Concordance= 0.691  (se = 0.029 )
Likelihood ratio test= 52.13  on 10 df,   p=1e-07
Wald test            = 54.82  on 10 df,   p=3e-08
Score (logrank) test = 59.3  on 10 df,   p=5e-09
```

UJI PARSIAL

Hipotesis:

$H_0 : \beta_j = 0$

$H_1 : \beta_j \neq 0$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $W_{hit}^2 = \dfrac{(\hat{\beta}_j)^2}{(SE(\hat{\beta}_j))^2}$

Daerah penolakan: Tolak H_0 jika $W_{hit}^2 > \chi_{\alpha,p}^2$ atau $P - value < \alpha$

Keputusan dan Kesimpulan:

Variabel yang berpengaruh signifikan terhadap model adalah **age, anaemia, high blood pressure, dan serum creatinine**.

Dikarenakan masih banyaknya variabel yang tidak signifikan disini melakukan beberapa pemodelan untuk model stratified, kami memilih **2 model**.

MODEL STRATIFIED COX 2

```
Call:
coxph(formula = y ~ age1 + anaemia + high_blood_pressure + ser_creatinine +
    ser_sodium + strata(ef), data = df)

  n= 299, number of events= 96

                        coef exp(coef) se(coef)      z Pr(>|z|)
age1Productive       -0.5793    0.5603   0.2079 -2.787  0.00533 **
anaemia               0.5311    1.7008   0.2097  2.533  0.01132 *
high_blood_pressure   0.4505    1.5691   0.2107  2.138  0.03250 *
ser_creatinineNormal -1.0339    0.3556   0.2195 -4.709 2.48e-06 ***
ser_sodiumNormal     -0.3757    0.6868   0.2225 -1.689  0.09122 .
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                    exp(coef) exp(-coef) lower .95 upper .95
age1Productive         0.5603     1.7848    0.3728    0.8421
anaemia                1.7008     0.5879    1.1276    2.5655
high_blood_pressure    1.5691     0.6373    1.0383    2.3713
ser_creatinineNormal   0.3556     2.8120    0.2313    0.5468
ser_sodiumNormal       0.6868     1.4561    0.4441    1.0621

Concordance= 0.681  (se = 0.029 )
Likelihood ratio test= 49.72  on 5 df,   p=2e-09
Wald test            = 52.03  on 5 df,   p=5e-10
Score (logrank) test = 56.29  on 5 df,   p=7e-11
```

UJI SIMULTAN

Hipotesis:

$H_0 : \beta_1 = \beta_2 = \beta_3 = \beta_4 = \beta_6 = \beta_7 = \beta_8 = \beta_9 = \beta_{10} = \beta_{11}$

$H_1 : Minimal\ ada\ satu\ \beta_j \neq 0, \quad j = 1,2,3,4,6,7,8,9,10,11$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: Likelihood ratio test = 49.72 $(p - value = 2\ x\ 10^{-9})$

Daerah penolakan: Tolak H_0 jika Likelihood Ratio $> \chi^2_{\alpha,p}$ atau $P - value < \alpha$

Keputusan dan Kesimpulan:

Tolak Ho karena $p - value < \alpha$ $(2\ x\ 10^{-9} < 0.05)$ sehingga minimal terdapat 1 $\beta_j \neq 0$ dengan j = 1,2,3,4,6,7,8,9,10,11

MODEL STRATIFIED COX 2

```
Call:
coxph(formula = y ~ age1 + anaemia + high_blood_pressure + ser_creatinine +
    ser_sodium + strata(ef), data = df)

  n= 299, number of events= 96

                       coef exp(coef) se(coef)      z Pr(>|z|)
age1Productive       -0.5793    0.5603   0.2079 -2.787  0.00533 **
anaemia               0.5311    1.7008   0.2097  2.533  0.01132 *
high_blood_pressure   0.4505    1.5691   0.2107  2.138  0.03250 *
ser_creatinineNormal -1.0339    0.3556   0.2195 -4.709 2.48e-06 ***
ser_sodiumNormal     -0.3757    0.6868   0.2225 -1.689  0.09122 .
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                     exp(coef) exp(-coef) lower .95 upper .95
age1Productive          0.5603     1.7848    0.3728    0.8421
anaemia                 1.7008     0.5879    1.1276    2.5655
high_blood_pressure     1.5691     0.6373    1.0383    2.3713
ser_creatinineNormal    0.3556     2.8120    0.2313    0.5468
ser_sodiumNormal        0.6868     1.4561    0.4441    1.0621

