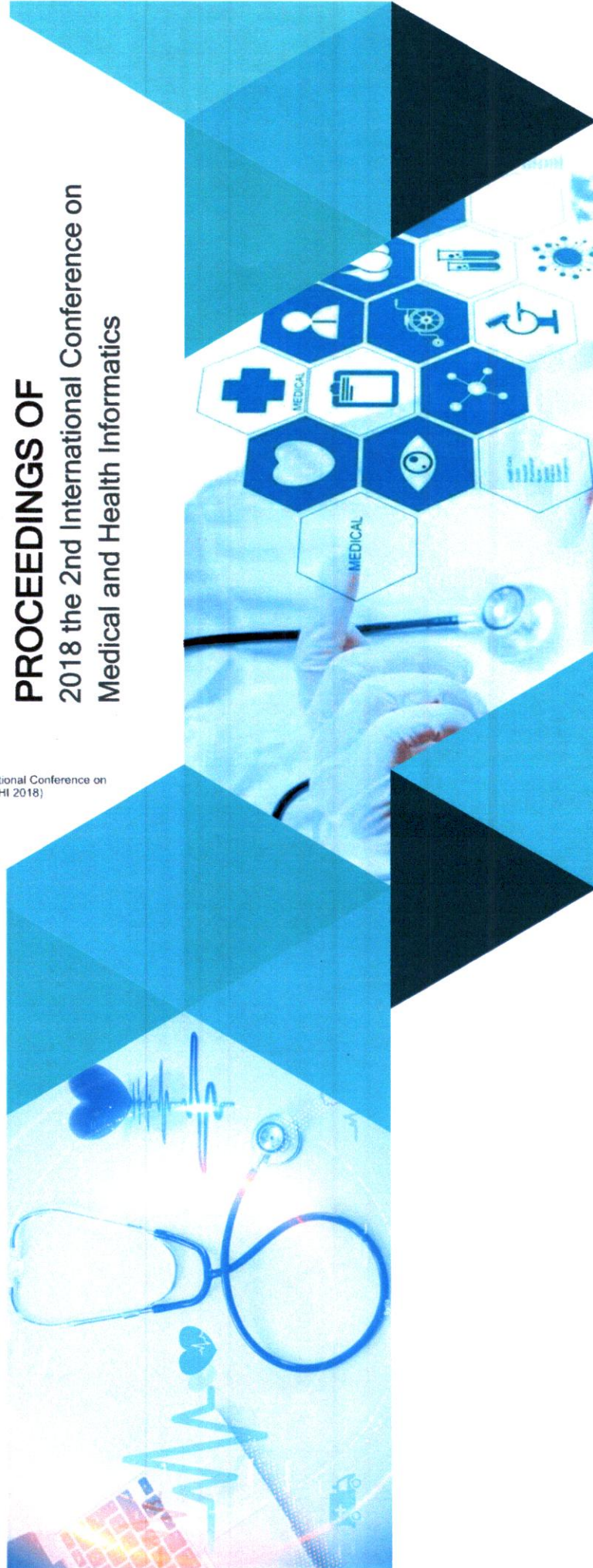


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Survival Analysis of Chronic Renal Failure Patients Undergoing Hemodialysis at Hospital in Makassar within 2012-2015

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ABSTRACT

The research aimed to investigate the prognostic factors most influential on the survival and the survival probability of the patients with the chronic kidney failures who underwent hemodialysis in the hospitals in Makassar city from 2012 through 2015. The research was conducted in Islam Faisal Hospital, Class II Pelamonia Hospital, Labuang Baji Regional Hospital and Dr. Wahidin Sudirohusodo Hospital. The research design used was the retrospective cohort design with the total samples of 454 patients. The collected data were then analyzed using life table method, Kaplan-meier and cox regression. The research result indicated that the survival probability of the patients until the end of the observation was 0%. The most influential factors on the patient survival were the age and albumin. The survival probability of the patients aging >55 years was 4% at the end of observation in the 25th month. While the survival probability of the patients aging ≤ 55 years was at the end of observation in the 38th month. As for the survival probability of the patients in relation for the albumin levels; if the albumin level <3.5 g/dl the survival probability was 8% at the end of observations in the 24th month, while if the albumin level was ≥ 3.5 g/dl, the survival probability was 0% at the end of observation in 38th month. The factors, which had no influences, were the gender, clinical stadium and the comorbidity

CCS Concepts

•Social and professional topics → User characteristics

Keywords

Chronic renal; hemodialysis; probability; survival; age; albumin levels

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1. INTRODUCTION

The development of non-communicable diseases has been a major cause of death globally, WHO stated that in 2012 there were 56 million deaths occurred in the world and non-communicable diseases cause 38 million of them. Globally, it is predicted that by 2030 the epidemiological transition from infectious disease to non-communicable diseases will increase, morbidity from non-communicable diseases increases while infectious diseases will decline [1].

