A Highly Nonlinear Survival Network for Hospital Readmission Prediction of Cardiac Patients

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Keywords: Survival Network, Hospital Readmission, Cardiac Patients.

Abstract:

Hospital readmission prediction of cardiac patients is an increasingly important survival analysis problem these days. So far, three groups of methods for cardiac readmission have been proposed: statistical-based, machine learning-based and deep learning-based. However, the assumptions of the statistical-based methods limit their practicality in real-world applications. The traditional machine learning-based methods suffer from the problem of over-reliance on feature engineering. Deep learning-based methods can be further classified into two groups in terms of how they deal with first hitting times: discrete strategy-based and continuous strategy-based. It is nontrivial for the discrete strategy-based methods to find the optimal granularity of output time intervals. The continuous strategy-based methods assume nonlinear proportional hazards condition, which often limits the model performance in practical applications. Besides, existing deep learning-based methods still have room for improvement in calculating the mean value of fitted dropout models. To address these issues, in this paper, we propose a highly nonlinear survival network called Environment-Aware Maxout Deep Survival Neural Network (EMaxSurv) to predict the risk value of hospital readmission of cardiac patients. EMaxSurv is based on a key observation that environmental conditions have a significant impact on the health of cardiac patients. The basic idea of EMaxSurv is to adopt maxout deep networks combined with environmental information to better capture the relationship between covariates and the distribution of the first-hitting times. To evaluate the proposed model, we conduct extensive experiments on three real world datasets. The experimental results show that EMaxSurv outperforms the other baselines in all three datasets.

1 INTRODUCTION

Hospital readmission prediction is a widely recognised survival analysis problem which aims to predict the likelihood of a patient experiencing hospital readmission before a specific time. Effective prediction of hospital readmission has many benefits, such as improving medical treatment plans, reducing the financial burden of both patients and governments, optimising hospital resource arrangements, etc. According to the study report (Heidenreich et al., 2022) of the American Heart Association (AHA) in 2022, millions of people worldwide are hospitalised for acute heart failure each year. The report shows that the risk of readmission within one month after discharge is 20%, the risk of death is 5%, the risk of readmission within one year after discharge is 60%, and the risk of death is 25%, and these data are on an upward trend (Joglar

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et al., 2024). In this paper, we focus on hospital readmission prediction of cardiac patients.

Existing methods for predicting readmission can be divided into three categories: statistical-based, machine learning-based and deep learning-based. Statistical-based models mainly adopted statistical methods such as Kaplan-Meier estimator (KM) (Kaplan and Meier, 1958) and Cox (Cox, 1972). However, statistical methods usually assume that the log risk of patient readmission is a linear combination of patient covariates (i.e., linear proportional hazards condition) or can only analyse a single factor at a time, which is too simple and impractical in realworld applications. Machine learning-based models (Zhai et al., 2023) usually utilise machine learning methods to do readmission prediction, and do not assume the linear proportional hazards condition. However, when dealing with complex nonlinear survival data, the performance of machine learningbased methods often suffers from severe degradation due to over-reliance on feature engineering.

Deep learning-based models have superior ability in automatic feature detection, and they focus on detect the relationship between covariates and the distribution of first-hitting times, i.e., the risk of hospital readmission. Specifically, there are two different ways in dealing with first hitting times: discrete strategy and continuous strategy. Discrete strategy (Lee et al., 2018) transforms the first hitting times into predefined discrete intervals. However, this approach inconveniently introduces a trade-off between the number of parameters and the granularity of the output time intervals, which increases the training difficulty. On the contrary, the continuous strategy (Katzman et al., 2018) regards the variation of first-hitting times as a continuous variable, thereby avoiding the aforementioned problem. However, continuous strategybased models assume that the log risk of patient readmission is a nonlinear combination of patient covariates. This assumption often results in suboptimal performance in many application scenarios (Gensheimer and Narasimhan, 2019). The reason is that the existing continuous strategy-based models cannot fit the non-linear relationship between covariates and firsthitting time distribution well.