Concordance= 0.681  (se = 0.029 )
Likelihood ratio test= 49.72  on 5 df,   p=2e-09
Wald test            = 52.03  on 5 df,   p=5e-10
Score (logrank) test = 56.29  on 5 df,   p=7e-11
```

UJI PARSIAL

Hipotesis:

$H_0 : \beta_j = 0$

$H_1 : \beta_j \neq 0$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $W_{hit}^2 = \dfrac{(\hat{\beta}_j)^2}{(SE(\hat{\beta}_j))^2}$

Daerah penolakan: Tolak H_0 jika $W_{hit}^2 > \chi_{\alpha,p}^2$ atau $P - value < \alpha$

Keputusan dan Kesimpulan:

Variabel yang berpengaruh signifikan terhadap model adalah **age, anaemia, high blood pressure, dan serum creatinine**.

Untuk memastikan kedua model ini maka dilakukan **uji signifikansi** agar lebih meyakinkan model dengan **variabel sederhana** apakah lebih baik dibanding dengan **model dengan variabel lain.**

UJI SIGINIFIKANSI VARIABEL PADA MODEL

```
Analysis of Deviance Table
 Cox model: response is  y
 Model 1: ~ age1 + anaemia + high_blood_pressure + ser_creatinine + ser_sodium + strata(ef)
 Model 2: ~ age1 + anaemia + creatinine + diabetes + high_blood_pressure + platelets1 + ser_creatinine + ser_sodium + sex + smoking + strata(ef)
   loglik  Chisq Df Pr(>|Chi|)
1 -426.76
2 -425.56 2.4061  5     0.7906
```

Hipotesis

H_0 : *Variabel tambahan tidak signifikan* ($\beta_{variabel\ tambahan} = 0$).

H_1 : *Setidaknya Satu Variabel tambahan signifikan* ($\beta_{variabel\ tambahan} \neq 0$).

Taraf Signifikansi

alfa = 0.05

Statistik Uji

$$G = -2lnL_{reduced} - \left(-2lnL_{full}\right)$$

$$G = -2(-426.76) - (-2(-425.56))$$

$$G = 2.0461$$

Daerah Kritis

Tolak H_0 jika $G > X^2_{1-\alpha;5}$ atau $p - value < \alpha$ dimana $X^2_{1-\alpha;5} = 11.07$

Kesimpulan

Karena $G < X^2_{1-\alpha;5}$ yaitu $2.041 < 11.07$ maka **gagal tolak H_0**. Oleh karena itu, dapat dismpulkan bahwa variabel tambahan tidak siginifikan atau model sederhana lebih baik.

MODEL STRATIFIED COX DENGAN INTERAKSI DAN UJI SIGNIFIKANSI VARIABEL PADA MODEL

```
Call:
coxph(formula = y ~ age1 + anaemia + high_blood_pressure + ser_creatinine +
    ser_sodium + strata(ef) * age1 + strata(ef) * ser_creatinine +
    strata(ef) * ser_sodium, data = df)

  n= 299, number of events= 96

                                              coef exp(coef) se(coef)      z Pr(>|z|)
age1Productive                             -0.4784    0.6198   0.2409 -1.986 0.047006 *
anaemia                                     0.5013    1.6509   0.2101  2.387 0.017007 *
high_blood_pressure                         0.4382    1.5500   0.2117  2.070 0.038449 *
ser_creatinineNormal                       -0.9581    0.3836   0.2508 -3.821 0.000133 ***
ser_sodiumNormal                           -0.2096    0.8109   0.2571 -0.815 0.415007
age1Productive:strata(ef)No-Heart Failure  -0.5902    0.5542   0.5043 -1.170 0.241899
ser_creatinineNormal:strata(ef)No-Heart Failure -0.4390    0.6447   0.5018 -0.875 0.381636
ser_sodiumNormal:strata(ef)No-Heart Failure     -0.9095    0.4027   0.5050 -1.801 0.071725 .
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                                           exp(coef) exp(-coef) lower .95 upper .95
age1Productive                                0.6198     1.6135    0.3865    0.9937
anaemia                                       1.6509     0.6057    1.0937    2.4918
high_blood_pressure                           1.5500     0.6452    1.0236    2.3471
ser_creatinineNormal                          0.3836     2.6068    0.2347    0.6271
ser_sodiumNormal                              0.8109     1.2331    0.4900    1.3422
age1Productive:strata(ef)No-Heart Failure     0.5542     1.8043    0.2063    1.4892
ser_creatinineNormal:strata(ef)No-Heart Failure 0.6447     1.5512    0.2411    1.7238
ser_sodiumNormal:strata(ef)No-Heart Failure     0.4027     2.4831    0.1497    1.0837

Concordance= 0.689  (se = 0.029 )
Likelihood ratio test= 55.7  on 8 df,   p=3e-09
Wald test            = 60.16  on 8 df,   p=4e-10
Score (logrank) test = 66.51  on 8 df,   p=2e-11
```