One of the chronic diseases whose incidence rate is estimated to increase annually is chronic renal failure, renal disease sometimes called silent disease and most commonly after advanced clinical stage. The kidneys are the organs that have an important role to maintain health, if the kidneys do not work properly or glomerular filtration rate <60ml / min, then one can be declared to have chronic kidney disorder. A person with chronic kidney disease, his kidney will not be able to perform its functions properly so that dialysis action needs to be done until the implementation of kidney transplant [2,3].

According to the report by Bruck [4], the prevalence of chronic kidney failure in stage 3-5 in Europe increased 20% from the previous year. The rough prevalence of stage 1-5 patients with chronic renal failure at age 20 and old age in the Netherlands ranges from 4.4% and 31.1% in northeastern Germany. Then the prevalence of stage 3-5 in adults aged 65 to 74 in Switzerland ranged from 4.1% and 25.4% in north eastern Germany [4].

Asian residents are reported to have a higher prevalence of kidney failure than native Caucasians. In Singapore in 2013, the prevalence of end-stage renal disease amounts to 1436.1 per 1,000,000 inhabitants and annually dialysis patients increase by an average of 8% per year from 1999 to 2013 and are projected to continue to increase in terms of increased life expectancy and high prevalence of diabetes [5].

According to Riskesdas RI [6], the prevalence of chronic renal failure in Indonesia is 0.5 percent in Central Sulawesi province, then 0.4 percent in Aceh, Gorontalo and North Sulawesi provinces. East Nusa Tenggara, South Sulawesi, Lampung, West Java, Central Java, DI Yogyakarta and East Java were 0.3 percent and 0.2 percent, respectively, of North Sumatera Province.

According to the Indonesian Renal Registry [7] the number of new patients in 2012 ranged from 19621 people but the active patients who underwent therapy ranged from 9161 people.

Related to the gender distribution of hemodialysis patients ie 5602 male patients or 61% and 3559 female patients or around 39%. Associated distribution of patient age, the highest at age 45-54 years about 29.21% and lowest age 1-14 years about 0.19%.

In Indonesia, the estimated survival of patients with chronic renal failure is not known with certainty, this is because there is still a lack of research on the estimated survival of a person suffering from chronic renal failure undergoing hemodialysis. The Beladi-Mousavi et al. [8] in Iran stated the estimated survival of patients with chronic renal failure in general from 1 year, 5 years, 10 years, 15 years was 83%, 25.2%, 3.8%, and 1.0%. Patients with renal failure who undergo hemodialysis are predicted to have survival for years > 20s or older are able to survive for up to 20 years or more, but ≥ 75 adults may only last for two to three years [9].

According to the Jha et al. [10] there are several risk factors that predict the survival of patients with chronic renal failure, comorbidity or comorbidities, glomerular filtration rate associated with clinical stage, albumin degree, age, gender, race and some associated risk others.

Assessment of the proportion of survival of chronic renal failure patients undergoing hemodialysis is important to know In terms of clinical view as doctors will be able to diagnose and recommend treatment.

Thus, in this work, the authors conducted a study related to gender variables, age, albumin levels, clinical stages and comorbidities as a predictor associated with long survival of patients with chronic renal failure who underwent hemodialysis. . This study aims to see the most influential predictors related to survival, proportion, and median survival of patients with chronic renal failure who underwent hemodialysis at the Hospital in Makassar City 2012-2015

2. METHODOLOGY

2.1 Research Design

The type of research used in this research is analytic observational study with retrospective cohort design method that is risk factor studied by using retrospective approach. The reason for the selection of retrospective cohort methods is that one of the hallmarks of cohort studies is to both explain the relationship between risk factors and temporal effects and to calculate incidence rates so that the design is suitable for survival research. Related to this research, the data used is secondary data that is medical record data of patients with chronic renal failure diagnosed in 2012-2015 at Makassar City Hospital. The observed medical record data were prognostic factors such as age, sex, albumin level, stage, and comorbidity to estimate survival probability and prognostic factors affecting survival of patients with chronic renal failure.

