Explainable artificial intelligence model to predict mortality in patients presenting with acute coronary syndromes

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Business Understanding

Introduction

Cardiovascular diseases (CVDs), principally ischemic heart disease (IHD) and cardiac stroke, are the leading cause of mortality globally and are often associated with poor survival(Roth 2020).

Acute Coronary Syndrome (ACS) is a term given to diverse presentations related to cardic myopathies of quick onset. Accurate estimation of risk for untoward outcomes after a suspected onset of an ACS may help clinicians chose the type and intensity of therapy. For example, patients predicted to be at higher risk may receive more aggressive surveillance and/or treatment, while patients predicted to be at lower risk may be managed less aggressively.

Problem statement The establishment of prognosis model for patients with suspected ACS is important in critical care medicine.Numerous risk-prediction models for differing outcomes exist for the different types of ACS.

These models however have some limitations. First, most models have been developed from large randomized clinical trial populations in which the generalizability to risk prediction in the average clinician's experience is questionable(Eagle KA Lim MJ 2004).Second, given the dynamic nature of the treatment environment, predicting future behavior while the treatment is underway may help the clinicians make decisions proactively.

Project Objectives

1. Developing a risk-prediction machine learning classifier, focusing on clinical end point of all-cause mortality after one hour of treatment(golden hour). The chances of a patient to have good outcomes are usually high if substantive medical attention is given within an hour of the cardiac event(Johnson 2016). In this study the golden hour cut-off was 60 minutes after initial contact with the hospital. This included all interventions that were done prior to admission.
2. Explanation of the predicted outcome based on the care pathway using process mining. This AHA guideline(ACLS 2020) was was used as the gold standard for ACS clinical pathway (ACLS 2020).

Project plan

Sources of Data and Knowledge

MIMIC III Database MIMIC-III is a large, freely-available database comprising deidentified health-related data associated with 46,520 patients who stayed in critical care units of the Beth Israel Deaconess Medical Center between 2001 and 2012. The database includes information such as demographics, vital sign measurements made at the bedside , laboratory test results, procedures, medications, caregiver notes, imaging reports, and mortality (including post-hospital discharge).

Researchers seeking to use the database are required to :

1. Become a credentialed user on PhysioNet. This involves completion of a training course in human subjects research.
2. Sign the data use agreement. Adherence to the terms of the DUA is paramount.

The Loin(Institute 2021) data tables will be used to enrich the laboratory dataset.

The British National Formulary (BNF) drug formularly was used to identify the drugs prescribed.

American Heart Association guidelines for CPR and ECC The AHA guideline(ACLS 2020) was used to identify the various services used in teh clinical pathwasy in the management of the patients with suspected ACS.

2. A glossary of data mining terminology, illustrated with examples relevant to the business problem in question

- Check prior availability of glossaries; otherwise begin to draft glossaries
- Talk to domain experts to understand their terminology
- Become familiar with the business terminology

Inventory of resources

Software For this project the following software will be used:

1. SQL - Database storage and queries.
2. R - Data manipulation, model building.

3. Python - Machine learning modeling
4. Celonis - Visualization of process

Computing resources The analysis was done on a Windows desktop and a Linux server. Github repository was used for the CI/CD pipeline.

Requirements, Assumptions, and Constraints

The de-identification step used to obstruct identifiable times through random date shifting is expected to be a limitations in the interpretation of the data. It is also assumed that:

- The patients in this population were only treated in this hospital, therefore mortality are only captured in this hospital.
- All the pre-hospitalization interventions were captured.
- All the pre-hospitalization interventions were captured.
- The unit of analysis is the admission, and a patient may have multiple admissions.