```
Analysis of Deviance Table
 Cox model: response is  y
 Model 1: ~ age1 + anaemia + high_blood_pressure + ser_creatinine + ser_sodium + strata(ef)
 Model 2: ~ age1 + anaemia + high_blood_pressure + ser_creatinine + ser_sodium + strata(ef) * age1 + strata(ef) * ser_creatinine + strata(ef) *
_sodium
   loglik  Chisq Df Pr(>|Chi|)
1 -426.76
2 -423.77 5.9837  3     0.1124
```

Hipotesis

H_0 : *Variabel tambahan tidak signifikan* ($\beta_{variabel\ tambahan} = 0$).

H_1 : *Setidaknya Satu Variabel tambahan signifikan* ($\beta_{variabel\ tambahan} \neq 0$).

Taraf Signifikansi

alfa = 0.05

Statistik Uji

$$G = -2lnL_{reduced} - (-2lnL_{full})$$

$$G = -2(-426.76) - (-2(-423.77))$$

$$G = 5.9837$$

Daerah Kritis

Tolak H_0 jika $G > X^2_{1-\alpha;3}$ atau $p - value < \alpha$ dimana $X^2_{1-\alpha;3} = 7.815$

Kesimpulan

Karena $G < X^2_{1-\alpha;5}$ yaitu $5.9837 < 7.815$ maka **gagal tolak H_0**. Oleh karena itu, dapat dismpulkan bahwa variabel tambahan tidak siginifikan atau model sederhana lebih baik.

MODEL FINAL STRATIFIED

```
Call:
coxph(formula = y ~ age1 + anaemia + high_blood_pressure + ser_creatinine +
    ser_sodium + strata(ef), data = df)

  n= 299, number of events= 96

                       coef exp(coef) se(coef)      z Pr(>|z|)
age1Productive       -0.5793    0.5603   0.2079 -2.787  0.00533 **
anaemia               0.5311    1.7008   0.2097  2.533  0.01132 *
high_blood_pressure   0.4505    1.5691   0.2107  2.138  0.03250 *
ser_creatinineNormal -1.0339    0.3556   0.2195 -4.709 2.48e-06 ***
ser_sodiumNormal     -0.3757    0.6868   0.2225 -1.689  0.09122 .
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                     exp(coef) exp(-coef) lower .95 upper .95
age1Productive          0.5603     1.7848    0.3728    0.8421
anaemia                 1.7008     0.5879    1.1276    2.5655
high_blood_pressure     1.5691     0.6373    1.0383    2.3713
ser_creatinineNormal    0.3556     2.8120    0.2313    0.5468
ser_sodiumNormal        0.6868     1.4561    0.4441    1.0621

Concordance= 0.681  (se = 0.029 )
Likelihood ratio test= 49.72  on 5 df,   p=2e-09
Wald test            = 52.03  on 5 df,   p=5e-10
Score (logrank) test = 56.29  on 5 df,   p=7e-11
```

Model

$$h_g(t,X) = h_{0g}\exp\left[\beta_1 Age + \beta_2 Anaemia + \beta_3 HighBloodPressure + \beta_4 SerumCreatinine + \beta_5 SerumSodium\right.$$

$$g = 1,2$$

EF (No-Heart Failure) g=1

$$\hat{h}_g(t,X) = \hat{h}_{01}\exp\left[-0.5793 Age + 0.5311 Anaemia + 0.4505 HighBloodPressure + -1.0039 SerumCreatinine + -0.3757 SerumSodium\right.$$

EF (Heart Failure) g=2

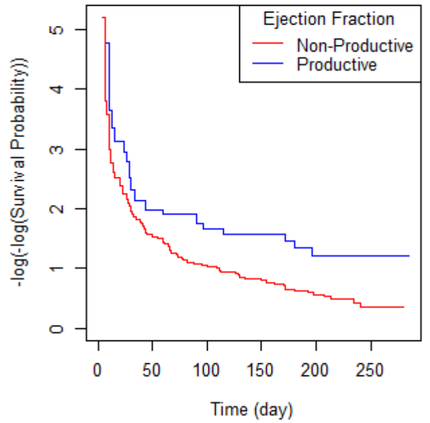
$$\hat{h}_g(t,X) = \hat{h}_{02}\exp\left[-0.5793 Age + 0.5311 Anaemia + 0.4505 HighBloodPressure + -1.0039 SerumCreatinine + -0.3757 SerumSodium\right.$$

Stratified Cox Model berdasarkan variabel ef menunjukkan bahwa variabel **age, anaemia, high blood pressure, dan serum creatinine** memiliki pengaruh signifikan terhadap hazard dengan serum creatinine memiliki pengaruh negatif paling kuat (HR=0.3556HR, p-value<0.05), sementara **serum sodium** tidak signifikan secara statistik.

MODEL EXTENDED COX

MODEL EXTENDED COX

Ejection Fraction



Secara visual, variabel Ejection Fraction tidak memenuhi asumsi PH karena tidak paralel.