2.2 Location and Time of Study

The study was conducted in several Makassar City Hospital in 2016, consisting of Dr. Wahidin Sudirohusodo, Labuang Baji Hospital, RSI Faisal, and TK II Pelamonia Hospital. The study was conducted on 27 February 2016 - 20 May 2016.

2.3 Population and Sample

The population in this study were all patients with chronic renal failure who underwent hemodialysis in 2012-2015 as many as 454 patients in four Makassar City Hospital. Sample in this research is patient of chronic renal failure first diagnosed and undergoing hemodialysis year 2012-2015 and fulfill criteria. total samples were 454 samples. The samples were taken from Dr. Wahidin

Sudirohusodo as many as 409 patients, Labuang Baji as many as 10 patients. RSI Faisal counted 24 patients TK II Pelamonia Hospital as many as 11 patients.

2.4 Sampling Method

The authors collect the respondent's data in the hospital medical record where the research takes place, the data is collected by searching the data of patients diagnosed with chronic renal failure and undergoing hemodialysis in 2012-2015. Then screening the data if it meets the inclusion criteria then the data entered as the study population. Selection of the sample is done by tracing data and information related research questions in accordance with the question of questionnaires in all patients with chronic renal failure who underwent hemodialysis. Instrument used in this research is comorbidity variable using standardized instrument that is charlson comorbidity index instrument, while for other variables using instrument made by researcher by using theoretical reference. Furthermore the authors will follow up the survival of chronic renal failure patients undergoing hemodialysis through medical record data or if possible using telephone survey and if there is no patient phone number, but the address is clear then the authors will visit sample house which is domiciled in Makassar. Previously authors will introduce themselves and state the intent to the respondent, then conduct interviews related to the condition of the sample or patient.

2.5 Data Collection Method

Data collection is required based on medical record data for 2012-2015 period at Makassar City Hospital according to inclusion criteria.

2.6 Data Analysis

Data analysis was performed by univariate, bivariate, and multivariate analysis using SPSS program. Univariate analysis aims to describe the distribution of research variables by presenting the value and size of data variations. These variables are gender, age, clinical stage, albumin, and comorbidity. The analysis was done to find the probability and the survival graph and the survival probability difference for the independent variable to the dependent variable. The analysis was done with Kaplan-Meier and analyzed life table as additional information related to time per interval group. Multivariate analysis aims to obtain the best model that can estimate the influence of independent variables. Before the tested variable is tested proportional hazard assumption by using kaplan meier method then can be tested multivariate using cox proportional hazard. The variables included in the multivariate analysis are variables that bivariate analysis has $p < 0.25$ and the variable that does not meet the assumption of PH, but theoretically important, can be incorporated into multivariate analysis. If all variables meet the assumption of PH, then a multivariate analysis is selected is an independent time cox regression analysis. However, if there are variables that do not meet the assumption PH, then the multivariate analysis is done cox regression model interaction or cox regression model stratification.

3. RESULT AND DISCUSSION

3.1 Univariate Analysis

3.1.1 Proportion of Survival of Chronic Renal Failure Patients Undergoing Hemodialysis

Patients with chronic renal failure who underwent hemodialysis in 2012-2015 total samples of 454 cases. The median score indicates that about 50% of chronic renal failure patients undergoing hemodialysis in 2012-2015 have died in the first month of visit. In

addition, survival of patients with chronic renal failure who underwent the lowest hemodialysis was 1 month, and the highest was 38 months.

3.1.2 Age

The result of univariate analysis related to age group shows that age group > 55 years have percentage 33% and age group ≤55 year percentage equal to 67%.

3.1.3 Gender

The result of univariate analysis related to sex depicts that woman have percentage 44% and man percentage equal to 56%.

3.1.4 Albumin content

The univariate analysis of albumin levels showed that albumin <3.5 g / dl had 74% percentage and albumin ≥3.5 g / dl percentage of 26%.

3.1.5 Clinical Stage

The results of univariate analyzes related to clinical stage illustrate that stage 5 has a percentage of 98%, stage 4 and stage 3 each of 1%.

3.1.6 Comorbidity (Complicated disease)

The result of univariate analysis related to comorbidity or disease the accompanist illustrates that severe comorbidities have percentage 48% and mild comorbidity 52%.