Data Mining Success Criteria

Since the aim of the model was to identify the patients who were at the highest risk of dying, the F-beta score was chosen. It was assumed that misclassification of a patient who survived was less costly as compared to misclassifying a patient who was at a high risk dying. Therfore the F-beta measure was used (set at 2 to give less weight to precision and more weight to recall)

$$Recall = \frac{TP}{TP + FN}$$

$$Precision = \frac{TP}{TP + FP}$$

$$F - score = 2 * \frac{Recall * Precision}{Precision + Recall}$$

| | | Ground Truth Values | |:————————-: |———- |:————————-: |:————————-: | | | | Positive | Negative | | Predicted Values | Positive | true positive (tp) | false positive (fp) | | | Negative | false negative (fn) | true negative (tn) |

Data Understanding

Data collection

Upon gaining access to the MIMIC-III database, all the data was transferred into a RDMS (relational database management system). This was done with the help of open source scripts(Ganas 2018). Subsequently, SQL queries were used to connect and access the data. Although the database includes 26 tables, only the following tables were be included in the analysis:

- **ADMISSIONS:** Contains information regarding a patients admission to the hospital. Information available includes timing information for admission and discharge, demographic information, the source of the admission, and so on. Record of 58,976 unique admissions.
- **PATIENTS:**Defines each patient in the database, i.e. defines a single patient. There are 46,520 patients recorded.
- **SERVICES:**Lists services that a patient was admitted/transferred under.This table contains 73,343 entries.
- **DIAGNOSIS_ICD:**Identify type of data sources (online sources, experts, written documentation, etc.)
- **MICROBIOLOGYEVENTS:**Contains microbiology information, including cultures acquired and associated sensitivities.There are 631,726 rows in this table.
- **PRESCRIPTIONS:**Contains medication related order entries, i.e. prescriptions.This table contains 4,156,450 rows.

- **PROCEDUREEVENTS_MV:**Contains procedures for patients. This table has 258,066 rows.
- **D_ITEMS:** Definition table for all 12,487 items in the ICU databases.
- **D_LABITEMS:** Definition table for 753 laboratory measurements. The **D_LABITEMS** and **D_ITEMS** tables were not used in teh analysis.

Selection criteria

For this analysis only the patients admitted with suspected acute cardiac syndrome were included. In this subset, patients who died within the first hour of treatment were also excluded. The keywords identified for the selection of the patient subset is listed in the Appendix.

Data exploration

The MIMIC III dataset contained 20399 43.85 female and % and 26121 56.15 male patients. The cumulative incidence of suspected ACS was 24.11%. The report is summarized in Table 1 below.

These data was subset using a total of unique subset of the words as shown below.

In addition the patients were seen over a span of time ranging from 2100-07-09 to 2209-07-14. This temporal distribution is shown in the chart below:

Volumetric analysis of data

The total dataset was estimated to be more than 100GBs of data. The selected subset of data tables was about 3.47 GBs.

Attribute types and values

And see Table @Table 2.

Data Preparation

Data quality was assessed dimensions of completeness, uniqueness, validity, accuracy and consistency. Any issue picked was addressed in the data cleaning step below. Thereafter, data standardization and dimension reduction was done.

Data Cleaning

1. There were no duplicates.
2. Completeness:

- Any treatment offered before admission had missing admission ID(*ADMISSION.HADM_ID*). This was inferred from the patient id (*ADMISSION.SUBJECT_ID*) and treatment period.
- The language(*ADMISSION.LANGUAGE*) and ethnicity (*ADMISSION.ETHNICITY*). These were replaced with "UNKNOWN"

3. Consistency:

- The diagnosis(*ADMISSION.DIAGNOSIS*) provides a preliminary, free text diagnosis for the patient on hospital admission as assigned by the admitting clinician and does not use a systematic ontology. Data cleaning was done by removing unnecessary text and ensuring common acronyms and abbreviations referred to the same diagnosis.
- The Loinc table was used to identify the actual test.
- British National Formularly (BNF) was used to identify the drugs administered to the patients.

Derived variables of data

The following derived variables were calculated:

1. Age - The age was computed by subtracting the *DOB* from the *ADMITTIME*. Any figure above 300 was adjusted by subtracting 211, since any age above 300 was ages over 89 had been shifted such that the patient age appears to be 300 in the database.
2. Splitting of Datetime Features - The following features were extracted from teh *ADMITTIME* feature:

- Day of the year
- Week of the year
- Month
- Year
- Hour of day

3. The Length of stay: This was calculated from the previous admissions.
4. Admission cycle: If the patient had multiple admissions, what was the admission cycle in this case.

Categorical variable encoding

1. Categorical variables with high cardinality: diagnoses, medicine, procedures.

- This target encoding/hash encoding was used.