```
> gof1 <- cox.zph(model, transform = "identity")
> gof1
                            chisq df     p
age                       0.22543  1 0.635
anaemia                   0.00479  1 0.945
creatinine_phosphokinase  1.35159  1 0.245
diabetes                  0.58638  1 0.444
ejection_fraction         4.66861  1 0.031
high_blood_pressure       0.07043  1 0.791
platelets                 0.29627  1 0.586
serum_creatinine          1.75892  1 0.185
serum_sodium              0.03032  1 0.862
sex                       0.03416  1 0.853
smoking                   0.64081  1 0.423
GLOBAL                   12.51231 11 0.326
```

Variabel **ejection fraction tidak memenuhi asumsi PH**, sehingga pada model extended Cox perlu dimasukkan interaksi antara waktu dengan variabel ejection fraction.

MODEL EXTENDED COX

```
coxph(formula = Surv(df.cp$start, df.cp$time, df.cp$status) ~
    age + anaemia + creatinine_phosphokinase + diabetes + ejection_fraction +
        high_blood_pressure + platelets + serum_creatinine +
        serum_sodium + sex + smoking + ejection_fraction:time,
    data = df.cp)

  n= 14254, number of events= 96

                               coef  exp(coef)   se(coef)      z Pr(>|z|)
age                        4.690e-02  1.048e+00  9.382e-03  4.998 5.78e-07 ***
anaemia                    4.873e-01  1.628e+00  2.173e-01  2.242   0.0250 *
creatinine_phosphokinase   2.264e-04  1.000e+00  9.945e-05  2.277   0.0228 *
diabetes                   1.283e-01  1.137e+00  2.222e-01  0.577   0.5638
ejection_fraction         -2.406e-02  9.762e-01  1.491e-02 -1.614   0.1065
high_blood_pressure        5.016e-01  1.651e+00  2.167e-01  2.315   0.0206 *
platelets                 -5.673e-07  1.000e+00  1.149e-06 -0.494   0.6216
serum_creatinine           3.174e-01  1.373e+00  6.983e-02  4.545 5.50e-06 ***
serum_sodium              -4.214e-02  9.587e-01  2.365e-02 -1.781   0.0749 .
sex                       -2.380e-01  7.882e-01  2.514e-01 -0.947   0.3438
smoking                    1.097e-01  1.116e+00  2.519e-01  0.436   0.6631
ejection_fraction:time    -4.143e-04  9.996e-01  1.906e-04 -2.174   0.0297 *
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                          exp(coef) exp(-coef) lower .95 upper .95
age                          1.0480     0.9542    1.0289     1.067
anaemia                      1.6278     0.6143    1.0632     2.492
creatinine_phosphokinase     1.0002     0.9998    1.0000     1.000
diabetes                     1.1368     0.8796    0.7354     1.757
ejection_fraction            0.9762     1.0243    0.9481     1.005
high_blood_pressure          1.6513     0.6056    1.0799     2.525
platelets                    1.0000     1.0000    1.0000     1.000
serum_creatinine             1.3735     0.7281    1.1978     1.575
serum_sodium                 0.9587     1.0430    0.9153     1.004
sex                          0.7882     1.2687    0.4816     1.290
smoking                      1.1160     0.8961    0.6811     1.829
ejection_fraction:time       0.9996     1.0004    0.9992     1.000

Concordance= 0.743  (se = 0.027 )
Likelihood ratio test= 86.92  on 12 df,   p=2e-13
Wald test            = 90.49  on 12 df,   p=4e-14
Score (logrank) test = 92.38  on 12 df,   p=2e-14
```

UJI SIMULTAN

Hipotesis:

$H_0: \beta_1 = \beta_2 = \beta_3 = \beta_4 = \beta_5 = \beta_6 = \beta_7 = \beta_8 = \beta_9 = \beta_{10} = \beta_{11} = \delta_5$

H_1: Minimal ada satu $\beta_j \; atau \; \delta_5 \neq 0, \; j = 1,2,3,4,5,6,7,8,9,10,11$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: Likelihood ratio test = 86,92 ($p\text{-}value = 2 \times 10^{-13}$)

Daerah penolakan: Tolak H_0 jika Likelihood Ratio $> \chi^2_{\alpha,p}$ atau $P - value < \alpha$

Keputusan dan Kesimpulan:

Tolak H_0 karena $p\text{-}value < \alpha$ ($2 \times 10^{-13} < 0{,}05$) sehingga minimal terdapat 1 $\beta_j \; atau \; \delta_5 \neq 0$ dengan j = 1,2,3,4,5,6,7,8,9,10,11

MODEL EXTENDED COX