3.1.7 Life Analysis

At the beginning of the observation, there has been a death in 147 patients so that the proportion of survival of chronic renal failure patients undergoing hemodialysis at baseline was 0.68 or 68%. Then after six months of diagnostic attack, the proportion of patient survival was 0.39 or 39%. Furthermore, the observation within 12 months (1 year) survival rate of patients with chronic renal failure who underwent hemodialysis were 0.28 or 28%. The 24th or 2nd month of the proportion of survival of patients with chronic renal failure who underwent second-year hemodialysis lived 0.15 or 15%. The higher the time (t) the proportion of survival decreases, the end of observation of the 38th month no longer found surviving patients or survival of chronic renal failure patients undergoing hemodialysis has 0%. Thus it can be stated that no chronic renal failure patients undergoing hemodialysis who survive or survive until the 4th year. Figure 1 shows the relationship of observation time and chronic renal failure chances of experiencing death, chronic renal failure chance to experience death until the end of observation of 38th month is 0.00%.

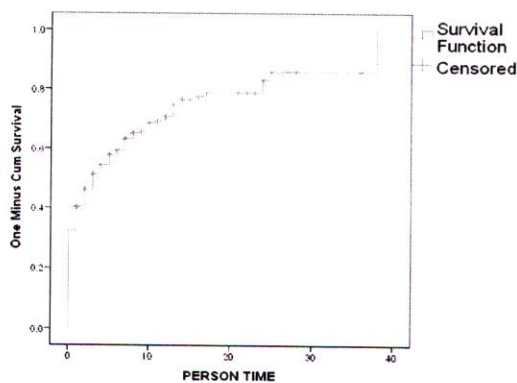


Figure 1. Proportion of Chronic Kidney Failure Patients Who Underwent Hemodialysis To Death At Several Hospitals In Makassar City Year 2012-2015.

3.2 Bivariate Analysis

3.2.1 Analysis of Chronic Kidney Failure Patients Undergoing Hemodialysis Year 2012-2015

Results of the analysis showed that patients with chronic renal failure who underwent hemodialysis, died the highest at age ≤55 years at 60.3%. The result of statistical test shows that p value is 0.001 or there is a correlation between age and death of chronic renal failure patients undergoing hemodialysis. Associated with gender, patients who died the highest in men ie by 54.9%. Value p = 0.474 or no relationship between gender with death of chronic renal failure patients. Analysis of albumin-related levels, death was highest in the albumin group <3.5 g / dl at 76.5%. P value was 0.120, which showed no association between albumin levels and death of chronic renal failure patients undergoing hemodialysis. Based on the clinical stage of the patient, ie the highest death in stage 5 ie 97.1% and p = 0.652 or no relationship between clinical stages with the death of chronic renal failure patients undergoing hemodialysis. Associated with comorbidity of patients, death was highest in mild comorbidity of 51.6% and p value of 1,000 or no association between comorbidity with death of chronic renal failure patients undergoing hemodialysis.

3.2.2 Life Table and Kaplan Meier Analysis Related Age

Results showed that shows the proportion of deaths > 55 years of early observation month of 0.428 or 42.8% with the survival proportion being 0.57 or 57%. The last event case occurred in the 25th month with a survival proportion of 0.04 or 4%. This means no chronic renal failure patients > 55 years of age survive up to 3 years. While age ≤55 years at the beginning of observation month after the diagnosis of the proportion of death was 0.272 or 27.2%. With the end of observation at month 38 and the survival proportion of 0.00 or 0%. Figure 2 shows that the survival curve of chronic renal failure patients with age groups does not intersect with each other. This means that there is a difference of survival probability and fulfill the proportional hazard assumption. This difference is significant indicated by log rank value <0.05. It can be concluded that, age-related chronic renal failure patients have different event times

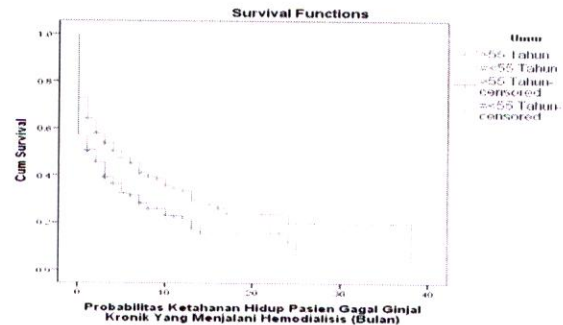


Figure 2 Proportion of survival of chronic renal failure patients undergoing hemodialysis by age in some hospitals in Makassar City 2012-2015.