2. Categorical variables with less cardinality but need to preserve the variance: gender,

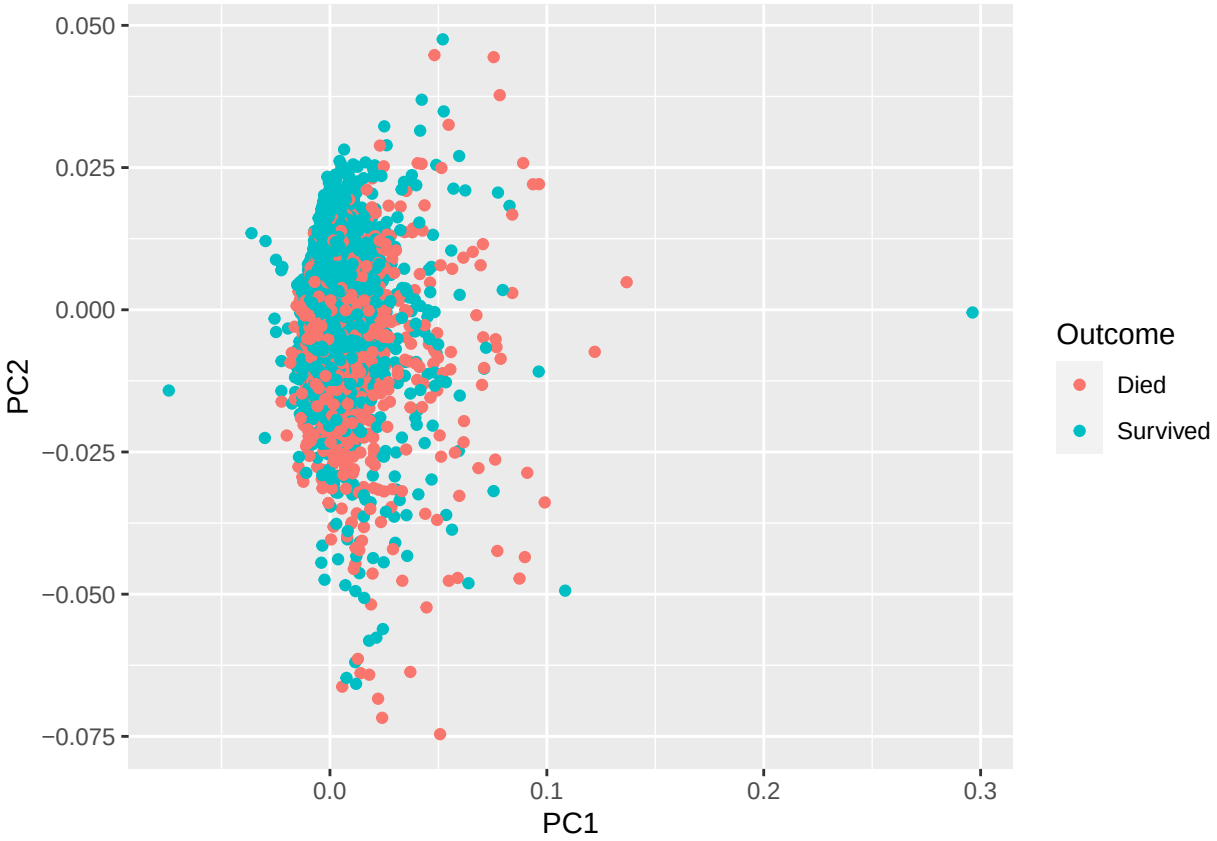
- Frequency encoding was used

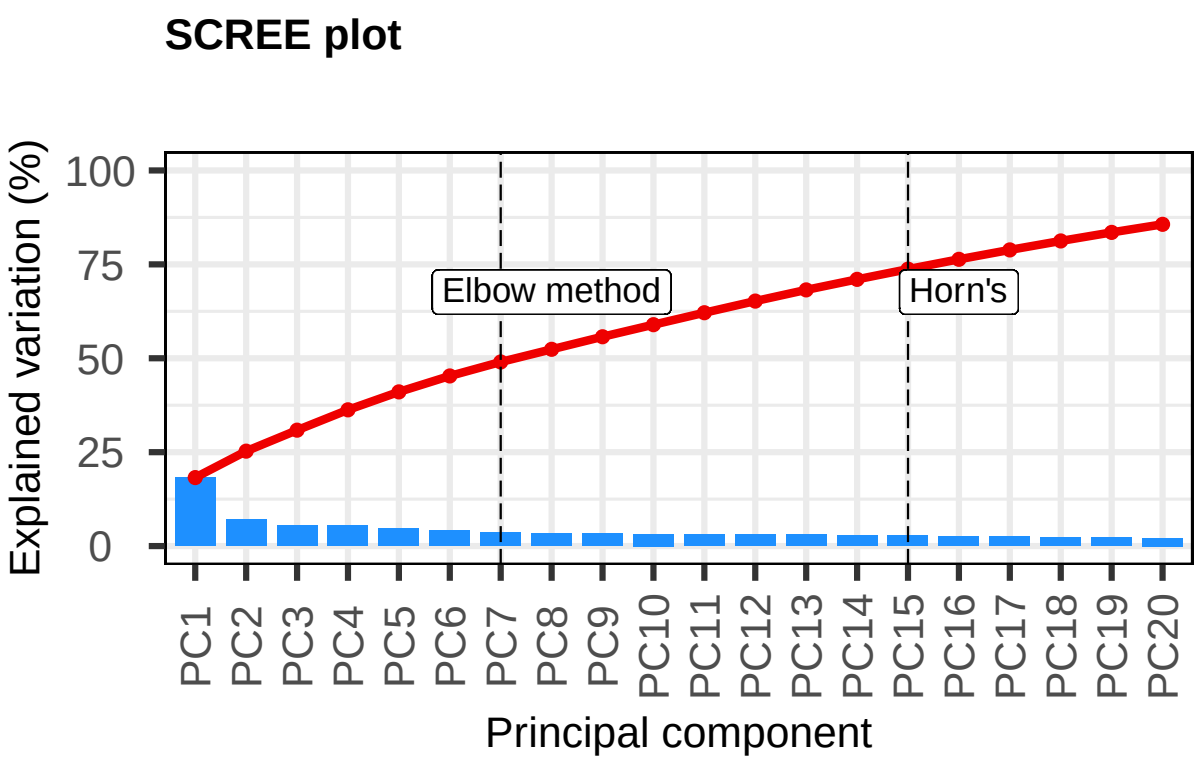
Data standardization.

Dimension reduction.

Dimension reduction

Principal component analysis was used to reduce the dimensionality of the data.


0.050
0.025
0.000
−0.025
−0.050
−0.075
PC2
0.0
0.1
0.2
0.3
PC1
Outcome
Died
Survived



Final Dataset

The Elbow method suggested 7 components, the 15 suggested. However, 23 components (accounting for 90% of variance were however chosen) were selected for further analysis. This was selected after experimentation for the model performance.

Construction of event logs

- Activities and activity instances: Each event related to the service offered to the patient as per the AHA care pathway.