```
coxph(formula = Surv(df.cp$start, df.cp$time, df.cp$status) ~
    age + anaemia + creatinine_phosphokinase + diabetes + ejection_fraction +
        high_blood_pressure + platelets + serum_creatinine +
        serum_sodium + sex + smoking + ejection_fraction:time,
    data = df.cp)

  n= 14254, number of events= 96

                               coef  exp(coef)   se(coef)      z Pr(>|z|)
age                        4.690e-02  1.048e+00  9.382e-03  4.998 5.78e-07 ***
anaemia                    4.873e-01  1.628e+00  2.173e-01  2.242   0.0250 *
creatinine_phosphokinase   2.264e-04  1.000e+00  9.945e-05  2.277   0.0228 *
diabetes                   1.283e-01  1.137e+00  2.222e-01  0.577   0.5638
ejection_fraction         -2.406e-02  9.762e-01  1.491e-02 -1.614   0.1065
high_blood_pressure        5.016e-01  1.651e+00  2.167e-01  2.315   0.0206 *
platelets                 -5.673e-07  1.000e+00  1.149e-06 -0.494   0.6216
serum_creatinine           3.174e-01  1.373e+00  6.983e-02  4.545 5.50e-06 ***
serum_sodium              -4.214e-02  9.587e-01  2.365e-02 -1.781   0.0749 .
sex                       -2.380e-01  7.882e-01  2.514e-01 -0.947   0.3438
smoking                    1.097e-01  1.116e+00  2.519e-01  0.436   0.6631
ejection_fraction:time    -4.143e-04  9.996e-01  1.906e-04 -2.174   0.0297 *
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                          exp(coef) exp(-coef) lower .95 upper .95
age                          1.0480     0.9542    1.0289     1.067
anaemia                      1.6278     0.6143    1.0632     2.492
creatinine_phosphokinase     1.0002     0.9998    1.0000     1.000
diabetes                     1.1368     0.8796    0.7354     1.757
ejection_fraction            0.9762     1.0243    0.9481     1.005
high_blood_pressure          1.6513     0.6056    1.0799     2.525
platelets                    1.0000     1.0000    1.0000     1.000
serum_creatinine             1.3735     0.7281    1.1978     1.575
serum_sodium                 0.9587     1.0430    0.9153     1.004
sex                          0.7882     1.2687    0.4816     1.290
smoking                      1.1160     0.8961    0.6811     1.829
ejection_fraction:time       0.9996     1.0004    0.9992     1.000

Concordance= 0.743  (se = 0.027 )
Likelihood ratio test= 86.92  on 12 df,   p=2e-13
Wald test            = 90.49  on 12 df,   p=4e-14
Score (logrank) test = 92.38  on 12 df,   p=2e-14
```

UJI PARSIAL

Hipotesis:

$H_0: \beta_j, \delta_5 = 0$

$H_1: \beta_j, \delta_5 \neq 0$

Taraf signifikansi: $\alpha = 5\%$

Statistik uji: $W_{hit}^2 = \dfrac{(\hat{\beta}_j)^2}{(SE(\hat{\beta}_j))^2}$

Daerah penolakan: Tolak H_0 jika $W_{hit}^2 > \chi_{\alpha,p}^2$ atau $P - value < \alpha$

Keputusan dan Kesimpulan:

Variabel yang berpengaruh signifikan terhadap model adalah **age, anaemia, creatinine phosphokinase, high blood pressure, serum creatinine, dan interaksi antara ejection fraction dengan waktu.**

MODEL EXTENDED COX

```
coxph(formula = Surv(df.cp$start, df.cp$time, df.cp$status) ~
    age + anaemia + creatinine_phosphokinase + diabetes + ejection_fraction +
        high_blood_pressure + platelets + serum_creatinine +
        serum_sodium + sex + smoking + ejection_fraction:time,
    data = df.cp)