Another problem of the deep learning-based category is that most of them contain dropout layers, which are essentially the mean of multiple neural networks. However, these models typically use curved activation functions almost everywhere, resulting in lower accuracy. In addition, some studies (Mišić et al., 2020) (Chen et al., 2022) treat the readmission prediction as a traditional classification problem. The major problem of these studies is that they cannot fully utilise the patient information. For example, these studies often remove information about the patients who died during hospitalisation. However, information on patients who died often helps predict readmission rates. Last, existing readmission models fail to note the impact of environmental conditions on the physical well-being of cardiac patients, which limits the performance of the models.

To address the above issues, in this paper, we propose a highly nonlinear survival network called Environment-Aware Maxout Deep Survival Neural Network (EMaxSurv) to predict the risk value of hospital readmission of cardiac patients. The basic idea is to adopt maxout deep networks (Goodfellow et al., 2013) combined with environmental information to better capture the relationship between covariates and the distribution of the first-hitting times. The maxout network has a more powerful nonlinear modelling ability. It can fit any convex function and learn more complex features and patterns without using nonlin-

ear activation functions. Thus, the linear and maximisation operations in the maxout network allow the dropout's fitted model to be averaged with high accuracy. Additionally, the multiple activation paths of the maxout network act like a built-in regularization mechanism, helping to reduce the risk of over fitting the model.

Besides, EMaxSurv is based on a key observation that environmental conditions have a significant impact on the health of cardiac patients. For example, high ambient temperatures can increase the patient's metabolism, blood flow, and heart's demand for oxygen, thereby increasing the burden on the heart (Bai et al., 2018) (Schwartz et al., 2004). Conversely, low ambient temperatures can narrow blood vessels and increase vascular resistance, thereby increasing the risk of hypertension and blood clots (Pan et al., 1995). To the best of our knowledge, we are the first to use environmental information for hospital readmission prediction of heart disease patients.

In summary, the main contributions of this paper are listed as follows:

- We propose a network called EMaxSurv for hospital readmission prediction of heart disease patients. The EMaxSurv consists of two modules: preprocessing and MaxSurv.
- We proposed to utilise the maxout network and the environmental information to better detect the relationship between covariates and the distribution of first-hitting times.
- We validated the performance of EMaxSurv and MaxSurv on three real-world datasets. Experimental results show that EMaxSurv outperforms the baseline, with a c-index improvement of 33% compared to the best baseline model.

The remainder of this paper is organised as follows. Section 2 presents the related work. Section 3 describes the components of EMaxSurv in detail. In Section 4, we evaluate the performance of EMaxSurv in real-world datasets. We conclude the paper in Section 5.

2 RELATED WORK

Statistical-Based Survival Method: One of the first survival models that began to be used was the Kaplan-Meier estimator (KM), a non-parametric technique. Pepe (Pepe and Fleming, 1989) introduced the weighted Kaplan-Meier statistic as a distance test for a class of censored data, providing a new perspective for analysing survival data. However, the KM

method can only analyse a single factor, cannot simultaneously consider the effects of multiple risk factors, and may produce unstable estimates for small samples and low event count data.

In contrast, the Cox proportional risk model can incorporate multiple risk factors simultaneously. The Cox model is the most commonly used regression analysis method for survival data. It is based on the proportional hazards assumption and uses partial likelihood for parameter estimation. Grzyb (Model, 2017) extended the Cox proportional risk model with multitask learning by exploring alternatives to existing models. However, Statistical methods often assume a linear combination of patient covariates or can only analyze a single factor, making them impractical for real-world applications.

Machine Learning and Deep Learning-Based Models: Assuming a linear function is too simplistic. Therefore, the survival model must accurately fit the survival data to the nonlinear log hazard function. Support Vector Machine (SVM) (Van Belle et al., 2011) is a supervised learning method, mainly used for classification, but can also be modified for regression problems, however, the disadvantage of this approach is that the information contained in the censored instances will be completely ignored. Random Survival Forest (RSF) (Ishwaran et al., 2008) extends the random forest method by using a forest of survival trees for prediction. DeepSurv and its variants predictive and modelling capabilities will enable medical researchers to use deep neural networks to explore the impact of patient characteristics on their risk of failure. DeepHit builds a deep network to directly learn the distribution of discrete time first to hit. However, discretising the first hitting time will increase the difficulty of training, and it is necessary to measure the relationship between the time step and the amount of network parameters.