- Time stamp: The time corresponding to the service delivery.

Modeling

Data splitting

For the data splitting strategy, 20% of the hospital admissions were reserved to the test set.

The k-fold cross-validation resampling method was used to create 5 different resamples of the training set which were further split into analysis and assessment sets, producing 5 different performance metrics that were then aggregated. In these re-sampled datasets, 20% of the hospital admissions were allocated to the validation set and 80% of the hospital stays to the training set.

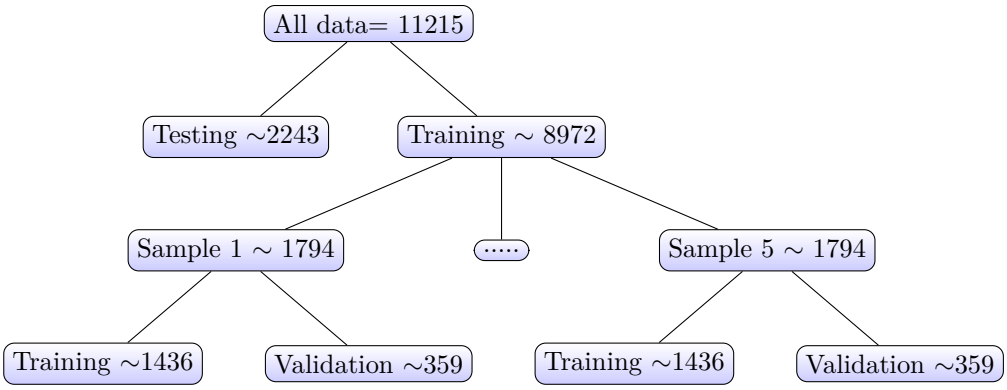


Figure 1: Data splitting algorithm

Model building and tuning

Candidate models Candidate models were selected from the candidate classification models in a multi step way:

Step 1: A representative model was chosen from the broad categories of classification models:

1. Linear models:Regression model.
2. Tree based models: Random forest.
3. Kernel based model: KNN.
4. Quadratic classification model
5. Neural networks: This was not done due to computational limitations

Results were as below:

Step 2: Other models in the Linear classification models were intoduced:

Generative models: Naive Bayes, LDA

Discriminative: logistic regression, SVM

These were compare with the earlier categories to pick the best model.

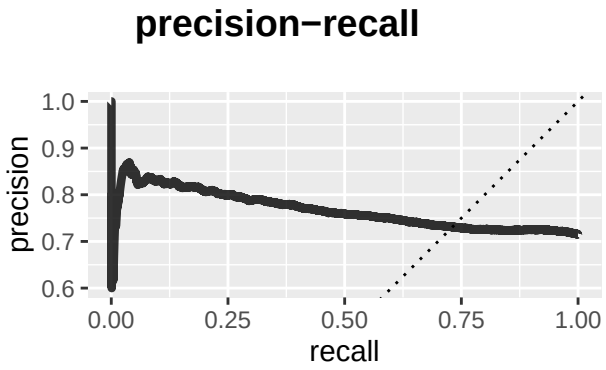
Step 3: Tuning of the best two performers

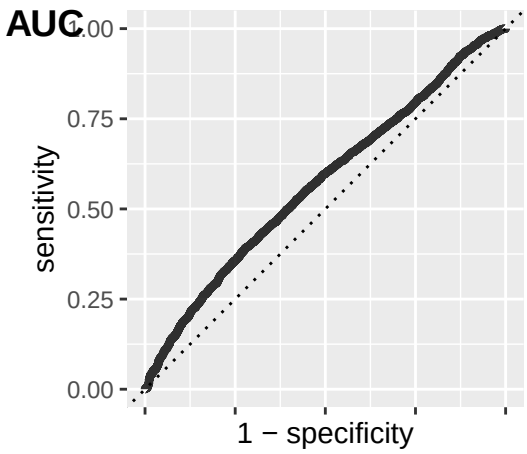
Model building and tuning Grid search algorithm was used to train multiple models simultaneously. The parameters for each model were captured and saved. The area under the recall-precision curve was used to quantify how well the model performs across a continuum of event thresholds .

This was implemented by use of a space-filling design to tune, with 25 candidate models. The random forest is uniformly better across event probability thresholds.

Best model Description

The best model was a logistic regression model with the penalty of 0.01 and mixture of 0.5





Model explanation

Process discovery was done by the implementation of the heuristics miner algorithm.

![Patients who survived](Dead.png)

![Patients who survived](Alive.png)

	Asprin	No
Alive	5330	873
Dead	3446	312

	Outcome +	Outcome -	Total	Inc risk *	Odds
Exposed +	5330	873	6203	85.9	6.11
Exposed -	3446	312	3758	91.7	11.04
Total	8776	1185	9961	88.1	7.41

Point estimates and 95% CIs:

Inc risk ratio	0.94 (0.92, 0.95)
Odds ratio	0.55 (0.48, 0.63)
Attrib risk in the exposed *	-5.77 (-7.01, -4.54)
Attrib fraction in the exposed (%)	-6.72 (-8.21, -5.24)
Attrib risk in the population *	-3.59 (-4.68, -2.51)
Attrib fraction in the population (%)	-4.08 (-4.97, -3.20)