3.2.3 Life Table and Kaplan Meier Analysis Related Age

Results of the analysis showed that the proportion of female deaths at baseline after diagnosis was 0.348 or 34.8% with a survival proportion of 0.65 or 65%. The last event case is in the 38th month with a cumulative proportion of 0.00 or 0%. This means there are no female patients with chronic renal failure who underwent hemodialysis that survived until the 4th year.

The male patient group event occurrence also occurred at the beginning of the observation with the proportion of deaths of 0.305 or 30.5% with the survival proportion being 0.70 or 70%. Up to the end of the observation, the proportion of survival was 0.00 or 0%, or in other words, patients with chronic renal failure who underwent hemodialysis with female sex as a whole only survived at 25 months. Figure 3 shows that the survival curve of patients with chronic renal failure who undergo hemodialysis based on gender intersect each other. This suggests the proportional hazard assumption or comparison of death rates between the sexes is not met. Differences reinforced with indigo log rank = 0.641 ($p > 0.05$). So it is concluded that statistically there is no difference in event occurrence between chronic renal failure patients undergoing hemodialysis in female and male patients in Makassar City hospital.

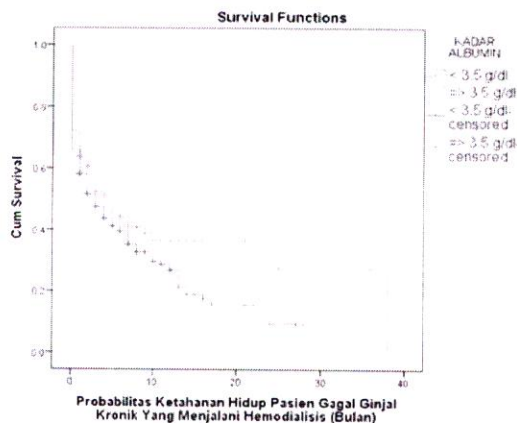


Figure 3 Proportion of Chronic Kidney Failure Patients Living Under Hemodialysis by gender at Makassar City Hospital 2012-2015

3.2.4 Life Table and Kaplan Meier Analysis Related Age

Results showed that the proportion of deaths of the albumin group < 3.5 g / dl at baseline after diagnosis was 0.340 or 34% with the proportion of survival was 0.66 or 66%. The last event case occurred in the 24th month with a survival proportion of 0.08 or 8%. This means that no chronic renal failure patients undergoing hemodialysis with albumin < 3.5 g / dl survive up to 3 years. Meanwhile, the albumin level of ≥ 3.5 g / dl event occurrence at the beginning of observation of the proportion of death was 0.277 or 27.7%. Up to the end of the observation, the proportion of survival was 0.00 or 0% or in other words, patients with albumin ≥ 3.5 g / dl overall survived at month 38. Figure 4 shows that the survival curves of chronic renal failure patients undergoing hemodialysis on the basis of albumin levels do not intersect. This suggests that the proportional hazard assumption or comparison of mortality rates between groups of albumin levels is accomplished this is reinforced by log rank values = 0.049 ($p > 0.05$). So it can be concluded, statistically there is a difference of event occurrence between patients with chronic renal failure who underwent hemodialysis in albumin group < 3.5 g / dl and albumin ≥ 3.5 g / dl

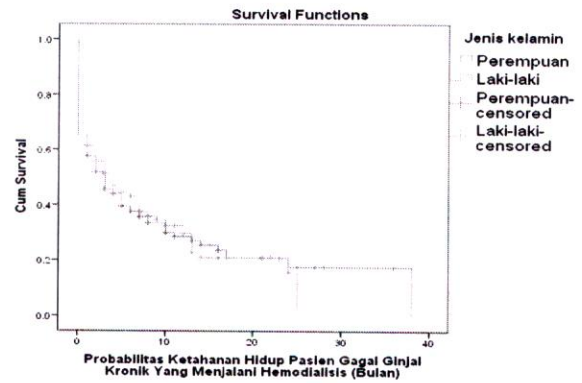


Figure 4 Proportion of Chronic Kidney Failure Patients Living Under Hemodialysis Based on Albumin Level In Makassar City Hospital 2012 -2015