The common goal of statistical methods and machine learning & deep learning methods is to predict survival time and estimate the survival probability at the estimated survival time. However, statistical methods focus more on characterizing the distribution of event times and the statistical properties of parameter estimation by estimating survival curves, while machine learning & deep learning methods focus more on predicting the occurrence of events at a given time point by combining traditional survival analysis methods with various machine learning techniques.

3 METHODOLOGY

In this section, we first give the formalised description of the problem of readmission prediction of heart disease patients. Then, we describe the main modules and loss functions of EMaxSurv in detail. Finally, we introduce the loss function.

3.1 Problem Formulation

When studying the survival analysis problem, there may be cases where the event of interest is not observed. This concept is called censoring, which can be divided into three categories:

- Right-censored, the observed survival time is less than the true survival time.
- Left-censored, the observed survival time is greater than the true survival time.
- Interval-censored, only the event is known to occur within a given time interval.

Right-censored is the most common case, our research is also based on right-censored data. In our work, we use survival data as input for EMaxSurv.

Survival Data: Survival data consist of three types of information for each patient: 1) observed covariates (demographic information, physical condition, and past treatments), 2) time elapsed since the covariates were collected, and 3) an indication of the labels for the type of event (e.g., readmission event).

Let "0" denote the right censoring. Let $S = \{0, 1, \dots, 1\}$ be the set of events. Each record can be denoted as $r_i = (x, t, s)$, where $x = \{x_1, x_2, \dots, x_d\}$ is covariates, t is the time interval from the beginning of the observation to the occurrence of the event or the end of the observation, and s is the label that marks whether censoring occurs during t. Thus we denote the patient survival data R below.

$$R = \left\{ \begin{array}{c} r_1 \\ \vdots \\ r_o \end{array} \right\} = \left\{ \begin{array}{cccc} x_{1,1} & \cdots & x_{1,d} & t_1 & s_1 \\ \vdots & & & \\ x_{o,1} & \cdots & x_{o,d} & t_o & s_o \end{array} \right\}$$
 (1)

Problem Statement: Given survival data $R = (r_1, r_2, \dots, r_o)^T$, r_k and time interval d_t , the problem of cardiac patient readmission prediction is to predict the risk of readmission $\lambda(R, r_k, d_t)$ for the corresponding cardiac patient of r_k within d_t after being discharged from the hospital. The higher the risk value, the greater the likelihood that the patient will be readmitted to the hospital within d_t after discharge.

3.2 EMaxSurv

The MaxSurv predicts the effect of a patient's covariates on their hazard rate, which is parameterized by the network weights θ . Figure 1 illustrates the main structure of EMaxSurv.

Data Preprocessing: In this module, we first preprocess each record r_i of R. Then, we organise the preprocessed results into a matrix shown in equation 1 in Section 3.1. To determine the season of each patient's admission, we use the year and month of the admission time to clas-For the record with admission time sify them. $Doa = \{2018/1/12, 2018/5/1, 2018/10/0\},$ we construct the season vector $Season = \{1, 2, 3\}$. Meanwhile, based on the year and month information of each record, we collect the temperature data of the corresponding time in the local area of the hospital from the Internet and construct three vectors of maximum temperature, minimum temperature. Specifically, for the record with admission time Doa = $\{2018/1/12, 2018/5/1, 2018/10/0\}$, we construct the maximum temperature $max - temp = \{8, 35, 20\},\$ minimum temperature $min - temp = \{-3, 8, 18\}$, and temperature difference $diff - temp = \{11, 27, 2\}$. In addition, we categorise patients according to their age data.

As a result, the data we feed into module (b) is as follows:

$$\widehat{R} = \left\{ \begin{array}{cccc} & max_1 & min_1 & diff_1 & sea_1 \\ R' & \vdots & & & \\ & max_o & min_o & diff_o & sea_o \end{array} \right\} (2)$$

where the difference between R' and R is that R' include the discrete age information.

MaxSurv Deep Network: This module aims to learn the correlation between covariates and the distribution of first-hitting times. We input each row of R into a network to train. The intuitive differences between RuLU-Like activation and maxout are shown in Figure. 2, as we can see, a single maxout unit can be interpreted as making a piece-wise linear approximation to an arbitrary convex function. At the same time, since maxout only selects the maximum activation value, only the selected path will update the weight during the gradient propagation process, which helps to accelerate convergence. Secondly, the maxout network can adapt to a variety of different data distributions because it can approximate complex function forms through a combination of multiple activation functions.