  n= 14254, number of events= 96

                               coef  exp(coef)   se(coef)      z Pr(>|z|)
age                        4.690e-02  1.048e+00  9.382e-03  4.998 5.78e-07 ***
anaemia                    4.873e-01  1.628e+00  2.173e-01  2.242   0.0250 *
creatinine_phosphokinase   2.264e-04  1.000e+00  9.945e-05  2.277   0.0228 *
diabetes                   1.283e-01  1.137e+00  2.222e-01  0.577   0.5638
ejection_fraction         -2.406e-02  9.762e-01  1.491e-02 -1.614   0.1065
high_blood_pressure        5.016e-01  1.651e+00  2.167e-01  2.315   0.0206 *
platelets                 -5.673e-07  1.000e+00  1.149e-06 -0.494   0.6216
serum_creatinine           3.174e-01  1.373e+00  6.983e-02  4.545 5.50e-06 ***
serum_sodium              -4.214e-02  9.587e-01  2.365e-02 -1.781   0.0749 .
sex                       -2.380e-01  7.882e-01  2.514e-01 -0.947   0.3438
smoking                    1.097e-01  1.116e+00  2.519e-01  0.436   0.6631
ejection_fraction:time    -4.143e-04  9.996e-01  1.906e-04 -2.174   0.0297 *
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                          exp(coef) exp(-coef) lower .95 upper .95
age                          1.0480     0.9542    1.0289     1.067
anaemia                      1.6278     0.6143    1.0632     2.492
creatinine_phosphokinase     1.0002     0.9998    1.0000     1.000
diabetes                     1.1368     0.8796    0.7354     1.757
ejection_fraction            0.9762     1.0243    0.9481     1.005
high_blood_pressure          1.6513     0.6056    1.0799     2.525
platelets                    1.0000     1.0000    1.0000     1.000
serum_creatinine             1.3735     0.7281    1.1978     1.575
serum_sodium                 0.9587     1.0430    0.9153     1.004
sex                          0.7882     1.2687    0.4816     1.290
smoking                      1.1160     0.8961    0.6811     1.829
ejection_fraction:time       0.9996     1.0004    0.9992     1.000

Concordance= 0.743  (se = 0.027 )
Likelihood ratio test= 86.92  on 12 df,   p=2e-13
Wald test            = 90.49  on 12 df,   p=4e-14
Score (logrank) test = 92.38  on 12 df,   p=2e-14
```

MODEL EXTENDED COX

$$h(t,\boldsymbol{X}) = h_0(t)exp[\beta_1 age + \beta_2 anaemia + \beta_3 creatinine\ phosphokinase + \beta_4 diabetes + \beta_5 ejection\ fraction + \beta_6 high\ blood\ pressure + \beta_7 platelets + \beta_8 serum\ creatinine + \beta_9 serum\ sodium + \beta_{10} sex + \beta_{11} smoking + \delta_5 (ejection\ fraction) g_5\ (t)]$$

$$\hat{h}(t,\boldsymbol{X}) = \widehat{h_0}(t)exp[\widehat{\beta_1} age + \widehat{\beta_2} anaemia + \widehat{\beta_3} creatinine\ phosphokinase + \widehat{\beta_4} diabetes + \widehat{\beta_5} ejection\ fraction + \widehat{\beta_6} high\ blood\ pressure + \widehat{\beta_7} platelets + \widehat{\beta_8} serum\ creatinine + \widehat{\beta_9} serum\ sodium + \widehat{\beta_{10}} sex + \widehat{\beta_{11}} smoking + \widehat{\delta_5} (ejection\ fraction) g_5\ (t)]$$

$$\hat{h}(t,\boldsymbol{X}) = \widehat{h_0}(t)exp[0{,}047\ age + 0{,}487\ anaemia + 0{,}000\ creatinine\ phosphokinase + 0{,}128\ diabetes - 0{,}024\ ejection\ fraction + 0{,}502\ high\ blood\ pressure - 0{,}000\ platelets + 0{,}317\ serum\ creatinine - 0{,}042\ serum\ sodium - 0{,}238\ sex + 0{,}109\ smoking - 0{,}000\ (ejection\ fraction) g_5(t)]$$

HAZARD RATIO

$\widehat{HR}_{age} = \exp(\widehat{\beta_1}) = \exp(0{,}047) = 1{,}048$

$\widehat{HR}_{anaemia} = \exp(\widehat{\beta_2}) = \exp(0{,}487) = 1{,}628$

$\widehat{HR}_{creatinine\ phosphokinase} = \exp(\widehat{\beta_3}) = \exp(0{,}000) = 1{,}000$

$\widehat{HR}_{diabetes} = \exp(\widehat{\beta_4}) = \exp(0{,}128) = 1{,}137$

$\widehat{HR}_{ejection\ fraction} = \exp(\widehat{\beta_5}) = \exp(0{,}024) = 0{,}976$

$\widehat{HR}_{high\ blod\ pressure} = \exp(\widehat{\beta_6}) = \exp(0{,}502) = 1{,}651$

$\widehat{HR}_{platelets} = \exp(\widehat{\beta_7}) = \exp(0{,}000) = 1{,}000$

$\widehat{HR}_{serum\ creatinine} = \exp(\widehat{\beta_8}) = \exp(0{,}317) = 1{,}376$

$\widehat{HR}_{serum\ sodium} = \exp(\widehat{\beta_9}) = \exp(0{,}042) = 0{,}958$

$\widehat{HR}_{sex} = \exp(\widehat{\beta_{10}}) = \exp(0{,}238) = 0{,}788$

$\widehat{HR}_{smoking} = \exp(\widehat{\beta_{11}}) = \exp(0{,}109) = 1{,}116$

MODEL EXTENDED COX