3.2.5 Life Table and Kaplan Meier Analysis Related Clinical Stage

Results showed the proportion of stage 5 mortality at the beginning of the first month after diagnosis was 0.325 or 32.5% with the survival proportion being 0.67 or 67%. The last event case in the 38th month was with a survival proportion of 0.00 or 0%. This means that no chronic renal failure patients undergoing hemodialysis with stage 5 survive until the 4th year. Group 4 clinical stage events also occurred at the beginning of the first month after the diagnosis of death proportion of 0.167 or 16.7%. Until the observation, the proportion of survival was 0.83 or 83%. Meanwhile, in stage 3 the event also occurred in the first month after diagnosis, the proportion of deaths of 0.4000 or 40%. Then, the last 3 clinical-related observations at 4th month, the survival proportion were 0.30 or 30%. Figure 5 shows that the survival curve of chronic renal failure patients with clinical stages intersected with each other. This means there is no difference in the probability of survival and does not meet the proportional hazard assumptions. This difference is not significant as indicated by log rank value > 0.05 , so it can be concluded that patients with clinical stage 5 have no time difference of death incidence with clinical stage 4 and clinical stage 3.

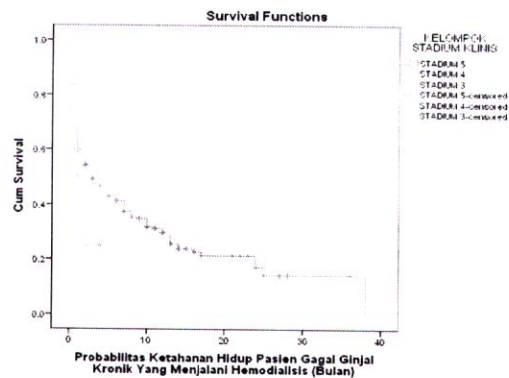


Figure 5 Proportion of Chronic Kidney Failure Patients Living Under Hemodialysis Based on Clinical Stages in Several Hospitals In Makassar City Year 2012-2015

3.2.6 Life Table and Kaplan Meier Analysis Related to comorbidities

Results showed that the proportion of deaths of severe comorbidities in the first month after diagnosis was 0.311 or 31.1%

with the survival proportion being 0.69 or 69%. The last event case occurred in the 38th month with a survival proportion of 0.00 or 0%. This means that there are no chronic renal failure patients undergoing hemodialysis with severe comorbidities that lasted until the 4th year. For mild comorbidity groups the event also occurred in the first month after diagnosis, with the proportion of deaths of 0.336 or 33.6% with the survival proportion being 0.66 or 66%. Until the end of the observation, the proportion of survival was 0.15 or 15% at month 24. Figure 6 shows that the survival curve of chronic renal failure patients undergoing hemodialysis based on comorbidity intersect each other. This means there is no difference in survival probability and does not meet proportional hazard assumptions. This difference was not significant as indicated by log rank values $p > 0.05$, so it can be concluded that patients with severe comorbidity did not have time difference in incidence of death with mild comorbidity group.

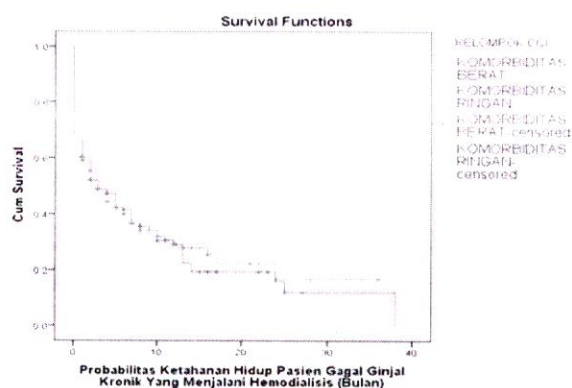


Figure 6 Proportion of Chronic Renal Failure Patients Living Under Hemodialysis Based on Comorbidity at Makassar City Hospital Year 2012-2015

3.2.7 Analysis Cox Regression

Kaplan Meier curve of age group variables did not intersect, so it can be said that at any time, chronic renal failure patients undergoing hemodialysis with age > 55 years (CI = 1.127-1.836) are likely to die compared with patients with chronic renal failure who underwent hemodialysis with age ≤ 55 years, statistically significant.