Assume that the input feature vector for a particular network layer is

$$x_i = (x_{i,1}, x_{i,2}, \cdots, x_{i,d}, max_i, min_i, diff_i, sea_i)_{1 \times n}$$
(3)

The formula in each neuron of the maxout layer is $h_i(x) = \max_{i \in [1, k]} z_{ij}$.

Above is the formula for neuron i in the maxout hidden layer. Where k is the parameter needed for the max out layer. The formula for Z is $z_{ij} = W_{ij}x^T + b_{ij}$. The weight W is a matrix of size (n,m,k), and b is a matrix of size (m,k). For an arbitrary continuous segmented linear function g(x), two convex segmented linear functions, $h_1(v)$ and $h_2(v)$, can be found such that the difference between these two convex functions is g(x). g(x) is used as the input of the next network layer to continue iteration.

After maxout layer is a Batch Norm layer, its role is to standardise the features in the network. Suppose that during training, a batch of maxout layers outputs features as $x = \{x_1, \dots, x_m\}$, where $x_i = (g_{i,1}, \dots, g_{i,k})$. We first find the mean and variance of the batch of features along the dimensions of the

batch:
$$\mu_i^{(1\times d)} = \frac{1}{m} \sum_{i=1}^m g_i, \ \sigma_i^{(1\times d)} = \sqrt{\frac{1}{m} \sum_{i=1}^m (g_i - \mu_i)};$$

Next, normalise the features $\hat{g}_i^{(1 \times d)} = \frac{g_i - \mu_i}{\sigma_i + \epsilon}$ and compute the output of the Batch Norm layer:

s as
$$x_{i} = (B\widetilde{N}_{i,1}, B\widetilde{N}_{i,2}, \cdots, B\widetilde{N}_{i,k}), \\ B\widetilde{N}_{i,j} = \gamma \odot \widehat{g}_{i,j} + \beta$$
 (4)

where γ and β are two parameters of the Batch Norm layer to train.

The last structure is a dropout layer, with its parameter p (per neuron dropout probability). When training with dropout, we perform the element-wise multiplication with the dropout mask immediately prior to the multiplication by the weights in all cases—we do not drop inputs to the max operator.

Finally, the output of the network $f_{\theta}(x)$ (the log-risk function) is a linearly activated single node that estimates the risk function $\lambda(t|x) = \lambda_0(t) \cdot e^{f(x)}$, where $\lambda_0(t)$ is the baseline risk function related to time, we calculated the $\lambda_0(t)$ from t=0 to t=dt. Note that no matter how $\lambda_0(t)$ is equal to, it does not affect the result of the likelihood function, so we don't assume a form for it here. For the loss function, we set it to average negative log partial likelihood with regularisation for training:

$$L_{fun} = \frac{\lambda \|\theta\|_2^2 - \sum_i (f_{\theta}(x_i) - \log \sum_{j \in \Re(T_i)} e^{f_{\theta}(x_j)})}{N_{cens}} \quad (5)$$

where N_{cens} is the number of patients who had an event of interest to us (i.e. readmission), λ is the

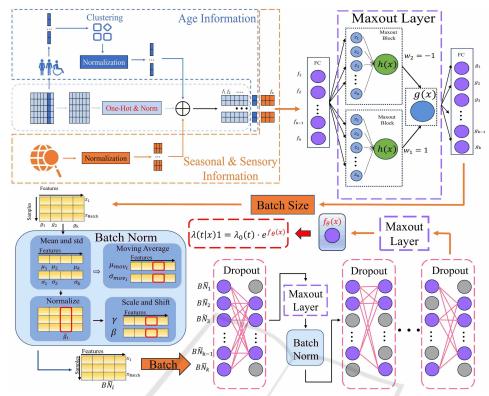


Figure 1: Overview of EMaxSurv. EMaxSurv consists of a Data Preprocessing module and a MaxSurv module. The MaxSurv module consists of three components: the maxout component (Purple dashed box), the Batch Norm component (Blue box) and the Drop component (Pink dashed box). The Data Preprocessing module takes R as input and generates data sets \hat{R} with richer features.