```
coxph(formula = Surv(df.cp$start, df.cp$time, df.cp$status) ~
    age + anaemia + creatinine_phosphokinase + diabetes + ejection_fraction +
        high_blood_pressure + platelets + serum_creatinine +
        serum_sodium + sex + smoking + ejection_fraction:time,
    data = df.cp)

  n= 14254, number of events= 96

                               coef  exp(coef)   se(coef)      z Pr(>|z|)
age                        4.690e-02  1.048e+00  9.382e-03  4.998 5.78e-07 ***
anaemia                    4.873e-01  1.628e+00  2.173e-01  2.242   0.0250 *
creatinine_phosphokinase   2.264e-04  1.000e+00  9.945e-05  2.277   0.0228 *
diabetes                   1.283e-01  1.137e+00  2.222e-01  0.577   0.5638
ejection_fraction         -2.406e-02  9.762e-01  1.491e-02 -1.614   0.1065
high_blood_pressure        5.016e-01  1.651e+00  2.167e-01  2.315   0.0206 *
platelets                 -5.673e-07  1.000e+00  1.149e-06 -0.494   0.6216
serum_creatinine           3.174e-01  1.373e+00  6.983e-02  4.545 5.50e-06 ***
serum_sodium              -4.214e-02  9.587e-01  2.365e-02 -1.781   0.0749 .
sex                       -2.380e-01  7.882e-01  2.514e-01 -0.947   0.3438
smoking                    1.097e-01  1.116e+00  2.519e-01  0.436   0.6631
ejection_fraction:time    -4.143e-04  9.996e-01  1.906e-04 -2.174   0.0297 *
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                          exp(coef) exp(-coef) lower .95 upper .95
age                          1.0480     0.9542    1.0289     1.067
anaemia                      1.6278     0.6143    1.0632     2.492
creatinine_phosphokinase     1.0002     0.9998    1.0000     1.000
diabetes                     1.1368     0.8796    0.7354     1.757
ejection_fraction            0.9762     1.0243    0.9481     1.005
high_blood_pressure          1.6513     0.6056    1.0799     2.525
platelets                    1.0000     1.0000    1.0000     1.000
serum_creatinine             1.3735     0.7281    1.1978     1.575
serum_sodium                 0.9587     1.0430    0.9153     1.004
sex                          0.7882     1.2687    0.4816     1.290
smoking                      1.1160     0.8961    0.6811     1.829
ejection_fraction:time       0.9996     1.0004    0.9992     1.000

Concordance= 0.743  (se = 0.027 )
Likelihood ratio test= 86.92  on 12 df,   p=2e-13
Wald test            = 90.49  on 12 df,   p=4e-14
Score (logrank) test = 92.38  on 12 df,   p=2e-14
```

HAZARD RATIO UNTUK INTERAKSI EJECTION FRACTION DENGAN WAKTU

$$\widehat{HR} = \exp\left(\widehat{\beta_5} + \widehat{\delta_5} t\right)$$

Berikut hazard ratio untuk pasien dengan id 8:

	id	start	time	status	ejection_fraction	HR
23	8	0	4	0	60	0.9746107
24	8	4	6	0	60	0.9738034
25	8	6	7	0	60	0.9734001
26	8	7	8	0	60	0.9729969
27	8	8	10	1	60	0.9721910

KESIMPULAN

PERBANDINGAN MODEL

$$h_g(t,X) = h_{0g}\exp\left[\beta_1 Age + \beta_2 Anaemia + \beta_3 HighBloodPressure + \beta_4 SerumCreatinine + \beta_5 SerumSodium\right]$$

$$g = 1,2$$

```
Call:
coxph(formula = y ~ age1 + anaemia + high_blood_pressure + ser_creatinine +
    ser_sodium + strata(ef), data = df)

  n= 299, number of events= 96

                       coef exp(coef) se(coef)      z Pr(>|z|)
age1Productive       -0.5793    0.5603   0.2079 -2.787  0.00533 **
anaemia               0.5311    1.7008   0.2097  2.533  0.01132 *
high_blood_pressure   0.4505    1.5691   0.2107  2.138  0.03250 *
ser_creatinineNormal -1.0339    0.3556   0.2195 -4.709 2.48e-06 ***
ser_sodiumNormal     -0.3757    0.6868   0.2225 -1.689  0.09122 .
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                     exp(coef) exp(-coef) lower .95 upper .95
age1Productive          0.5603     1.7848    0.3728    0.8421
anaemia                 1.7008     0.5879    1.1276    2.5655
high_blood_pressure     1.5691     0.6373    1.0383    2.3713
ser_creatinineNormal    0.3556     2.8120    0.2313    0.5468
ser_sodiumNormal        0.6868     1.4561    0.4441    1.0621