Table 1: Attributes and the level of measurement

	variables	types	missing_percent	unique_count	unique_rate
7	ADMISSION_TYPE	character	0	3	0.0002675
8	ADMISSION_LOCATION	character	0	6	0.0005350
10	INSURANCE	character	0	5	0.0004458
11	LANGUAGE	character	0	47	0.0041908
12	RELIGION	character	0	20	0.0017833
13	MARITAL_STATUS	character	0	8	0.0007133
14	ETHNICITY	character	0	35	0.0031208
20	GENDER	character	0	2	0.0001783
23	AGE	integer	0	84	0.0074900
27	admissionCycle	integer	0	26	0.0023183
29	deadBefore	numeric	0	926	0.0825680
31	dayOfYear	integer	0	366	0.0326349
32	Month	integer	0	12	0.0010700
33	week	integer	0	53	0.0047258
34	weekday	integer	0	7	0.0006242
35	year	integer	0	110	0.0098083
36	hour	integer	0	24	0.0021400

```
Uncorrected chi2 test that OR = 1: chi2(1) = 74.376 Pr>chi2 = <0.001
Fisher exact test that OR = 1: Pr>chi2 = <0.001
 Wald confidence limits
 CI: confidence interval
 * Outcomes per 100 population units
```

Summary

References

Appendix

```
con <- DBI::dbConnect(RPostgreSQL::PostgreSQL(),
  host = "AWS end point",
  user = "eKagereki",
  password = rstudioapi::askForPassword("Database password")
)

data <- tbl(con, "ADMISSIONS")
```

Data attibutes and levels of measurements

Terms and terminologies used

Terminology

1. **Acute Cardiac syndrome:** Acute coronary syndrome (ACS) refers to a spectrum of clinical presentations ranging from those for ST-segment elevation myocardial infarction (STEMI) to presentations found in non–ST-segment elevation myocardial infarction (NSTEMI) or in unstable angina. It is almost always associated with rupture of an atherosclerotic plaque and partial or complete thrombosis of the infarct-related artery. Candidates of acute cardiac syndrome were identified using the *DIAGNOSIS* in

the *ADMISSIONS* table which provides a preliminary. This column was is a free text diagnosis for the patient on hospital admission. The diagnosis was assigned by the admitting clinician and did use a systematic ontology. Candidate cased were identified by using the key words commonly used in the diagnosis of acute coronary syndrome and the related differential diagnosis. These were:

"stemi,""acute coronary syndrome,""angina,""tachycardia,""aortic aneurysm,""pericardi,""ortic dissection,""coronary artery dissection,""cardiomyopathy,""heart failure,""mitral valve disease,""mitral stenosis,""coronary artery disease,""chf,""congestive heart failure,""heart failure,""telemetry,""myocardial infaction,""cardiac arrest,""myocardial infarction,""aortic stenosis,""st elevated,""pericardial effusion," "cardiomyopathy,""cath lab,""tamponade,""tamponede"

2. Angiotensin-converting enzyme (ACE) inhibitors are medications that help relax the veins and arteries to lower blood pressure. ACE inhibitors prevent an enzyme in the body from producing angiotensin II, a substance that narrows blood vessels. The following terms were used to identify ACE's from the list of *DRUG* column of the *PRESCRIPTIONS TABLE* table:

"benazepril," "captopril," "enalapril,""enalaprilat,""fosinopril," "lisinopril," "moexipril," "perindopril," "quinapril," "ramipril,""trandolapril"

3. Beta blockers (beta-adrenergic blocking agents)

Medications that reduce blood pressure. Beta blockers work by blocking the effects of the hormone epinephrine, also known as adrenaline.The following terms were used to identify Beta blocker from the list of *DRUG* column of the *PRESCRIPTIONS TABLE* table:

"acebutolol,""atenolol,""betaxolol,""bisoprolol,""carteolol,""carvedilol,""labetalol,""metoprolol,""nadolol,""nebivolol," "penbutolol,""pindolol,""propanolol,""sotalol,""timolol"

4. Glycoprotein IIb/IIIa inhibitors

These drugs are frequently used during percutaneous coronary intervention (angioplasty with or without intracoronary stent placement). They work by preventing platelet aggregation and thrombus formation.

The following terms were used to identify Glycoprotein IIb/IIIa inhibitors's from the list of *DRUG* column of the *PRESCRIPTIONS TABLE* table:

"abciximab,""eptifibatide,""tirofiban,""roxifiban,""orbofiban"

5. P2Y12 inhibitors *"clopidogrel,""prasugrel,""ticlopidine,""ticagrelor"*

6. HMGCoA *"altoprev,""amlodipine,""atorvastatin,""caduet,""crestor,""ezallor,""fluvastatin,""lescol,""lipitor,""livalo,""lo*

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