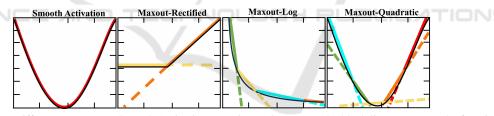


Figure 2: Intuitive Differences Between Smooth Activation Function and maxout. The black line represents the function that needs to be fitted, while the colored line represents the process of activating the function to approximate it.

 l_2 regularisation parameter. We combine the risk predicted by observed covariates $X=(x_1,x_2,\cdots,x_o)$ with time $T=(t_1,t_2,\cdots,t_o)$ and censored label $S=(s_1,s_2,\cdots,s_o)$ to update the parameters Θ . During network training, the input data x is first normalised, and the optimiser chooses Adam, incorporating the learning rate schedule and Nestorv mechanism.

4 EXPERIMENTS

In this section, we conduct an empirical study on the performance of EMaxSurv. First, we describe the dataset and the baseline methods. After that, we intro-

duce our performance metrics and experimental environment. Finally, we discuss the experimental results (including ablation experiments).

4.1 Dataset and Baselines

We conduct our experiments in three real-world datasets: the cardiac readmission dataset (Bollepalli et al., 2022), GBSG2 (Schumacher et al., 1994) and Veterans (Davis et al., 1982). The Readmissions dataset was collected from patients over a two-year period (2017 to 2019). There were 14,845 patient admissions to the Cardiology Department, of which 1921 patients were admitted multiple times. And GBSG2 contains breast cancer records of 720 pa-

tients, while Veterans contains lung cancer records of 138 patients.

Besides the EMaxSurv and the MaxSurv, we also implement the following baselines in the three datasets.

- COXPH is a important statistical model used for survival data analysis.
- GBoost (Saigo et al., 2009) is a sequential training method with higher weights for misclassified samples. The final prediction is obtained based on the weighted results.
- *DeepSurv* is a multilayer perceptron similar to the Faragi-Simon network.
- DeepHit does not rely on any assumptions about underlying stochastic processes. Thus, network learning models the evolution of the relationship between covariates and risk over time.
- ResDeepS(RDS) (Weibin, 2022) improves Deep-Surv using residual networks to solve the gradient vanishing problem for deep networks. RDE, RDC, RDG denote ResDeepS using ELU, CELU and GELU activation function, respectively.

We use 4-fold cross-validation: randomly divide the data into a training set (80%) and a test set (20%). The main code will be released as soon as the paper is published.

4.2 Performance Metric

We choose the Concordance Index (C-Index, CI) (Harrell et al., 1982) as the primary metric and Integrated Brier scores (IBS) (Ishikawa et al., 2019) as the secondary metric.

The formulaic representation of C-Index is $P(score(A) > score(B) | Y_A > Y_B)$, where *score* represents the output of the model, and Y is the time before a readmission.

The formulaic representation of Brier score is as follows:

$$BrierScore = \frac{1}{N} \sum_{i=1}^{N} \sum_{j=1}^{R} (predict_{ij} - observe_{ij})^{2}$$
 (6)

where N is the sample size, R is the number of categories, $predict_{ij}$ is the probability that the i_{th} individual is classified as j, and $observe_{ij}$ is the actual state of whether the i_{th} individual is classified as j. The $observe_{ij}$ value is 1 if the proper classification is j and 0 otherwise. Integrating the BS yields the Integrated Brier score (IBS): $IBS = \int_0^{\max(t)} BS(t) dt$. The lower the IBS, the higher the C-index, i.e., the higher the model's prediction accuracy.

4.3 Results and Analysis

We chose to add environmental information to the heart disease dataset after careful consideration: First, temperature changes can affect the body's physiological responses. Extreme temperatures can increase the burden on the cardiovascular system. Second, existing heart disease prediction features mainly focus on individual internal factors, while temperature features provide information about the external environment. Furthermore, the temperature data is obtained from the public data source of the meteorological department, which has high accessibility and reliability. Finally, different individuals have different sensitivities to temperature changes. Adding temperature features can help build a more personalized heart disease prediction model.