Concordance= 0.681  (se = 0.029 )
Likelihood ratio test= 49.72  on 5 df,   p=2e-09
Wald test            = 52.03  on 5 df,   p=5e-10
Score (logrank) test = 56.29  on 5 df,   p=7e-11

> # AIC
> extractAIC(model_stra4)[2]
[1] 863.5244
>
```

AIC : 863,5244

Concordance : 0,681

$$\hat{h}(t,\boldsymbol{X}) = \widehat{h_0}(t)exp[0{,}047\ age + 0{,}487\ anaemia + 0{,}000\ creatinine\ phosphokinase + 0{,}128\ diabetes - 0{,}024\ ejection\ fraction + 0{,}502\ high\ blood\ pressure - 0{,}000\ platelets + 0{,}317\ serum\ creatinine - 0{,}042\ serum\ sodium - 0{,}238\ sex + 0{,}109\ smoking - 0{,}000\ (ejection\ fraction)g_5(t)]$$

```
Call:
coxph(formula = Surv(df.cp$start, df.cp$time, df.cp$status) ~
    age + anaemia + creatinine_phosphokinase + diabetes + ejection_fraction +
        high_blood_pressure + platelets + serum_creatinine +
        serum_sodium + sex + smoking + ejection_fraction:time,
    data = df.cp)

  n= 14254, number of events= 96

                                coef  exp(coef)   se(coef)      z Pr(>|z|)
age                         4.690e-02  1.048e+00  9.382e-03  4.998 5.78e-07 ***
anaemia                     4.873e-01  1.628e+00  2.173e-01  2.242   0.0250 *
creatinine_phosphokinase    2.264e-04  1.000e+00  9.945e-05  2.277   0.0228 *
diabetes                    1.283e-01  1.137e+00  2.222e-01  0.577   0.5638
ejection_fraction          -2.406e-02  9.762e-01  1.491e-02 -1.614   0.1065
high_blood_pressure         5.016e-01  1.651e+00  2.167e-01  2.315   0.0206 *
platelets                  -5.673e-07  1.000e+00  1.149e-06 -0.494   0.6216
serum_creatinine            3.174e-01  1.373e+00  6.983e-02  4.545 5.50e-06 ***
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sex                        -2.380e-01  7.882e-01  2.514e-01 -0.947   0.3438
smoking                     1.097e-01  1.116e+00  2.519e-01  0.436   0.6631
ejection_fraction:time     -4.143e-04  9.996e-01  1.906e-04 -2.174   0.0297 *
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                           exp(coef) exp(-coef) lower .95 upper .95
age                           1.0480     0.9542    1.0289     1.067
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ejection_fraction             0.9762     1.0243    0.9481     1.005
high_blood_pressure           1.6513     0.6056    1.0799     2.525
platelets                     1.0000     1.0000    1.0000     1.000
serum_creatinine              1.3735     0.7281    1.1978     1.575
serum_sodium                  0.9587     1.0430    0.9153     1.004
sex                           0.7882     1.2687    0.4816     1.290
smoking                       1.1160     0.8961    0.6811     1.829
ejection_fraction:time        0.9996     1.0004    0.9992     1.000

Concordance= 0.743  (se = 0.027 )
Likelihood ratio test= 86.92  on 12 df,   p=2e-13
Wald test            = 90.49  on 12 df,   p=4e-14
Score (logrank) test = 92.38  on 12 df,   p=2e-14

> extractAIC(mod.extended1)[2]
[1] 955.4854
>
```

AIC : 955,4854

Concordance : 0,743

MODEL TERBAIK

Model Stratified Cox
AIC : 863,5244
Concordance : 0,681

Model Extended Cox
AIC : 955,4854
Concordance : 0,743

Kami menggunakan nilai concordance sebagai acuan untuk memilih model terbaik karena nilai AIC terpengaruh banyaknya jumlah parameter.

Akaike information criterion / Formula

$$AIC = 2k - 2\ln(\hat{L})$$

AIC = Akaike information criterion
k = number of estimated parameters in the model
$\hat{L}$ = maximum value of the likelihood function for the model

Dengan nilai concordance yang lebih besar, maka model terbaik adalah **model Extended Cox**. Variabel yang berpengaruh signifikan terhadap model adalah **age, anaemia, creatinine phosphokinase, high blood pressure, serum creatinine, dan interaksi antara ejection fraction dengan waktu**. Variabel yang berperan sangat signifikan terhadap event gagal jantung pada pasien adalah age dan serum creatinine dengan hazard ratio untuk age sebesar 1,048 dan untuk serum creatinine 1,376.

TERIMA KASIH