Kaplan Meier curves of the gender variables intersect each other, so it is said that patients with chronic renal failure who undergo hemodialysis between sex groups have the same possibility in the occurrence of an event. However, the multivariate test results of women having 1,113 times (CI = 0.874-1.416) are likely to die as compared to male patients, statistically insignificant.

Kaplan Meier's curve of variable albumin levels does not intersect each other, so it is said that at any time, chronic renal failure patients undergoing hemodialysis with albumin levels < 3.5 g / dl have 1,297 times (CI = 0.979-1.718) is likely to die compared with patients with albumin ≥ 3.5 gr / dl, statistically significant.

Kaplan Meier curve of clinical staging variables intersect, so it can be said that at any time patients with chronic renal failure who undergo inter-stage hemodialysis may be the same in the occurrence of an event. However, patients with stage 5 had 0.519 times (CI = 0.191-1.405) likely to die compared to other clinical staging patients, and were not statistically significant.

Kaplan Meier's curves of comorbidity variables intersect, so it can be said that at any time patients with chronic renal failure who undergo hemodialysis with comorbidities are likely to be similar in the event of an event. However, patients with severe comorbidities 1,018 times (CI = 0.803-1.290) were likely to die

compared with patients with chronic renal failure who underwent hemodialysis with mild comorbidities, were not statistically significant.

3.3 Multivariate Analysis

The result of bivariate analysis shows that there are three variables that meet the assumptions to be included in the multivariate test ($p < 0.25$), other variables are excluded from multivariate testing. The final model in multivariate analysis revealed that the variables that meet the survival of chronic renal failure patients undergoing hemodialysis At Makassar City Hospital are age and albumin levels. The final modeling results can also be interpreted as follows:

- Hazard Ratio patients with chronic renal failure who underwent hemodialysis with age group > 55 years to die was 1,410 times compared with age group ≤ 55 years.
- Hazard Ratio patients with chronic renal failure who underwent hemodialysis with a group of albumin < 3.5 g / dl to die 1,291 times compared with the age group ≥ 3.5 g / dl

3.4 Overall Discussion

The proportion of survival to 0% in this study, almost in line with Valdivia et al. [11] in Havana Hospital Cuba City with estimated survival of chronic renal failure patients can reach 0%, ie in general 1 year, 3 years, and 5 years is 85%, 25.0%, and 0.0%.

This study is in line with the research of Chien et al. [12] in Taiwan which states that patients with chronic renal failure who initiate hemodialysis > 55 years of age significantly influence survival compared to patients under 55 years of age. Based on cox regression analysis, age had a statistically significant effect of $p = 0.001$, with HR 2.72. This effect strengthens the evidence that mortality rates increase with increasing age.

This study is in line with research conducted by Carrero et al. [13] states that gender is not an effect that can predict the survival of patients undergoing dialysis with hazard ratio 0.98. This is in line with the research conducted by Tze-Wah Kao et al. [14] which stated that hazard ratio of sex group in dialysis patients was 0.81 with p -value = 0.26 or gender variable was not significant with survival of chronic renal failure patients.

The results of this study are in line with research conducted Takahashi et al. [15] in 259 patients in Japan who stated that albumin < 3.5 g / dl was a factor affecting the survival of hemodialysis patients but the hazard ratio was low ie 0.185.

This is in line with the research of Odetunde et al. [16] in Nigerian hospitals but with overall respondents in children, indicating that patients with chronic kidney failure with stage 5 more than other clinical stages of chronic renal failure were as many as 25 people compared with stage 4 and stage 3 ie 19 people and 9 people.

Shih et al. [17] in the study also stated that in patients with chronic renal failure who underwent hemodialysis obtained a low hazard ratio value at comorbidity of 1.08 but different statistical test results, where Shih et al. [17] stated the significant comorbidity with the survival of patients with chronic renal failure with the value $p < 0.001$. This work is also line with the study of Da Silva-Gane et al., [18], where the value of $p < 0.001$ or comorbidity affects the survival of chronic renal failure patients undergoing hemodialysis but the hazard ratio is large, HR = 2.71.

4. CONCLUSION

This study was conducted to analyze the most influential predictors related to survival, proportion, and median survival of patients with chronic renal failure who underwent hemodialysis at the Hospital in Makassar City 2012-2015. Based on the analysis done, key results have shown that most influential factors on the

survival of patients with chronic renal failure who undergo hemodialysis namely age and albumin.

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