4.3.1 Comparison on all Baselines

Table 1 shows the experimental results of our proposed model and baseline models using the cardiac dataset. CoxPH and Gboost perform poorly due to their solid assumptions and reliance on feature engineering. The best deep learning model is Deep-Hit. Although will increase the difficulty of training, Deephit gets rid of the assumption of the risk function. Furthermore, we can learn that EMAXSurv achieves a 33% improvement in the C-index metric relative to the best baseline model DeepHit, and achieves a 10.9% improvement in the IBS metric relative to the best baseline model RDG, this is because EMaxSurv combines environmental information during prediction and more effectively capture the nonlinear relationship of covariates.

Table 1: Performance comparisons of EMaxSurv and baselines.

Models	C-Index	IBS
CoxPH	0.5994	0.1652
Gboost	0.5582	0.1713
DeepSurv	0.6911	0.1857
RDE	0.6922	0.1629
RDC	0.6919	0.1638
RDG	0.6897	0.1628
DeepHit	0.6930	0.1633
EMaxSurv	0.9221	0.1449

4.3.2 Comparison on Different Environmental Information

We added different environmental information to the readmission data, resulting in four different datasets, each containing the original information and an addi-

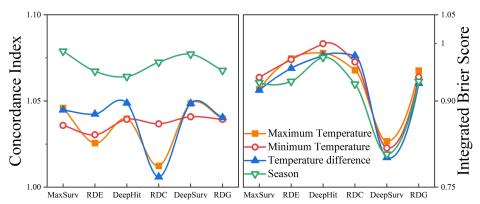


Figure 3: The ratio of model results after adding different environmental information. The horizontal axis represents different models, and lines of different colors represent the ratio after adding different environmental information.

Models	Veteran		GBSG2		Cardiac			
	C-Index	IBS	C-Index	IBS	C-Index	IBS		
CoxPH	0.6312	0.1487	0.6941	0.1105	0.5994	0.1652		
Gboost	0.6007	0.1490	0.6761	0.1383	0.5582	0.1713		
DeepSurv	0.6927	0.1411	0.7612	0.1064	0.6911	0.1857		
RDE	0.6919	0.1433	0.7418	0.1066	0.6922	0.1629		
RDC	0.6708	0.1478	0.7355	0.1051	0.6919	0.1638		
RDG	0.6885	0.1429	0.7630	0.1049	0.6897	0.1628		
DeepHit	0.7094	0.1445	0.7884	0.1048	0.6931	0.1633		
MaxSurv	0.7197	0 1400	0.8182	0 1045	0.6965	0.1627		

Table 2: Performance comparisons of MaxSurv and baselines on three disease survival datasets.

tional piece of environmental information. We trained the same predictor with the new and old datasets, and then divided the metric obtained with the new dataset by the metric obtained with the old dataset, as shown in Figure 3.

As shown in Figure 3, adding any kind of environmental information improves the performance of all models. For MaxSurv, it is the best model in most settings. This is because there is a close correlation between heart attacks and environmental information. In addition, the effect of inputting all environmental information into the data is better than all other configurations.

4.3.3 Comparison on Three Disease Survival Datasets

In order to verify the performance of the model on datasets without supplementary environmental information, we verified the performance of the MaxSurv module on three different disease datasets and compared it with other baseline models. Their performance is shown in Table 2.

As shown in Table 2 above, MaxSurv exhibits optimal performance in all three datasets. DeepSurv and DeepHit also perform well and are closer to the MaxSurv model, but there is still a gap. MaxSurv has

several features that can help the model achieve better performance: the generated representation is not sparse; the maxout structure is more compatible with the dropout structure; and the multi-way activation mechanism of maxout enables the network to capture more complex features and show stronger generalization ability.

5 CONCLUSION

In this paper, we propose a new method, EMax-Surv, to analyze cardiac readmission data. EMaxSurv maintains the basic assumptions of the Cox model and uses a neural network to model a nonlinear representation of the relationship between covariates and the risk of clinical events. We compare the performance of MaxSurv with that of previous models in conjunction with the patient's environmental perceptual information. In the data with environmental information, the performance of all models is effectively improved, with Maxsurv's performance being the most improved. The MaxSurv outperforms the previous model even with the original data and data from other disease types.

ACKNOWLEDGEMENTS

This work was supported in part by the Macao Polytechnic University – Research on Representation Learning in Decision Support for Medical Diagnosis (RP/FCA-11/2022). The submission of this research is controlled by the Macau Polytechnic University (fca.65b5.d61c.2).

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